Motility initiation in active gels

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Abstract

Motility initiation in crawling cells requires a symmetry breaking mechanism which transforms a symmetric state into a polarized state. Experiments on keratocytes suggest that polarization is triggered by increased contractility of motor proteins. In this paper we argue that contraction can be responsible not only for the symmetry breaking transition but also for the incipient translocation of the segment of an active gel mimicking the crawling cell. Our model suggests that when the contractility increases sufficiently far beyond the motility initiation threshold, the cell can stop and re-symmetrizes. The proposed theory reproduces the motility initiation pattern in fish keratocytes and the behavior of keratocytes prior to cell division.

1. Introduction

The ability of cells to self-propel is essential for many biological processes: in the early life of an embryo, stem cells move to form tissues and organs, during the immune response, leukocytes migrate through capillaries to attack infections and wound healing requires the motion of epithelial cells. While the biochemistry of cell motility is rather well understood, the underlying mechanics of active continuum media is still in the stage of development (Bray, 2000; Mogilner, 2009; Carlsson and Sept, 2008; Joanny and Prost, 2011; Adler and Givli, 2013; Ziebert and Aranson, 2013; Giomi and DeSimone, 2014).

At a very schematic level, a cell can be viewed as an elastic ‘bag’ whose interior is separated from the exterior by a bi-lipid membrane. The membrane is attached from inside to a thin cortex - an active muscle-type layer maintaining the cell’s shape. The interior is filled with a passive medium, cytosol, where all essential cell organelles are immersed. The active medium responsible for self propulsion, is a network of actin filaments (cytoskeleton) cross-linked by myosin motors that can inflict contractile stresses on the network. The cytoskeleton is mechanically linked to the cell exterior through adhesion proteins (Alberts et al., 2002).

The elementary mechanisms responsible for the steady crawling of keratocytes (flattened cells with fibroplastic functions) on rigid surfaces have been identified (Abercrombie, 1980; Bell, 1984; Bellairs, 2000; Stossel, 1993). The advance starts with protrusion through active polymerization of actin network in the frontal area of the cell (the lamellipodium) with a simultaneous formation of adhesion clusters at the edge. After the adhesion of the protruding part of the cell is secured, the cytoskeleton contracts due to activity of myosin motors. The contraction leads to detachment at the rear and lessening of the network through de-polymerization. All these phenomena are driven by ATP hydrolysis and are synchronized which allows the cell to move with a stable shape and constant velocity (Barnhart et al., 2011).

The initiation of motility requires a polarization of the cell which distinguishes the leading from the trailing edges. The implied spontaneous symmetry breaking turns a symmetric stationary configuration of a cell into a polar motile configuration. While both contraction and protrusion contribute to steady state cell migration, contraction
appears to be the dominating mechanism of polarization: it has been shown experimentally that motility initiation in keratocytes may be triggered by raising the contractility of myosin (Verkhovsky et al., 1999; Csucs et al., 2007; Lombardi et al., 2007; Yam et al., 2007; Vicente-Manzanares et al., 2009; Poincloux et al., 2011) and that cells may even self propel by contraction only Keller et al. (2002). In physical terms, the contraction driven motility is driven by ‘pullers’ (contractile agents) leaving the ‘pushers’ (protrusive agents) largely disabled. The relative role of ‘pushers’ and ‘pullers’ in cellular motility is tightly linked to the task (Simha and Ramaswamy, 2002; Saintillan and Shelley, 2012) or the nature of the cargo (Recho et al., 2013a). It is still not fully understood why in some cases motility initiation is primarily contraction centered.

In this paper we circumvent this fundamental question and simply posit that the initiation of motility is largely driven by contraction with only a minor role played by polymerization driven protrusion. We then study in detail the mechanical instabilities in a non-polar segment of an actively contracting gel and provide a compelling evidence that active contraction can be solely responsible for the symmetry breaking transition and that it can lead by itself to a steady translocation of the active segment. Quite remarkably, our prototypical model exhibits motility initiation pattern closely reproducing experiments performed on fish keratocytes. We also show that when the contractility increases sufficiently far beyond the motility initiation threshold, the active segment can again re-symmetrize. Such re-entrant transition, leading also to the motility arrest, can be directly associated with the behavior of keratocytes prior to cell division.

A large variety of modeling approaches to cell motility can be found in the literature, see the reviews (Rafelski and Theriot, 2004; Carlsson and Sept, 2008; Mogilner, 2009; Wang et al., 2012). In some models actin network is viewed as a highly viscous active fluid generating internal contractile stresses and moving through a fluid cytoplasm (Alt and Dembo, 1999; Oliver et al., 2005; Herant and Dembo, 2010; Kimpton et al., 2014). In other models, the cytoskeleton is modeled as an active gel whose polar nature is captured by the theory of liquid crystals (Kruse et al., 2005; Joanny et al., 2007; Julicher et al., 2007; Joanny and Prost, 2011; Callan-Jones and Julicher, 2011). The active gel theory, which we also adopt in this study, was particularly successful in reproducing rings, asters and vortices and some other observed sub cellular structures (Doubrovinski and Kruse, 2007; Sankararaman and Ramaswamy, 2009; Doubrovinski and Kruse, 2010; Du et al., 2012). Cytoskeleton can be also modeled as an active solid characterized by complex, scale free visco-elastic properties (Broedersz and MacKintosh, 2014; Pritchard et al., 2014).

Other elements of the motility mechanism have been also subjected to careful mechanical modeling. The plasmic membrane with an attached cortex is usually represented as a passive elastic surface and is modeled by phase field methods allowing one to deal with topological transitions (Wang et al., 2012; Giomi and DeSimone, 2014). The membrane may also play an active role: an asymmetrical distribution of channels on the surface of the membrane leads to a particular mechanism of cell motility relying on variation of osmotic pressure (Stroka et al., 2014). While most models assume that the cell membrane interacts with the exterior of the cell through passive viscous friction, active dynamics of adhesion complexes has recently become an area of intense research driven in part by the finding of a complex dependence of the crawling velocity on the adhesive properties of the substratum (Novak et al., 2004; Deshpande et al., 2008; Gao et al., 2011; Lin et al., 2008; Ronan et al., 2014; DiMilla et al., 1991; Lin, 2010; Ziebert and Aranson, 2013). The account of other relevant factors, including realistic geometry, G-actin transport, Rac/Rho-regulation, etc., has led to the development of rather comprehensive models that can serve as powerful predictive tools (Rubinstein et al., 2009; Wogemuth et al., 2011).

A sub-problem of finding the mechanism of motility initiation is most commonly addressed in the framework of the theories emphasizing polymerization driven protrusion (Mogilner and Edelstein-Keshet, 2002; Dawes et al., 2006; Bernheim-Gros Wass er et al., 2005; Hawkins et al., 2009; Schreiber et al., 2010; Campas et al., 2012; Hodge and Papadopoulos, 2012). With this emphasis in view, spontaneous polarization was studied in (Callan-Jones et al., 2008; John et al., 2008; Hawkins et al., 2009; Hawkins and Voituriez, 2010; Doubrovinski and Kruse, 2011; Blan ch-Mercader and Casademunt, 2013). In (Banerjee and Marchetti, 2011; Ziebert et al., 2012; Ziebert and Aranson, 2013) polarization was interpreted as a result of an inhomogeneity of adhesive interactions; other authors argued that cell polarity is induced by a Turing-type instability (Mori et al., 2008; Altschuler et al., 2008; Vanderlei et al., 2011; Jilkine and Edelstein-Keshet, 2011).

The idea that contraction may be an important factor behind cell polarization has been also discussed in the literature. First, it was realized that contraction can cause actin flow which in turn carries the regulators of contraction creating a positive feedback (Kruse et al., 2003; Ahmadi et al., 2006; Salbreux et al., 2009; Recho et al., 2013b). It was then shown that in constrained conditions the positive feedback generates peaks in the concentration of stress...
activator (myosin motors) (Bois et al., 2011; Howard et al., 2011); the same idea was used to model polarization induced by angular cortex flow (Hawkins et al., 2009, 2011). Closely related heuristic models of the Keller-Segel type (Perthame, 2008) were proposed in (Kruse and Jülicher, 2003; Calvez et al., 2010). In all these models, however, the effect of contraction was obscured by the account of other mechanisms, in particular, polymerization induced protrusion, and the focus was on generation of internal flow rather than on the motion of the center of mass of a cell. More recently, a model of contraction-induced polarization relying on splay instability of an active gel was proposed in (Tjhung et al., 2012; Giomi and Desimone, 2014). In this model the polarization is induced by a local transition from non-polar to polar gel. In (Callan-Jones and Voituriez, 2013) the motility initiation was attributed to a contraction-induced instability in a poro-elastic active gel permeated by a solvent. However, once again, since in these models the non-contractile active mechanisms were involved as well, the domineering role of contraction was not made explicit.

The goal of the present paper is to pinpoint the special role of contraction by studying a minimalistic, analytically transparent model of motility initiation in a linear segment of an active gel. Following previous work, we exploit the Keller-Segel mechanism but now in a free boundary setting and show that the instability is fundamentally similar to an uphill diffusion of the Cahn-Hilliard type. In contrast to previous results, our contraction driven translocation of a cell is caused exclusively by the internal flow generated by molecular motors. Each motor contributes to the stress field and simultaneously undergoes biased random motion resulting in an uphill diffusion along the corresponding stress gradient. In this way active cross-linkers use the passive actin network as a medium through which they interact and self-organize.

The proposed mechanism of instability is conceptually similar to chemotaxis, however, instead of chemical gradients, it is driven by convection of molecular motors. In turn, the motors propel the actin network by inflicting contraction which creates an autocatalytic effect (Mayer et al., 2010). The mechanical coupling between passive and active components leads to build up of local motor concentration. The localization is limited by diffusion which resists the runaway and provides the negative feedback. After the symmetry of the static configuration is broken, the resultant contraction driven flow inside the cell ensures both the perpetual renewal of the network and the steady translocation of the cell body.

To make the mechanism of motility initiation more transparent we study the problem in the simplest, one dimensional setting. We decouple the dynamics of actin and myosin by assuming infinite compressibility of the cross-linked actin network (Julicher et al., 2007; Rubinstein et al., 2009). In addition to active contractility, the model accounts for cortex-mediated long range elastic interaction between the front and the back of the self-propelling fragment (Banerjee and Marchetti, 2012; Barnhart et al., 2010; Du et al., 2012; Loosley and Tang, 2012); a comparison of such mean field elasticity with more conventional bulk elasticity models can be found in (Recho et al., 2013a). The implied ’global spring’, which largely controls the length of our moving segment, may also have an active origin and result from different rates of polymerization and depolymerization at the extremities of the lamellipodium (Recho et al., 2013a; Étienne et al., 2014).

Our main result is the demonstration that the initiation of motility is controlled by the average contractility of motor proteins. The increase of contractility beyond a well defined threshold leads to a bifurcation from a static symmetric regime to an asymmetric traveling wave (TW) regime describing a steadily moving cell. While several TW regimes may be available at the same value of parameters, we show that stable TW solutions localize motors at the trailing edge of the cell in agreement with observations (Verkhovsky et al., 1999; Csucs et al., 2007; Lombardi et al., 2007; Yam et al., 2007; Vicente-Manzanares et al., 2009; Poincloux et al., 2011). The model shows the possibility of spontaneous polarization and self propulsion without engaging either active protrusion or liquid crystal elasticity.

The paper is organized as follows. In Section 2, we present a discrete ”model of a model” which conveys the main ideas of our approach in the simplest form. In Section 3 we develop a continuum analogue of the discrete model, study its general features and pose the mathematical problem of finding a set of TW solutions containing static and motile regimes. In Section 4, the static solutions of the TW problem are found analytically. In Section 5 we study the structure of the bifurcations producing motile solutions from the static ones. In Section 6 we investigate numerically the initial value problem which allows us to qualify some of the motile TW solutions as attractors. The reconstruction the background turnover of actin, which takes place in our model without active protrusion at the leading edge, is discussed in Section 7. In Section 8 we demonstrate that our model can quantitatively match the experiments carried on keratocytes. The last Section highlights our main conclusions and mentions some unsolved problems; three appendices contain material of technical nature.
Some of the results of this paper were previously announced in (Recho et al., 2013b, 2014).

2. The discrete model

Our point of departure is a conceptual discrete model explaining in the simplest possible terms the mechanism of contraction-driven crawling and emphasizing the role of symmetry breaking in achieving the state of steady self-propulsion. This "model of a model" allows us to clarify the role of different components of the contraction dominated motility machinery and link the proposed mechanism with the previous work on optimization of the crawling stroke irrespective of the underlying microscopic processes, e.g. (DeSimone and Tatone, 2012; Noselli et al., 2013).

Recall that in crawling cells, the 'motor part' containing contracting cytoskeleton (lamellipodium), is a thin active layer located close to the leading edge of the cell, see Fig.1. We assume that all mechanical action originates in lamellipodium and that from the mechanical viewpoint the rest of the cell, including the nucleus, can be interpreted as cargo. The main task will be to develop a model of lamellipodium which we schematize as a segment of active gel.

Figure 1: Conceptual discrete model of the motility mechanism in a crawling keratocyte cell.

The system (1) can be rewritten as three decoupled equations for the length of our active segment $L(t) = x_3(t) - x_1(t)$, its geometric center $G(t) = (x_3(t) + x_1(t))/2$ and the position of a central block $x_2(t)$ representing the internal flow:

\[
\begin{align*}
-l_0 \dot{\chi}_1 + k \frac{x_3-x_1-L_0}{L_0} + \chi_1 - \eta \frac{x_3-x_1}{\chi} &= 0 \\
-l_0 \dot{\chi}_2 - \chi_1 + \chi_2 - \eta \frac{x_3-x_1}{\chi_2} &= 0 \\
-l_0 \dot{\chi}_3 - k \frac{x_3-x_1-L_0}{L_0} - \chi_2 - \eta \frac{x_3-x_1}{\chi_2} &= 0,
\end{align*}
\]

where $x_1(t), x_2(t), x_3(t)$ are the current positions of the blocks and $L_0$ is the reference length of a linear spring. This spring describes the membrane-cortex 'bag' around the lamellipodium allowing the inhomogeneous contraction to be transformed into a protruding force. We assume that polarization have already taken place and therefore the contractile force dipoles $\chi_1 \geq 0$ and $\chi_2 \geq 0$ acting between the two pairs of blocks are not the same $\chi_1 \neq \chi_2$.

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\[
\begin{align*}
-l_0 \dot{\chi}_1 + k \frac{L_0}{L} L &= \chi_1 + \chi_2 + 2k(L/L_0 - 1) \\
2l_0 \dot{\chi}_2 + 3k \frac{L_0}{L} \dot{\chi}_2 &= \chi_1 - \chi_2 \\
-l_0 \dot{\chi}_2 + 3k \frac{L_0}{L} \dot{\chi}_2 &= \chi_1 - \chi_2
\end{align*}
\]
where $l_0 = \sqrt{\eta/\xi}$ is the internal (hydrodynamic) length scale which will ultimately play the role of a regularizing parameter. The first equation shows that the length is converging to a steady state value:

$$L_\infty = L_0(1 - (\chi_1 + \chi_2)/(2k)).$$

Notice that in order to avoid the collapse of the layer due to contraction, it is necessary to ensure that the spring has sufficiently large stiffness $k > (\chi_1 + \chi_2)/2$. We observe that independently of the value of the evolving length $L(t)$, the velocity of the geometrical center of our train of blocks $V$ is always the same

$$V = G = \frac{\chi_1 - \chi_2}{2l_0\xi(1 + 3l_0^2/l_0^2)}.$$

One can see that the system can move as a whole only if $\chi_1 \neq \chi_2$, which emphasizes the crucial role for motility of the *polarization* and the ensuing inhomogeneity of contraction.

Notice that the middle block moves in the direction opposite to the motion of the center of the system with a constant velocity $x_2 = -2V$. Therefore, it takes a finite time $\sim L_\infty/V$ for the central block to collide with the block at the rear and the dynamics described by (2) needs to be extended beyond the collision point.

To model circulation (turnover) of the cytoskeleton in a one dimensional setting we assume that while the flow is continuous along the contact surface, the cytoskeleton continuously disintegrates at the trailing edge and reintegrates at the leading edge. This assumption closes the treadmilling cycle, however, the details of the discontinuous part of the cycle, involving both reaction and an almost frictionless transport (in the absence of a contact with the substrate), are not resolved by the model. The reverse flow is replaced by instantaneous jumps maintaining the overall mass balance. We also neglect the active component of the treadmilling flow and view the polymerization reaction as equilibrium and the return mass flow as passive, driven exclusively by the contractile motors.

In the discrete formulation we assume that as a result of the collision a block at the rear is instantaneously removed from the chain and at the same time an identical block is added at the front. In other words, each (equilibrium) depolymerization event at the rear is matched by an (equilibrium) polimerization event at the front. We also assume at the time scale of frictional (continuous) dynamics the reverse transport of monomers takes place instantaneously: we implicitly assume the existence of a stationary gradient of the chemical potential for G-actin and of a large pool of blocks ready to be added to the network at the front as soon as one is released at the rear.

The structure of the resulting stroke in the $t,x$ plane and in the $x_2 - x_1, x_3 - x_2$ plane is shown in Fig. 2. One can see that each block maintains its identity through the whole cycle and that its trajectory involves a succession of continuous segments described by (1) that are interrupted by instantaneous jumps from the rear to the front. Another representation of the same cycle can be obtained if we trace the evolution of the distances between the first two blocks $l_1 = x_2 - x_1$ and the last two blocks $l_2 = x_3 - x_2$, where now the notations $x_1, x_2, x_3$ indicate positions only and can refer to different blocks in different times. In this representation the cycle collapses on a single line, which is traveled continuously in one direction and discontinuously in the other direction, see Fig. 3b.
Figure 3: Schematic representation of the continuous \((\alpha, \beta)\) and the jump \((\alpha', \beta')\) part of the crawling stroke. Continuous flows have to overcome friction while the jumps are assumed to be friction free.

Notice that the pair of elements \((l_1(t), l_2(t))\) undergoes a periodic sequence of extensions and contractions which resemble the mechanism propelling the swimming sheet (Taylor, 1951) and its crawling analogue (DeSimone and Tatone, 2012). The main difference is that in our case the loop in the \((l_1, l_2)\) plane is degenerate and the propulsion is achieved because of the asymmetry of friction forces acting in the different phases of the stroke. More specifically, during the continuous phase of the cycle the blocks move with friction (polymerized filaments experience effective drag transmitted by focal contacts), while during the jump stage the friction is absent (depolymerized monomers advance freely). The situation is remotely analogous to that of a rotating tank tread, see Fig. 3a.

Since the obtained solution remains basically the same in the limit \(\frac{l_2}{l_b} \to 0\) it appears that the dashpots play a redundant role and can be dropped. To illustrate the role of the dashpots we now consider the case of \(N\) coupled blocks. Then, the force balance for the central blocks \(j \in [2, N - 1]\) reads

\[-l_b \xi_j \dot{x}_j - \chi_j l_2 - \frac{\chi_j - \dot{x}_{j+1}}{l_b} - \frac{\chi_j - \dot{x}_{j-1}}{l_b} = 0.\]

This system of equations can be written in the matrix form,

\[T \dot{x} = b, \quad (4)\]

where we denoted by \(\dot{x}\) the unknown vector \(\dot{x}_2, ..., \dot{x}_{N-1}\). The tri-diagonal matrix

\[
T = \begin{bmatrix}
-(2 + \frac{l_2}{l_b}) & 1 & 0 & 0 & 0 \\
1 & -(2 + \frac{l_2}{l_b}) & 1 & 0 & 0 \\
0 & \cdots & \cdots & \cdots & 0 \\
0 & 0 & 1 & -(2 + \frac{l_2}{l_b}) & 1 \\
0 & 0 & 0 & 1 & -(2 + \frac{l_2}{l_b})
\end{bmatrix}
\]

describes viscous coupling and frictional interaction with the background while the vector

\[
b = \frac{l_b}{\xi l_0} \begin{bmatrix}
-\chi_1 + \sigma_0 - \frac{\xi_0}{l_b} x_1 \\
\chi_1 - \chi_2 \\
\vdots \\
\chi_{N-2} - \chi_{N-1} \\
\chi_{N-1} - \sigma_0 - \frac{\xi_0}{l_b} x_N
\end{bmatrix}
\]
with \( \sigma_0 = -k(x_N - x_1 - L_0)/L_0 \) carries the information about the active forcing, the mean field type elasticity and the boundary layer effects. To find the solution \( \chi \), we need to invert the matrix \( T \) and then solve a system of two coupled linear equations \( \dot{x}_i = (R \ b_i) \) and \( \dot{x}_N = (R \ b_N) \) where \( R = T^{-1} \). The components of the matrix \( R \) can be found explicitly (Meurant, 1992)

\[
R_{i,j} = \frac{\cosh((N + 1 - j - i)\lambda) - \cosh((N + 1 - |j - i|)\lambda)}{2 \sinh(\lambda) \sinh((N + 1)\lambda)}
\]

where \( \lambda = \text{arccosh}(1 + \frac{L_0^2}{2\xi^2}) \). Knowing the 'velocity field', we can now compute the steady state value of the length

\[
L_\infty = L_0 \left( 1 - \frac{\sum_{j=1}^{N-1} \sinh(\lambda j - \lambda N/2)\chi_j}{2\eta \sinh(\lambda N/2)} \right).
\]

We see again that a finite stiffness is necessary to prevent the collapse of the system under the action of contractile stresses: assuming for instance that \( \chi_1 = \bar{\chi} \) we obtain the low bound for the admissible elasticity modulus \( k > \bar{\chi} \).

The steady velocity \( V = (\dot{x}_N + \dot{x}_1)/2 \) of the geometrical center of the system can be also computed explicitly

\[
V = -\frac{l_0 \sum_{j=1}^{N-1} \sinh(\lambda j - \lambda N/2)\chi_j}{2\eta \sinh(\lambda N/2)}.
\]

By denoting \( M = [N/2] \), where \([x]\) is the largest integer not greater than \( x \), we can rewrite this expression in the form

\[
V = -\frac{l_0 \sum_{j=1}^{M-1} \sinh(\lambda j - \lambda N/2)\chi_{M+j - \chi_{M-j})}}{2\eta \sinh(\lambda M)}.
\]

from where it is clear that (as in the case of three blocks) the symmetry of the vector \( \chi \) with respect to the center must be broken for the system to be able to self-propel.

If we now formally drop the dashpots by assuming that \( l_0 = 0 \) we obtain the same expressions for the velocity and for the steady state length as in the three block model

\[
V = \frac{\chi_N - \chi_1}{2l_0}, \quad L_\infty = L_0 \left( 1 - \frac{\chi_1 + \chi_N}{2k} \right).
\]  

(5)

The reason of this 'coincidence' is that in this limit the 'flow' fully localizes in the two boundary elements, the only ones present in the case \( N = 3 \). More precisely, the general solution of the discrete problem, which depends singularly on the ratio \( l_0^2/L_0^2 \), becomes progressively localized around the boundary elements as \( l_0^2/L_0^2 \to \infty \). Such localization presents a major problem if we consider the continuum limit when \( N \to \infty \) and \( l_0 \to 0 \) while \( NL_0 \to L \) where \( L \) is the continuum length of the self-propelling segment. Thus, if \( l_0 \to 0 \) the size of boundary layers tend to zero and the solution converges to a distribution.

Observe also that the limits \( l_0 \to 0 \) (dropping dashpots) and \( l_0 \to 0 \) (continuum approximation) do not commute. Indeed, if we choose in (5) the motor distribution with all \( \chi_i = 0 \) except for one \( \chi_2 = \chi^* > 0 \) we obtain \( V = 0 \) for any value of \( l_0 \). In particular, when \( l_0 \to 0 \) we still have \( V \to 0 \). If instead we first perform the continuum limit while keeping \( l_0 \) finite we obtain

\[
L_\infty = L_0 \left( 1 - \frac{\int_0^{L_\infty} \cosh[(x - L_\infty/2)/l_0]\chi(x)dx}{2kl_0 \sinh[L_\infty/(2l_0)]} \right).
\]

(6)

and,

\[
V = -\frac{\int_0^{L_\infty} \sinh[(x - L_\infty/2)/l_0]\chi(x)dx}{2\eta \sinh[L_\infty/(2l_0)]}.
\]

(7)

If we now take a distribution of motors \( \chi(x) = \delta_0 \) where \( \delta_0 \) is the Dirac mass at \( x = 0 \), which can be viewed as (one of the continuum analogs of the discrete distribution considered above, we obtain that \( V = \chi^*/(2l_0^2) \)). Then in the limit \( l_0 \to 0 \) we obtain \( V \to \infty \) which is drastically different from the value \( V = 0 \) obtained when the order of limits was reversed.
To connect the two double limits we assume that $l_b \sim N^{-1}$ and hence $l_s^2/l_b^2 \sim 1/(\eta N^2)$. One can see that the crossover regimes with $\eta \sim N^{-2}$ separate two different limiting behaviors. Thus, for $l_s^2/l_b^2 \to \infty$ (which is a dimensionless version of $\eta \ll N^{-2}$) the internal flow localizes in the boundary layers whose thickness disappears when $\eta \to 0$. When we dropped the dashpots in the three element model we could not see this localization because the two boundary links were the only links in the system. In the other limit $l_s^2/l_b^2 \to 0$ (dimensionless version of $\eta \gg N^{-2}$) the viscosity dominates the dynamics and the internal flow becomes uniform. In the three block model the difference between these two cases was only qualitative.

In the next Sections the formulas (6) and (7) will be obtained directly from the continuum model. We will also see more clearly how the introduction of the viscosity-related internal length scale and the associated nonlocality regularizes the continuum model which otherwise has only singular solutions.

### 3. The continuum model

We model the lamellipodium as a one dimensional continuum layer in frictional contact with a rigid background, see Fig. 4. Assuming that the friction is viscous and neglecting inertia we can write the force balance in the form

$$\partial_x \sigma = \xi v,$$

where $\sigma(x, t)$ is the axial stress and $v(x, t)$ is the velocity of the cytoskeleton (actin network). Eq. (8) is the continuous analog of the system (4) in the discrete problem.

As in the discrete model, we denoted by $\xi$ the coefficient of viscous friction. Such representation of active adhesion is usual in the context of cell motility (Rubinstein et al., 2009; Larripa and Mogilner, 2006; Julicher et al., 2007; Shao et al., 2010; Doubovinski and Kruse, 2011; Hawkins et al., 2011). It implies that the time-averaged shear stress generated by constantly engaging and disengaging focal adhesions is proportional to the velocity of the retrograde flow, see (Tawada and Sekimoto, 1991) for a microscopic justification. There is evidence (both experimental (Gardel et al., 2008, 2010; Mogilner, 2009; Bois et al., 2011; Schwarz and Gardel, 2012) and theoretical (DiMilla et al., 1991; Mi et al., 2007)) that this assumption describes the behavior of focal adhesions accurately only when the retrograde flow is sufficiently slow. The behavior of adhesion strength in the broader range of velocities is biphasic and since we neglect this effect, we potentially misrepresent sufficiently fast dynamics. Observe though that for both keratocytes and PtK1 cells the rate of lamellar actin retrograde flow varies from 5 to 30 nm s$^{-1}$ in usual experimental conditions (Schwarz and Gardel, 2012) and in this range a direct proportionality relationship between traction stress and actin retrograde flow has been confirmed experimentally (Gardel et al., 2008; Fournier et al., 2010; Barnhart et al., 2011). The characteristic velocity of the flow in our problem is 20 nm s$^{-1}$ which falls well into the aforementioned interval where the biphasic behavior can be neglected.

Following (Kruse et al., 2006; Julicher et al., 2007; Bois et al., 2011; Howard et al., 2011), we assume that the cytoskeleton is a viscous gel with active pre-stress. We neglect the bulk elastic stresses that relax over time scale 1−10 s (Rubinstein et al., 2009; Wottawah et al., 2005; Kole et al., 2005; Panorchan et al., 2006; Mofrad, 2009; Recho et al., 2013a) which is much shorter than characteristic time scale of motility experiments (hours). We can then describe the constitutive behavior of the gel in the form

$$\sigma = \eta \partial_x v + \chi c,$$

where $\eta$ is the bulk viscosity, $c(x, t)$ is the concentration of motors and $\chi > 0$ is a contractile pre-stress (per motor) representing internal activity. The constitutive relation (9) generalizes the parallel bundling of dashpots and contractile units in the discrete model. The important new element is that the strength of the contractile elements may now vary in both space and time.

In the discrete model the concentration of motors $c$ was a given as a function of $x$. To obtain a more self consistent description we assume that the function $c(x, t)$ satisfies a convection-diffusion equation (Rubinstein et al., 2009; Bois et al., 2011; Barnhart et al., 2011; Wolgemuth et al., 2011; Hawkins et al., 2011)

$$\partial_t c + \partial_x (cv) = D \partial_x c,$$

where $D$ is the diffusion coefficient. Behind this equation is the assumption that myosin motors, actively cross-linking the actin network, are advected by the network flow and can also diffuse which accounts for thermal fluctuations.
To justify this model, consider a simple mixture model with two species representing attached and detached motors. The attached motors are advecting with the velocity of actin filaments and can detach. The detached motors are freely diffusing, and can also attach. Suppose that the attachment-detachment process can be described by a first order kinetic equation. Then the system of equations governing the evolution of the concentrations of attached $c_a$ and detached $c_d$ motors can be written as:

$$\begin{align*}
\frac{\partial}{\partial t} c_a + \frac{\partial}{\partial x} (c_a v) &= k_{\text{on}} c_d - k_{\text{off}} c_a \\
\frac{\partial}{\partial t} c_d - \tilde{D} \frac{\partial}{\partial x} c_d &= k_{\text{off}} c_a - k_{\text{on}} c_d
\end{align*}$$

where $k_{\text{on}}$ and $k_{\text{off}}$ are the chemical rates of attachment and detachment and $\tilde{D}$ is the diffusion coefficient of detached motors in the cytosol. Now suppose that the attachment-detachment process is chemically equilibrated and hence $c_a/c_d = K$, where $K = k_{\text{on}}/k_{\text{off}}$ is the reaction constant. Then for the attached motors performing contraction we obtain

$$K + \frac{1}{K} \frac{\partial}{\partial t} c_a + \frac{\partial}{\partial x} (c_a v) - \frac{\tilde{D}}{K} \frac{\partial}{\partial x} c_a = 0.$$  

Our equation (10) is obtained in the limit $K \rightarrow \infty$ (fast attachment) and $\tilde{D}/K \rightarrow D$ (fast diffusion).

To obtain boundary conditions we denote by $l^-(t)$ and $l^+(t)$ the rear and front boundaries of our gel segment. To account for cortex/membrane elasticity we assume as in the discrete model that the boundaries are linked through a linear spring (Barnhart et al., 2010; Du et al., 2012; Loosley and Tang, 2012; Recho et al., 2013a). This assumption affects the values of the stress in the moving points $l^-(t)$ and $l^+(t)$:

$$\sigma(l^-(t), t) = -k(L(t) - L_0)/L_0.$$  

Here $L(t) = l_+(t) - l_-(t)$ is the length of the segment, $k$ is the effective elastic stiffness and $L_0$ is the reference length. As we have seen in the discrete model, the presence of an elastic interaction plays a crucial role in preventing the collapse of the segment due to contractile activity of motors.

Our next assumption is that the external boundaries of the self propelling segment are isolated in the sense that they move with the internal flow $l_\pm = v(l_\pm)$. We imply here that the addition and deletion of F-actin particles inserted at the front and taken away at the rear does not contribute to propulsion. We also impose a zero exterior flux condition for motors $\frac{\partial}{\partial x} c(l_\pm(t), t) = 0$ ensuring that the average concentration of motors

$$c_0 = \frac{1}{L_0} \int_{L_0}^{L(t)} c(x, t) dx$$

is conserved. To complete the setting of the problem we need to impose the initial conditions $l_\pm(0) = L_0$ and $c(x, 0) = c_0(x)$.

Our assumption that the bulk stiffness of the cytoskeleton is equal to zero (known also as the infinite compressibility assumption (Julicher et al., 2007; Rubinstein et al., 2009)) allowed us to uncouple the force balance problem, which becomes statically determinate, from the mass balance problem. By solving the main system of governing equations (8)–(11) we obtain the velocity field and the concentration of motors but not the density distribution for the main flow. To recover the mass distribution of the cytoskeleton we need to solve the mass balance equation with a kinematically prescribed velocity field (Recho et al., 2013a).
Suppose that by solving the system (8)–(11) we found the velocity field $v(x,t)$. This means that we also know the trajectories of the free boundaries $l_-(t)$ and $l_+(t)$. To find the density $\rho(x,t)$, we need to solve the mass balance equation

$$\partial_\rho + \partial_\nu(\rho v) = 0. \quad (12)$$

with initial condition $\rho(x,0) = \rho_0(x)$. Here we neglected the diffusion of actin comparing to the diffusion of myosin. Since both the leading and the trailing edges of the moving lamellipodium coincide with the trajectories of particles, the total mass $M$ is conserved

$$M = \int_{l_-(t)}^{l_+(t)} \rho(x,t)dx.$$

To address the problem of continuous circulation and to close the cycles of the cytoskeleton flow we need to interpret the points of density singularities as sources and sinks. In Section 7 we show that even in the presence of singularities the solutions can be regularized if we cut out small regularization domains around sources and sink and appropriately reconnect the incoming and the outgoing flows of matter.

**Dimensionless problem.** If we now normalize length by $L_0$, time by $L_0^2/D$, stress by $k$, concentration by $c_0$ and density by $M/L_0$, we can rewrite the main system of equations in dimensionless form

$$-Z\partial_x\sigma + \sigma = PC, \quad \partial_t c + K\partial_x(c\partial_x\sigma) = \partial_{xx} c. \quad (13)$$

Here we introduced three main dimensionless constants of the problem: $Z = \eta/(\xi L_0^2)$ - the ratio of viscous and elastic length scales; $K = k/(\xi D)$ - the ratio of stiffness induced agglomeration over diffusion and finally $P = c_0\chi/k$ - the dimensionless measure of motor contractility. One can discern in (13) the structure of the Keller-Segel system from the theory of chemotaxis, e.g. (Perthame, 2008). The role of the distributed chemical attractant is played in our case by the stress field $\sigma$ whose gradient is the driving force affecting the ‘colony’ of myosin motors. Using dimensionless variables we can also rewrite the boundary conditions in the form

$$\dot{l}_-(t) = K \partial_x \sigma(l_-(t),t), \quad \sigma(l_+(t),t) = -(L(t) - 1), \quad \partial_t c(l_+(t),t) = 0. \quad (14-16)$$

The integral constraint (11) reduces to

$$\int_{L}^{l_+(t)} c(x,t)dx = 1. \quad (17)$$

Mass balance equation (12) becomes,

$$\partial_\rho + K\partial_x(\rho \partial_x \sigma) = 0. \quad (18)$$

while the total mass gets normalized

$$\int_{l_-(t)}^{l_+(t)} \rho(x,t)dx = 1.$$  

**Non local reformulation.** Since the first of the equations (13) is linear, it can be solved explicitly for $\sigma$

$$\sigma(x,t) = \frac{(L - 1) \cosh[(G - x)/\sqrt{Z}]}{\cosh[L/(2\sqrt{Z})]} + \frac{P}{\sqrt{Z}} \int_{l_-(t)}^{l_+(t)} \Psi(x,y)c(y)dy, \quad (19)$$

$$\Psi(x,y) = \frac{\sinh[(l_0 - x)/\sqrt{Z}] \sinh[(y - L)/\sqrt{Z}]}{\sinh[(L)/(\sqrt{Z})]} - H(y - x) \sinh[(y - x)/\sqrt{Z}].$$

where $H(x)$ - the Heaviside function and $G(t) = [L(t) + l_+(t)]/2$ is the position of the geometric center of the moving fragment. By eliminating $\sigma$ from (13) we obtain a single non local partial differential equation with quadratic non linearity for $c(x,t)$

$$\partial_t c(x,t) - K(L - 1)\partial_x[\partial_x c(x,t)] + \frac{PK}{\sqrt{Z}} \int_{l_-(t)}^{l_+(t)} \varphi(x,y)c(y)\varphi(x,t)dx = \partial_{xx} c(x,t), \quad (20)$$
where the auxiliary velocity field
\[ \theta(x) = \frac{\sinh[(x - G)/\sqrt{Z}]}{\cosh[L/(2\sqrt{Z})]} \]
describes advective flow induced by the elastic coupling between the rear and the front of the active segment. The feedback behind contraction-driven motility is contained in the kernel
\[ \varphi(x, y) = -\frac{\cosh[l_+ - x]/\sqrt{Z} \sinh[(y - l_+ - y)/\sqrt{Z}]}{\sinh[(L - y)/\sqrt{Z}]} + H(y - x) \cosh[(y - x)/\sqrt{Z}] \]
which is due to viscosity induced bulk mechanical interactions in the system and the effect of the boundaries. Notice that this kernel has the action/reaction symmetry \( \varphi(x, y) = -\varphi(l_+ + l_+ - x, l_+ + l_+ - y) \) which is a fundamental constraint imposed by the balance of momentum (Kruse and Jülicher, 2003; Kruse and Julicher, 2000; Torres et al., 2010).

**Inviscid limit.** To distinguish the bulk mechanical interactions from the effects of the boundaries, we use the following asymptotic expansion (Ren and Truskinovsky, 2000)
\[ \varphi_b(y - x) = \lim_{L \to \infty} \varphi(x + G/2, y + G/2) \]
\[ = \frac{1}{2} \begin{cases} \exp\left(-\frac{x - y}{\sqrt{Z}}\right) & \text{if } x - y < 0 \\ -\exp\left(-\frac{y - x}{\sqrt{Z}}\right) & \text{if } x - y > 0 \end{cases} \] (21)

In Fig. 5 we compare our viscosity induced interaction kernel with a long range kernel proposed in (Kruse and Jülicher, 2003; Kruse and Julicher, 2000; Torres et al., 2010) as a model of steric interactions between actin filaments with half size \( l_s \)
\[ \varphi_s(x - y) = \begin{cases} \frac{1}{2} \text{sgn}(x - y), & \text{if } |x - y| \leq l_s \\ 0, & \text{if } |x - y| > l_s \end{cases} \] (22)
The length \( l_s \) plays in (Kruse and Jülicher, 2003; Kruse and Julicher, 2000; Torres et al., 2010) the same role as our viscous length \( l_0 = \sqrt{\eta/\xi} \) represented in (21) by the dimensionless parameter \( Z \).

In Section 2 we anticipated a non trivial limit in the continuum theory when the bulk viscosity \( \eta \) goes to zero. Now we see that when \( Z \to 0 \) the kernel \( \varphi_b \) becomes singular and the nonlocality in the mechanical part of the model disappears. From (13) we also notice that parameter \( Z \) enters as a coefficient in front of the highest derivative. Therefore, outside the boundary layers of size \( \sim \sqrt{Z} \) we can formally assume that \( \sigma = Pc \) which make the main dynamic equation (20) local
\[ \partial_t c(x, t) + \mathcal{K} \partial_x (c(x, t) \partial_x c(x, t)) = \partial_x c(x, t). \] (23)

At small \( Z \) the non-bulk contributions to the kernel \( \varphi(x, y) \) will play a role only around the extremities of the moving segment and in the limit \( Z \to 0 \) will affect only the boundary conditions.

By using a new variable \( w = 1 - \mathcal{K}c \), we can rewrite Eq. (23) in the form
\[ \partial_t w(x, t) + \partial_x (w \partial_x w(x, t)) = 0. \]
Here we recognize the porous flow equation which is, however, unusual because the field \( w(x,t) \) may be sign-indefinite. In particular, in the regimes with \( c > \langle KP \rangle^{-1} \) one can expect an uphill diffusion similar to that of spinodal decomposition. A systematic study of the inviscid case, requiring the knowledge of the boundary conditions in the limiting problem, will be done elsewhere.

**Cell velocity.** Using the boundary conditions (14) we find from (19) an explicit formula for the (time dependent) velocity of the center of our active segment (see also Eq. (7) in Section 2)

\[
\dot{G} = \frac{\mathcal{K}P}{2Z} \int_{l}^{L} \frac{\sinh\left(\frac{G}{\sqrt{Z}}\right)}{\sinh\left(\frac{\sqrt{Z}}{\sqrt{Z}}\right)} c(x,t)dx. \tag{24}
\]

Similarly we obtain an equation for the evolving length of the segment (see also Eq. (6) in Section 2)

\[
L = -2 \frac{\mathcal{K}}{\sqrt{Z}}(L-1) \tanh\left(\frac{L}{2\sqrt{Z}}\right) - \frac{\mathcal{K}P}{\sqrt{Z}} \int_{l}^{L} \frac{\cosh\left(\frac{G}{\sqrt{Z}}\right)}{\cosh\left(\frac{\sqrt{Z}}{\sqrt{Z}}\right)} c(x,t)dx. \tag{25}
\]

Notice that in (24) only the odd component of the function \( c(x,t) \) (with respect to the moving center \( G(t) \)) contributes to the integral while in (25) only the even component matter. In particular, if the concentration of motors is an even function of \( x \) then \( \dot{G} = 0 \) and the segment does not move as a whole. This conclusion is a direct analog of Purcell’s theorem (Purcell, 1977) in the case of a crawling body with the emphasis on spatial asymmetry replacing the emphasis on temporal asymmetry.

From (24) we infer that the maximal velocity of the self propelling segment is equal to \( \mathcal{K}P/(2Z) \). In dimensional variables (Julicher et al., 2007; Bois et al., 2011; Howard et al., 2011), we get an estimate \( \chi L_{c}c_{0}/(2\pi) \approx 10 \mu m/min \) which is rather realistic in view of the data reviewed in (Jilkine and Edelstein-Keshet, 2011; Schreiber et al., 2010).

**Traveling waves.** Given our interest in the steady modes of cell motility, which are typical for keratocytes (Barnhart et al., 2011), we need to study the traveling wave (TW) solutions of the main system (13). To find such solutions we assume that the front and the rear of our segment travel with the same speed \( \dot{G}(t) \equiv V \), ensuring the constancy of the length \( L(t) \equiv L \), and that both the stress and the myosin concentration depend on \( x \) and \( t \) through a combination \( u = (x-Vt)/L \) only. Using this ansatz we find that the equation (13)_2 can be solved explicitly

\[
c(u) = \frac{\exp[s(u)] - VLu}{L \int_{0}^{1} \exp[s(u)] - VLu}du. \tag{26}
\]

Here for convenience we introduced a new stress variable \( s(u) = \mathcal{K}[\sigma(u) + (L-1)] \). After being non-dimensionalized by \( \xi D \), the function \( s(u) \) represents the inhomogeneous contribution to internal stress field due to active pre-stress. The system (13) reduces to the single nonlocal equation

\[
-\frac{Z}{L^2} s''(u) + s(u) - \mathcal{K}(L-1) = \mathcal{K}P \frac{\exp[s(u)] - VLu}{L \int_{0}^{1} \exp[s(u)] - VLu}du, \tag{27}
\]

which is supplemented by the boundary conditions

\[
s(0) = s(1) = 0 \quad \text{and} \quad s'(0) = s'(1) = LV. \tag{28}
\]

The two ‘additional’ boundary conditions in (28) allow one to determine parameters \( V \) and \( L \) along with the function \( s(u) \). After the problem (27, 28) is solved, the motor concentration profile can be found explicitly by using Eq. (26).

4. **Static regimes**

Initiation of motility is associated with a symmetry breaking instability of a static (non-motile) configuration. To identify non-motile configurations we need to find solutions of (27) with \( V = 0 \). These solutions may still characterize
Figure 6: Three families of trivial static solutions $\hat{L}_+$, $\hat{L}_-$ and $\hat{L}_0$ parameterized by $\mathcal{P}$. Solid lines and arrows show stable branches while dotted lines correspond to unstable branches (see Section 6).

the states with nontrivial active internal rearrangements of both actin and myosin. Static solutions with periodic boundary conditions were studied in (Bois et al., 2011) and here we complement and extend this analysis.

If $V = 0$ the Eq. (27) simplifies considerably

$$-rac{Z}{L^2} s'' + s - K (L - 1) = K \mathcal{P} \frac{\exp(s)}{L \int_0^1 \exp(s(u)) du}.$$  

(29)

The nonlocal equation (29) was studied extensively in many domains of science from chemotaxis (Senba and Suzuki, 2000) to turbulence (Caglioti et al., 1992) and gauge theory (Struwe and Tarantello, 1998). In our case, this equation where parameter $L$ remains unknown, has to be solved with three boundary conditions $s'(0) = s(0) = s(1) = 0$ because the forth boundary condition $s'(1) = 0$ is satisfied automatically.

We begin with the study of the regular solutions of (29). Instead of $K$ and $\mathcal{P}$, it will be convenient to use another set of parameters $A := K (L - 1) \leq 0$ and $B := K \mathcal{P} / (L \int_0^1 \exp(s(u)) du) \geq 0$. In terms of parameters $(A, B)$ the problem (29) reads

$$-\frac{Z}{L^2} s'' + s - A = B \exp(s) \quad \text{with} \quad s'(0) = s(0) = s(1) = 0.$$  

(30)

A trivial homogeneous solution of this problem $s(u) = 0$ exists when $A + B = 0$ which is equivalent in the $(\mathcal{P}, K)$ parametrization to $L = \hat{L}_+$ with,

$$\hat{L}_+ = \left(1 \pm \sqrt{1 - 4\mathcal{P}}\right)/2.$$  

(31)

The sub-branches with longer and shorter lengths $\hat{L}_-(\mathcal{P})$ and $\hat{L}_+(\mathcal{P})$, respectively, that meet at point $\alpha$ where $\hat{L}_-(\mathcal{P}) = \hat{L}_+(\mathcal{P})$ are illustrated in Fig. 6.

To obtain nontrivial static solutions we multiply (30) by $s'$, integrate and use the boundary conditions to obtain the ‘energy integral’ $s'^2 = W(s)$, where

$$W(s) = \frac{L^2}{Z} (s^2 - 2As - 2B [\exp(s) - 1]).$$

The general solution of this equation can be expressed as a quadrature, $u = \pm \int^{s(u)} W^{-1/2}(r) dr$. A detailed analysis of this equation is given in Appendix A, where different families of static solutions are identified as $S^+_m$ and $S^-_m$ where the index $\pm$ specifies the $\hat{L}_+$ trivial branch from which a particular solution bifurcates: the associated lengths $\hat{L}_+ \pm$ are defined in (31). The integer valued index $m$ corresponds to the number of spikes in the configuration $s(u)$. The prime differentiates between two subfamilies belonging to the same bifurcated branch with primed subfamily having the length $L$ larger than in the trivial configuration and non-primed subfamily having the length $L$ smaller than in the trivial configuration. Fig. 20 illustrates the families $S^+_1$ and $S^-_1$. For each family we plot the length of the fragment $L$ as a function of one of the controlling parameters, see Fig. 7.

In addition to regular solutions described above Eq. (29) has measure-valued solutions corresponding to collapsed cells. First of all, as we see in Fig. 6, $\hat{L}_-(\mathcal{P}) \rightarrow 0$ when $\mathcal{P} \rightarrow 0$ (point $\alpha'$) and the limiting distribution of motors
is concentrated on an infinitely small domain. To characterize the asymptotic structure of the singular solutions we suppose that \( L << 1 \) and that the maximum of \( s \) is of order \( L \). Then, by ignoring high order terms, we deduce from (29) a simplified boundary value problem

\[
-s'' \approx \frac{\mathcal{K}PL}{(Z \int_0^1 [1 + s(u)]du)} \quad \text{with} \quad s'(0) = s(0) = s(1) = 0.
\]  

(32)

Then \( s(u) \approx \frac{\mathcal{K}PLu(1-u)}{(2Z)} \), and the remaining boundary condition \( s'(0) = 0 \) is automatically satisfied in the limit \( L \to 0 \). We can then conclude that the singular solutions are of the form

\[ s(x) = \lim_{L \to 0} L f(x/L) \]

where \( f(u) = \frac{\mathcal{K}Pu(1-u)}{(2Z)} \). Singular solutions of this type can be implicated in the description of cell splitting in a cortical geometry (Turlier et al., 2014); they are also known in other fields where stationary states are described by equation (29) (Caglioti et al., 1992; Chen and Lin, 2001; Ohtsuka, 2002; Gladiali et al., 2012). The presence of such solutions is a sign that in a properly augmented theory, accounting for the vanishing length, one can expect localization with active contraction balanced by a regularization mechanism, which may be, for instance, active treadmilling (Recho et al. (2013a)). Our numerical solutions of a non-steady problem, which are naturally regularized because of the finite mesh size (see Section 6), show that the almost singular solutions of the type described above are indeed attractors for initial data with \( L < \hat{L} - \) when \( \mathcal{P} < 1/4 \). Moreover, numerical experiments suggest that they are the only attractors for \( \mathcal{P} > 1/4 \). This means that even in the presence of a cortex-type spring, an active segment fragment necessarily collapses after the contractility parameter reaches the threshold \( \mathcal{P}_{\text{max}} = 1/4 \).

5. Bifurcations from static regimes

We now show that motile branches with \( V \neq 0 \) can bifurcate only from trivial static solutions with \( s(u) = 0, V = 0 \) and \( L = \hat{L}_\pm \). For \( V \neq 0 \) equation (27) has an integral

\[
1 - \exp(-LV) = LV \int_0^1 \exp[s(u) - VLu]du.
\]  

(33)

Then in the limit \( V \to 0 \) we obtain that \( \int_0^1 \exp(s) = 1 \). Since static solutions \( s(u) \) must be necessarily sign definite, see Appendix A, Eq. 33 implies that the corresponding static solution can only be trivial \( s(u) = 0 \). As we have seen in Fig. 6, there are two non-singular families of trivial solutions: one with longer \( (\hat{L}_+, \text{family}) \) and the other with shorter \( (\hat{L}_- \text{family}) \) lengths.

**Bifurcation points.** To find the bifurcation points along the trivial branch \( (s = 0, V = 0, L = \hat{L}_\pm(\mathcal{P})) \), we introduce infinitesimal perturbations \( \delta s(u), \delta V, \delta L \) and linearize (27) together with boundary conditions (28). We obtain the boundary value problem

\[
\delta s'' - \omega^2 \delta s = \frac{Z(2L-1)}{L^2(2L-1)} \left( \frac{2L-1}{L} \delta L \frac{\hat{L}_3(L-1)}{2} (2u-1)\delta V \right).
\]  

(34)
As we show in the inset in Fig. 8, the two points may also bifurcate from the same branch $\hat{K}$ to infinity as $\omega$ has a zero determinant. This gives a transcendental equation for $\omega$

$$\delta s(0) = \delta s(1) = 0, \quad \delta s'(0) = \delta s'(1) = \hat{L}\delta V.$$  \tag{35}$$

Here we introduced the notation

$$\omega^2 = (\hat{L}^2 - \mathcal{K}\mathcal{P}\hat{L})/\mathcal{Z}.$$  \tag{36}$$

Since $\omega = 0$ at the trivial branch $\delta s = \delta V = \delta L = 0$, we can assume that $\omega \neq 0$. The general solution of the problem (34), (35) can be written explicitly

$$\delta s(u) = C_1 \exp(-\omega u) + C_2 \exp(-\omega u) - \frac{\mathcal{Z}\omega^2 - \hat{L}^2}{\omega^2 \hat{L}^2(L - 1)} \left( \mathcal{Z} \frac{2\hat{L} - 1}{L} \omega^2 \delta L + \frac{\hat{L}^3(\hat{L} - 1)}{2} (2u - 1) \delta V \right).$$  \tag{37}$$

The boundary conditions are satisfied if the matrix

$$\begin{pmatrix}
1 & 0 & \frac{2\hat{L} - 1}{L} & \frac{1}{\omega^2} \left( \frac{\hat{L}^2}{\mathcal{Z}} - 1 \right) \\
\cosh(\omega) & \sinh(\omega) & \frac{2\hat{L} - 1}{L} & \frac{1}{\omega^2} \\
0 & \omega & 0 & -\frac{\hat{L}^2}{\mathcal{Z}} \\
\omega \sinh(\omega) & \omega \cosh(\omega) & 0 & -\frac{\hat{L}^2}{\mathcal{Z}}
\end{pmatrix},$$  \tag{38}$$

has a zero determinant. This gives a transcendental equation for $\omega$

$$2\hat{L}[\cosh(\omega) - 1] - \mathcal{K}\mathcal{P}\omega \sinh(\omega) = 0.$$  \tag{39}$$

The detailed analysis of this equation is presented in Appendix B. The full locus of bifurcation points in the $(\mathcal{K}, \mathcal{P})$ plane is shown in Fig. 8. The lines of bifurcation points + and − originating on the trivial sub-branches $\hat{L}_+$ and $\hat{L}_-$ smoothly connect at $\mathcal{P} = 1/4$, see Fig. 6. When parameter $\mathcal{P}$ is held constant while $\mathcal{K}$ is changing each family $D_i$ and $S_i$ in Fig. 8 is represented by two points. For solutions bifurcating from the trivial branch $\hat{L}_+$, we have $\mathcal{K}_+ = (\hat{L}_+^2 - \mathcal{Z}\omega^2)/(\mathcal{P}\hat{L}_+)$, which gives points $D_1^+, S_1^+, D_2^+, S_2^+, \ldots$ and for the branch $\hat{L}_-$, we have $\mathcal{K}_- = (\hat{L}_-^2 - \mathcal{Z}\omega^2)/(\mathcal{P}\hat{L}_-)$ which gives points $D_1^-, S_1^-, D_2^-, S_2^-, \ldots$ Notice that the total number of bifurcation points increases to infinity as $\mathcal{K} \to \infty$. Now consider the case when $\mathcal{K} = \text{const}$ and $\mathcal{P}$ is varied. A line $\mathcal{K} = \text{const}$ in the $(\mathcal{K}, \mathcal{P})$ plane cuts again each line of the bifurcation points $D_i$ and $S_i$ in two points which we denote $D_1^+, S_1^+, \ldots$ (solutions with longer lengths) and $D_1^-, S_1^-, \ldots$ (solutions with shorter lengths), see Fig. 6 and Fig. 8. In most cases one of these two points is a bifurcation originating from the $\hat{L}_+$ trivial solution while the other is from the $\hat{L}_-$ trivial solution. However, as we show in the inset in Fig. 8 the two points may also bifurcate from the same branch $\hat{L}_+$. As we show later in the paper such bifurcations are of particular interest because they describe both motility initiation and motility arrest.
Figure 9: (a) Bifurcation diagram with $\mathcal{K}$ as a parameter showing nontrivial solutions branching from families of homogeneous static solutions $\hat{L}_+\text{ and } \hat{L}_-$. The value $\Phi = 0.245$ and $Z = 1$ are fixed. Solid lines show stable motile branches while all the dotted lines correspond to unstable solutions. The internal configurations corresponding to branches indicated by numbers (1, $1'$, 2, $2'$, etc) are shown in Fig. 9(b). The projection of the bifurcation diagram on the $(\mathcal{K}, L)$ plane is also shown below. (b) Internal profiles associated with successive bifurcated solutions shown in Fig. 9(a) for $\Phi = 0.245$ and $Z = 1$. Our notation (1,3) correspond to asymmetric motile branches while (2,4) describe symmetric static branches.
Structure of bifurcations. After the bifurcation points are known one can use the Lyapunov-Schmidt reduction technique to identify the nature of the corresponding bifurcations (Nirenberg, 1974; Koiter, 1976; Amazigo et al., 1970). The analysis presented in Appendix C shows that the bifurcations from the trivial to the nontrivial static branch are always transcritical. The bifurcations to motile branches can be either subcritical or supercritical. In particular, at a given \( K \) the bifurcation from a static homogeneous solution with longer length is always supercritical while the bifurcation from a static homogeneous solution with smaller length can be either subcritical or supercritical depending on the value of \( K \), see Section Appendix C.

Bifurcated branches. To illustrate different types of bifurcations we constructed the nonlinear continuation of the bifurcated branches by solving the boundary value problem (27)–(28) numerically for successive values of parameters \( K \) and \( P \) (tracking algorithm, see (Doedel et al., 2007)). In Fig. 9(a) we show the continuation in \( K \) for both static and motile configurations at fixed \( P \); the corresponding profiles of motor concentration, stress and velocity are shown in Fig. 9(b). One can see that each pitchfork (for motile branches) and each transcritical (for static branches) bifurcation points gives rise to two nontrivial solutions. For instance, along the static branch \( \hat{L}_c \), the bifurcation point \( \hat{D}_1 \) is associated with two motile supercritical branches whereas the point \( S_1 \) is associated with two transcritical static branches. Each pair of motile solutions is symmetric with two opposite polarizations corresponding to two different signs of the velocity. Along the first motile branch originating at \( \hat{D}_1 \), the myosin motors concentrate at the trailing edge. For the second motile branch originating at \( \hat{D}_2 \), there is an additional peak in the concentration profile, see Fig. 9(b). In contrast, the static bifurcation point \( S_1 \) gives rise to two symmetric configurations with different lengths and with myosin motors concentrated either in the middle of the cell or near the boundaries, see Fig. 9(b). As one would expect, the higher order static and motile bifurcation points produce solutions with more complex internal patterns. For the branches bifurcating from the trivial configurations belonging to \( \hat{L}_c \) family, the picture is similar, see Fig. 9(a).

In Fig. 10 we show in more detail the nontrivial solutions originating from the motile bifurcation points \( D_i \) at two values of parameter \( K \) which correspond to two sections \( a\beta \) and \( a\beta' \) shown in Fig. 8 (insert). Notice that a single...
solution connects the bifurcation points $D^*_r$ (supercritical) and $D^{1*}_r$ (sub- or supercritical) which may belong either to one family $L_+$ (where $D^*_r$ is the same as $D^{1*}_r$ or to two different families $L_+$ and $L_-$ (where $D^*_r$ is the same as $D^{1*}_r$). In the former case, the nontrivial motile branch has a turning point at a finite value of $\mathcal{P} < 1/4$ giving rise to a re-entrant behavior. Similar behavior was also observed in some other nonlocal models, e.g. (Kruse and Jülicher, 2003). In this regime, the increase of the average concentration of myosin first polarizes the cell and initiates motility, but then, if the concentration is increased further, the cell becomes symmetrical again and re-stabilizes in another static homogeneous configuration. Finally, if $\mathcal{P}$ is increased further, the cell collapses to a point. Following (Turlier et al., 2014), we can associate such collapse with cell division. We can then conclude that our simple model can reproduce a rather general pattern of cell behavior showing that it stabilizes in space and depolarizes before division.

**Nonlinear active stress.** The fact that the bifurcation leading to polarization and motility initiation is always a supercritical pitchfork indicates that this model does not allow for the metastability resulting in the coexistence of motile and non-motile configurations that was observed in other models, e.g. (Ziebert and Aranson, 2013; Tjhung et al., 2012; Giomi and DeSimone, 2014). To obtain such a coexistence in the present setting, we need to modify our model only slightly. The main idea is to consider a more realistic nonlinear dependence of the active stress on motor concentration which is linear for small values of $c$ but then saturates after around a threshold $c^r$. More specifically, we rewrite the main system of equations in the form

$$-\mathcal{Z} \partial_x^2 \sigma + \sigma = \Phi(\mathcal{P})/\mathcal{P} \, / r,$$

$$\partial_t c + \lambda \partial_x (c \partial_x \sigma) = \partial_x^2 c,$$

where, following Bois et al. (2011), we choose a particular form of nonlinearity $\Phi(x) = x/(1 + x)$. To simplify the analysis we consider only the ‘rigid’ limit when $k \rightarrow \infty$, $L \rightarrow L_0$ while the stress on the boundaries $-k(L/L_0 - 1)$ remains finite. We also had to re-scale the stress by $c_0\mathcal{X}$ instead of $k$. The new dimensionless parameters are then $r = c_0/c^r$ and $\lambda = c_0\mathcal{X}/(\xi \mathcal{D}) = \mathcal{K} \mathcal{P}$, see also Bois et al. (2011); Howard et al. (2011); Hawkins et al. (2009, 2011). In dimensionless variables the residual stress can be written as $\sigma_0 = -\lim_{\mathcal{P} \rightarrow 1/4} \lim_{L \rightarrow L_0}(L - 1)/\mathcal{P}$. Then the boundary conditions read

$$\dot{L}_+ = 0,$$

$$\partial_t \sigma(L_+(t), t) = \sigma_0,$$

$$\partial_t c(L_+(t), t) = 0,$$

$$\dot{L}_- = \lambda \partial_x \sigma(L_-(t), t).$$

For TW solutions we can write the analogue of (27)

$$-\mathcal{Z} s'' + s + s_0 = \frac{\lambda}{r} \Phi \left( \frac{\exp(s - V u)}{\int_0^1 \exp(s - V u) du} \right),$$

where $s = \lambda(\sigma - \sigma_0)$ and $s_0 = \lambda \sigma_0$. The boundary conditions take the form $s(0) = s(1) = 0$ and $s'(0) = s'(1) = V$. The difference with our static solutions, described in Section 4, is that now we have to find the stress at the boundary $s_0$ instead of the length $L$. 

\[ \text{Figure 11: Bifurcation diagrams in the nonlinear model with fixed length (infinite stiffness) (40) showing the possibility of a switch from supercritical to subcritical bifurcation. Parameters: } \mathcal{Z} = 1. \]
Figure 12: Cell length $L(t)$, velocity $G(t)$ and profiles $c/L(u, t)$, $s/L(u, t)$ and $v(u, t) - G(t)$ for the case with initial data shown at $t = 0$ with $L(0) = 0.4$. Parameters $P = 0.245$, $K = 150$ and $Z = 1$ as in Fig. 9(a). The layer collapses due to the contractile stress.

The analysis of the motility initiation bifurcation in this case is presented in Appendix D. The results are illustrated in Fig. 11. As we see, when the nondimensional parameter $r$ is small, which means that we are in the linear regime, the bifurcation from static to motile regime is a supercritical pitchfork. However, at larger values of $r$ the nature of the bifurcation changes from supercritical to subcritical. This creates a domain of parameters where static and motile regime can coexist and where the system may exhibit metastability and hysteresis. Another important effect is that in this range of parameters the motility initiation/arrest is a discontinuous transition which may explain why experimenters were unable to observe particularly small velocities of self propulsion in keratocytes Barnhart et al. (2011). An alternative explanation of this experimental fact based on the idea of optimality and compatible with the supercritical nature of the motility initiation bifurcation was can be found in Recho et al. (2014)

6. Stability of post-bifurcational regimes

Stability of various branches of the TW solutions identified in the previous sections was studied numerically. Since we have to deal with a moving segment, it is convenient to map system (13) onto the fixed domain $[0, 1]$ which makes the coefficients of the governing equations time dependent. To this end, we introduce the new space variable $u(x, t) = [x - L(t)]/L(t) \in [0, 1]$ and denote the new unknown functions $\hat{\sigma}(u, t) = \sigma[L + L(t)u, t]$ and $\hat{c}(u, t) = L(t)c[L + L(t)u, t]$. Then the original problem (13), (15)–(16) takes the form

$$- \frac{Z}{L^2} \partial_{uu} \hat{\sigma} + \hat{\rho} = \frac{P}{L} \hat{\sigma}$$

and

$$\partial_t \hat{c} + \frac{1}{L} \partial_u (\hat{\rho} \hat{c}) = \frac{1}{L^2} \partial_{uu} \hat{c},$$

(41)

Here we defined the relative velocity $\hat{v} := K \partial_u \hat{\sigma}/L - G - (u - 1/2)L$, where

$$G = (K/L) [\partial_u \hat{\sigma}(1, t) + \partial_u \hat{\sigma}(0, t)]/2,$$

$$L = (K/L) [\partial_u \hat{\sigma}(1, t) - \partial_u \hat{\sigma}(0, t)].$$

(42)

The remaining boundary conditions can be written as

$$\hat{\sigma}(u, t) = -(L - 1) \quad \text{and} \quad \partial_u \hat{c}(u, t) = 0 \quad \text{at} \quad u = [0, 1].$$

(43)

while the initial data take the form $\hat{c}(u, 0) = \hat{c}^0(u)$, $G(0) = G^0$ and $L(0) = L^0$.

We integrated the dynamical system (41)–(43) with initial data chosen close to one of the known steady states. The numerical scheme was based on the finite volume method (LeVeque, 2002). We used two dual regularly-spaced
Figure 13: Cell length $L(t)$, velocity $\dot{G}(t)$ and profiles $c/L(u,t)$, $s/L(u,t)$ and $\nu(u,t) - \dot{G}(t)$ for the test with initial data shown at $t = 0$ with $L(0) = 0.5$. Parameters $\mathcal{P} = 0.245$, $\mathcal{K} = 150$ and $\mathcal{Z} = 1$ as in Fig. 9(a). The layer polarizes to one of the motile attractor (depending of the initial bias).

grids on the interval $[0, 1]$: $Z$ and $Z_d$. Given the initial condition $\hat{c}$ we solved (41)$_1$ on $Z$ and computed the effective drift term $\hat{\nu}$ on $Z_d$. We then applied the upwind finite volume scheme to (41)$_2$ and updated the concentration profile $\hat{c}$ on $Z$ which provided us with the new initial data for the next time step. The time interval for each time step was adapted to ensure that the Courant-Friedrichs-Lewy condition is uniformly satisfied on $Z_d$.

Our numerical experiments suggest that the trivial branch $\hat{L}_-$ is unstable together with all nontrivial non-singular static solutions. The singular static solutions from the $L_0$ family appear to be locally stable. To illustrate the attractive nature of the singular static solutions we choose in Fig. 12 the initial configuration with a length smaller than $\hat{L}_-$ with an internal initial profile biased to the front associated to a motile solution. We observe that the length collapses to zero in finite time and cell velocity goes to zero. In accordance with the computations made in Section 4, the stress profile converges to $s(u)/L \sim \mathcal{K}P(u - 1)/2$, velocity to $\nu(u) \sim \mathcal{K}P(u - 1/2)$ and concentration to $c(u) = 1$.

Next, we observed numerically that the dynamic solutions are all unstable except for the branches bifurcating from the points $D_1^+$ on the trivial branch $L_+$. The trivial branch $\hat{L}_+$ branch is locally stable until the first (motile) bifurcation $D_1^+$. Both symmetric subbranches of $D_1^+$ (subfamilies 1 and 1$'$ in Fig. 9(a) and Fig. 9(b)) are stable. To illustrate the instability of a nontrivial static solution, we show in Fig. 14 the escape of the phase trajectory from the neighborhood of the trivial static solution $\hat{L}_-$. Since in this numerical test the value of $\mathcal{K}$ was chosen to be smaller than the critical value, corresponding to the bifurcation of the first motile branch $D_1^+$, the system originally placed near $\hat{L}_-$ becomes unstable and then re-equilibrates on another trivial static branch $\hat{L}_+$ without moving its geometrical center.

In Fig. 13 we illustrate motility initiation in two initially almost identical and nearly homogeneous static configurations which differ by a localized concentration peak introduced either at the rear or at the front of the cell. We see that with time these two initial profiles converge to the different stable motile solutions $D_1$ and $D_1'$. The initial inhomogeneity is remembered and selects the subfamily of the $D_1$ solutions with the same bias. As we see, independently of the direction of motion the cell recovers its length after a short transient period.

As in (Bois et al., 2011; Howard et al., 2011; Kruse and Jülicher, 2003) who considered the problem with fixed boundaries, we find that some unstable multi-peaked static and dynamic solutions are long living. This behavior is reminiscent of the spinodal decomposition in a 1D Cahn-Hilliard model where the coarsening process gets critically slowed down near multiple saddle points (Carr and Pego, 1989). To illustrate the long transients near the unstable solutions we study in Fig. 15 evolution of two initially homogeneous concentration profiles with different initial length. We observe that the phase trajectory first approaches the unstable branch from subfamily 2 from Figs. 9(a) and Figs. 9(b) before being finally attracted by the stable configuration from the subfamily 1$'$. Interestingly, the symmetric subfamily 2$'$ can be also initially approached if we choose slightly different initial data, however, this regime is abandoned much faster than the solution from the subfamily 2, see Fig. 15b. Based on our simulation, we conjecture that the lifespan of an unstable branch is linked to the distribution of motors and the states with higher localization of
motors on the periphery of the cell survive longer than the states where motors are spread near the center of the cell. To summarize, we found considerable numerical evidence that in a problem with free boundaries only trivial static solutions can be stable and only solutions with monotone profiles can describe configurations of steadily moving cells. To confirm these results a more systematic mathematical analysis of stability of the obtained TW solutions is needed. Cells with constrained or loaded boundaries may show different stability patterns as it is evidenced by the study of a related problem with a periodic boundary conditions (Bois et al., 2011; Howard et al., 2011; Kruse and Jülicher, 2003).

7. Mass transport of actin

As we have already mentioned, the infinite compressibility assumption allowed us to decouple the force balance equation from the mass balance equation. Once the velocity field \( v(x, t) = \mathcal{K} \partial_x \sigma(x, t) \) is known, the latter can be solved \textit{a posteriori} by the method of characteristics.

Denote the trajectories of the mass particles by \( x = \phi(\zeta, t) \), where \( l_-(0) \leq \zeta \leq l_+(0) \) is the Lagrangian coordinate.
at $t = 0$ and $L_-(t) \leq \phi(\zeta, t) \leq L_+(t)$. The characteristic curves can be found from the equations

$$\frac{d\phi(\zeta, s)}{ds} = v(\phi(\zeta, s), s).$$

(44)

Along these curves we must have

$$\frac{d\rho(\phi(\zeta, s), s)}{ds} = -\rho(\phi(\zeta, s), s) \partial_s v(\phi(\zeta, s), s),$$

Integration of this equation gives gives an explicit formula for the mass density

$$\rho(\phi(\zeta, t), t) = \rho(0) \exp\left( - \int_0^t \partial_s v(\phi(\zeta, s), s) ds \right).$$

(45)

As we are going to see below, this solution is applicable only outside the singular points describing the sinks and the sources.

Consider a TW solution of (13) which satisfies the boundary conditions $L_-(t) = Vt$ and $L_+(t) = L + Vt$. Introducing the normalized co-moving variable $\hat{\phi} = (\phi - Vt)/L$ and the normalized Lagrangian variable $\hat{\zeta} = \zeta/L(0)$, both in the interval $[0, 1]$, we obtain that $v = v(\hat{\phi})$ and Eq. (44) reduces to

$$\frac{d\hat{\phi}(\hat{x}, t)}{dt} = \frac{\nu(\hat{\phi}(\hat{x}, t)) - V}{L}.$$  

(46)

For TW solutions the general formula (45) describing the mass distribution simplifies

$$L\hat{\rho}(\hat{\phi}(\hat{x}, t), t)[\nu(\hat{\phi}(\hat{x})) - V] = L(0)\rho(0)\hat{\zeta}[\nu(\hat{\zeta}) - V].$$

(47)

According to (46) the points of the body where $v = V$ are singular because the relative flow there is stagnated. If at such point the slope of the function $v(\hat{\phi})$ is negative we obtain a sink of particle trajectories $\hat{\phi} = \gamma_+$ (i.e. an attractor for particles as $t \to \infty$) whereas if the slope of the function $v(\hat{\phi})$ is positive, the singular point $\hat{\phi} = \gamma_-$ corresponds to a source of particle trajectories (an attractor as $t \to -\infty$). An important feature of the flows described by (46) is that it takes an infinite time for a mass particle to reach a sink or to leave a source because $(v(\hat{\phi}) - V)^{-1}$ is not integrable in the neighborhood of $\gamma_-$ and $\gamma_+$.

$$\tau = \int_{\gamma_-}^{\gamma_+} \frac{d\phi}{|v(\phi) - V|} = \infty.$$

This implies that mass density infinitely localizes in the singular points (sources and sinks) because $L\hat{\rho}(\hat{\phi})[\nu(\hat{\phi}) - V] = \tau^{-1} = 0$. Then all mass points (corresponding to different values of $\hat{x}$) come from the sources where the characteristic curves accumulate at large negative times and disappear in the sinks where the characteristic curves accumulate at large positive time.

For the trivial static solutions characterized by the lengths $\hat{L}_a$, there is no flow $(v = 0)$ and the mass density does not depend on either space or time. The density profiles for nontrivial static and motile solutions can be illustrated near the bifurcation points where the velocity profiles are known explicitly.

For instance, in the case of the nontrivial static branches $\hat{S}_m^n$ introduced in Section 5, we obtain

$$\frac{d\hat{\phi}(\hat{x}, t)}{dt} = \zeta \sin(\omega_\phi \hat{\phi}(\hat{x}, t)),$$

(48)

where $\omega_\phi = -2\pi n$. For determinacy, we choose the value of the amplitude $\zeta$ in such a way that the maximum of our dimensionless velocity field is equal to one. The approximate value of $\zeta$ can be computed in the vicinity of the bifurcation point from the amplitude equations presented in Appendix C. In Fig. 16(a) we show sample solutions of (48) corresponding to homogeneous initial conditions $\hat{\phi}(\hat{x}, 0) = \hat{\zeta}$ for positive and negative values of $\zeta$ corresponding to the two possible branching directions. The corresponding density profiles are illustrated in Fig. 17 where the passive treadmilling cycles are shown by arrows.
Figure 16: (a) Trajectories of particles from sources to sinks for the first two static bifurcation points for initially homogeneously distributed set of particles. Labels 1, 1', 3, 3' and labels 2, 2', 4, 4' are related to Fig. 9(a) and Fig. 9(b).

Figure 17: Density profiles for the first two motile and static branches for $\varsigma > 0$, the profiles for $\varsigma < 0$ are the same; only the treadmilling cycles (indicated by black circles) are going in the opposite direction. Labels are related to Fig. 9(a) and Fig. 9(b). Parameter is $\epsilon = 0.01$.

Similarly, for the motile branches $D_m^\pm$ we need to solve the characteristic equation

$$\frac{d\hat{\phi}(\hat{\zeta}, t)}{dt} = \varsigma \left\{ -\frac{L^2}{\omega_c^2 \cos(\omega_c/2)} \left[ \omega_c \cos(\omega_c(\hat{\phi}(\hat{\zeta}, t) - 1/2)) - 2 \sin(\omega_c/2) \right] - 1 \right\},$$

(49)

where $\omega_c$ is a solution of the equation (54). Both equations can be solved analytically by separation of variables. In Fig. 16(b), we show the sample solutions of (49) corresponding to homogeneous initial conditions $\phi(\hat{\zeta}, 0) = \hat{\zeta}$ again for the positive and negative values of $\varsigma$.

We reiterate that this model is singular because in a one dimensional setting we are obliged to over-schematize the treadmilling of actin.

To recover the circulation aspect of the flow in a one-dimensional setting, we need to regularize the problem near the singular points and make the mass flux finite. For instance, we can cut out small regularizing domains of size $\epsilon$ around sinks and sources. In this way we obtain an effective ‘polymerization zone’ around each source $\Gamma_- = \{\phi \in [0, 1]/|\phi - \gamma_-| < \epsilon\}$ and an effective ‘depolymerization zone’ around each sink $\Gamma_+ = \{\phi \in [0, 1]/|\phi - \gamma_+| < \epsilon\}$. We assume that in the domain $\Gamma_-$ the network is constantly assembled from the abundant monomers while in the domain $\Gamma_+$ it is constantly disassembled so that the pool of monomers is replenished. The ensuing closure of the treadmilling cycle is instantaneous (jump process) allowing the monomers to avoid the frictional contact with the
environment. More precisely, we assume that the jump part of the treadmilling cycle is a passive equilibrium process driven exclusively by myosin contraction. The turnover time

\[ \tau = \int_{\phi = \phi_0}^{\phi_1} \frac{d\phi}{v(\phi) - V} \]

is now finite and the corresponding density profiles are illustrated in Fig. 17. Notice that the flow between the neighboring source and sink can be interpreted as a treadmilling cluster. Thus, for the \( m \)\textsuperscript{th} static branch, we have \( 2^m \) such clusters and for the \( m \)\textsuperscript{th} motile branch we have \( 2^m - 1 \) clusters.

8. Experimental verification of the model

We can now compare the predictions of the model with experiments describing motility initiation in keratocytes. For instance, in the experiment of Verkhovsky (Verkhovsky et al., 1999) a mechanical force was applied via a micropipette on one side of a keratocyte fragment. Since the data presented in Fig. 5 of (Verkhovsky et al., 1999) (and reproduced with permission in our Fig. 18) are of one dimensional nature we can directly apply our model after adjusting it to account for mechanical loading.

In order to make quantitative predictions we need to specify the values of parameters relevant for fish keratocytes. In (Barnhart et al., 2011) we find the values of viscosity \( \eta \sim 10^5 \text{ Pa} \cdot \text{s} \) and active stress \( \chi c_0 \sim 10^3 \text{ Pa} \). Friction coefficient can vary over several orders of magnitude depending on the substrate whose physical properties have not been specified in (Verkhovsky et al., 1999). However, based on the fact that in (Verkhovsky et al., 1999) the velocity of the fragment after initiation of motility was approximately \( 0.08 \mu \text{m} \cdot \text{s}^{-1} \), we can infer from Fig. 5 of (Barnhart et al., 2011) that \( \xi \sim 2 \times 10^{16} \text{ Pa} \cdot \text{m}^{-2} \cdot \text{s} \). From (Barnhart et al., 2011; Luo et al., 2012) we can also obtain the value of the diffusion coefficient \( D \sim \frac{25}{10^{-13} \text{m}^2 \cdot \text{s}^{-1}} \) and from (Barnhart et al., 2010; Du et al., 2012; Loosley and Tang, 2012), we estimate the stiffness of the cortex \( k \sim 10^4 \text{Pa} \). Finally, directly from (Verkhovsky et al., 1999), we infer that the characteristic length of the keratocyte fragment is \( L_0 \sim 20 \times 10^{-6} \text{m} \). Based on these estimates we conclude that \( Z \sim 0.0125, \mathcal{P} \sim 0.1 \) and \( \mathcal{K} \sim 20 \).

In (Verkhovsky et al., 1999) (Fig. 5) the initially round fragment with diameter \( L_i = 22 \mu \text{m} \), was subjected to applied stress of the order of \( q_- = 15 - 20 \text{ kPa} \). The loading was applied after 830 s and lasted for about 80 s. The
additional surface tractions can be easily incorporated into our model through the boundary condition at the rear of the cell: \( \sigma(l(t), t) = -\left[ \frac{L(t)}{L_0} - 1 \right] - q(t) \).

In Fig. 18 (a) we present the results of our numerical simulation of the motility initiation experiment of Verkhovsky (Verkhovsky et al., 1999). We start with a uniform initial state where motors are distributed homogeneously. We chose a generic value of the length \( L(0) \) that is slightly different from the value \( \hat{L} \) which is unstable in this range of parameters. The length first decays towards the value corresponding to the branch \( S^{+1} \) as one could expect based on Figs. 9(a), 9(b) and 15. This is an unstable state which we found rather robust to selected perturbations. The distribution of motors remains non-polar with the development of two contractile zones characteristic of the nontrivial static regime \( S^{+2} \). The system then remains in this long living unstable state until we apply an additional one-sided force on the boundary breaking the symmetry of the \( S^{+2} \) state. The destabilized system evolves towards the motile state on the \( D^{+1} \) branch with both velocity and length well captured by our model.

We can now compare with experiment the stationary density profiles (for both myosin and actin) generated by the model. In the static regime the flow of actin is absent (\( v = 0 \)) and the model then predicts uniform distribution of actin and myosin. From Fig. 19 (left) we see that this prediction is in agreement with experimental observations given that we disregard fluctuations and neglect near-membrane effects.

From (Rubinstein et al., 2009), the turnover time of actin can be estimated to be 30 s. Therefore we obtain in non-dimensional units that \( \tau = 0.018 \) which leads to the estimate \( \epsilon = 0.015 \), see Section 7. Knowing the value of \( \epsilon \), we can reconstruct the mass density distribution \( \rho(u) \) which we show in Fig. 19 (right) together with the motor concentration distribution \( c(u) \). One can see that outside the boundary layers the model captures the main effect: the sweeping of actin towards the de-polymerization zone at the back of the cell by the retrograde flow and its regeneration on the polymerization zone at the front of the cell. A more detailed quantitative comparison with experiment requires an account of the two (or even three) dimensional nature of the flow.

Overall, we can conclude that the model reproduces rather well the motility initiation pattern observed in Verkhovsky’s experiment. Moreover, the ensuing dynamics is described adequately by the stable motile branch predicted by our theory formerly Fig. 18 (b).

In another experiment by Yam (Yam et al., 2007), which we can interpret here only qualitatively because of the absence of a natural 1D representation, motility was induced by injection of calyculin A, known to be a factor increasing the activity of myosin motors. The conventional interpretation of this experiment refers to the local variation of contractility which disrupts the actin flow and affects the cascade of polymerization and depolymerization (Paluch et al., 2006), from the perspective of our model it is natural to conjecture that the injection calyculin A affects the value of parameter \( \mathcal{P} \) pushing it beyond the threshold where the static symmetric configuration is stable and initiating in this way polarization and motility.

Notice that in both experiments (Verkhovsky et al., 1999) and (Yam et al., 2007), a fraction of keratocyte cells did not move at all after being exposed to the same mechanical or chemical perturbation as the cells that did become
motile. This can be explained by the fact that the realistic values for $P$ and $K$ lay rather close to the boundary separating static and motile regimes, see Fig. 18 (b). It is then feasible that some cells remain in the symmetric regime despite the perturbation. It is also possible that the realistic nonlinear dependence of active stress on myosin concentration saturates above a certain threshold and the nature of the motility initiation bifurcation $D_1$ changes into a subcritical pitchfork, see discussion in Section 5. This opens a finite range of bi-stability where both the homogeneous static state and the inhomogeneous motile state are locally stable which may be an alternative explanation of the simultaneous presence of motile and nonmotile cells with seemingly equal level of contractility.

9. Conclusions

We studied in this paper a prototypical model of a crawling segment of an active gel showing the possibility of spontaneous polarization and steady self propulsion in the conditions when contraction is the only active process. This model, which focuses on ‘pullers’, complements the existing theories of polarization and motility which place the main emphasis on ‘pushers’ and links motility initiation with active treadmilling and protrusion. Mathematically, the proposed model reduces to a Keller-Segel type dynamical system, however, in contrast to its chemotaxic analog, the nonlocality in this model is due to mechanical rather than chemical feedback.

As we argue in the paper, the motor proteins with sufficient contractility induce internal stress which can overcome the hydrodynamic resistance and induce flow. The flow produces a drift of motors in the direction of the regions where they concentrate and this autocatalytic amplification is the mechanism of the positive feedback in this model. The ensuing run away is countered by diffusion of motors which penalizes creation of concentration gradients and thus plays the role of a negative feedback. When a critical contractility of motors is reached, the homogeneous concentration of motors becomes unstable and a balance between drift and diffusion leads to the formation of a non trivial pattern. Among all possible patterns of this type, whose number increases with contractility, the stable ones localize motors at the trailing edge as observed in experiments. When the motor distribution loses symmetry the contraction asymmetry induces a flow of actin filaments towards the trailing edge thus producing frictional forces which propel the cell forward.

It is important to emphasize that our model generates polarization and steady crawling in the conditions when active protrusion is disabled. This provides an alternative explanation of the experiments of Verkhovsky et al (Verkhovsky et al., 1999) and Yam et al (Yam et al., 2007) that have been so far interpreted in terms of active polymerization inducing the growth of actin network (Blanch-Mercader and Casademunt, 2013). The predictions of the model are in agreement with experimental data presented in (Verkhovsky et al., 1999) which is rather striking in view of rather schematic nature of the model and the absence of fitting parameters.

Despite the overall success of the model, it leaves several important questions unanswered. Thus, our focus on a one dimensional representation of the motility process obscured the detailed description of the reverse flow of actin monomers which we have replaced with an opaque jump process. Similarly, our desire to maximally limit the number of allowed activity mechanisms, forced us to assume that polymerization of actin monomers and their transport are fast, equilibrium processes. These assumptions would have to be reconsidered in a richer setting with realistic flow geometry and an explicit account of the non-equilibrium aspects of treadmilling. A realistic 2D or 3D formulation will also open a way towards more adequate description of the membrane (cortex) elasticity and will allow one to account for the polar nature of the gel Marchetti et al. (2013). An assumption about the infinite compressibility of the cytoskeleton, which is behind our decoupling of the mass transport from the momentum balance, has to be reconsidered as well in the light of recent advances in the understanding of cytoskeletal constitutive response Broedersz and MacKintosh (2014); Pritchard et al. (2014). Finally, our oversimplified depiction of focal adhesions as passive frictional pads needs to be corrected by the account of the ATP driven integrin centered activity and the mechanical feedback from the binders to the cytoskeleton Schwarz and Safran (2013). The adequacy of the proposed mechanism as a fundamental explanation of motility initiation in keratocytes will depend on the extent to which the inclusion of all these and other related factors affects the main conclusions of the paper. A more thorough analysis will also open the way towards deeper understanding of the remarkable optimality of this mechanism discovered in the case of infinite stiffness (Recho et al., 2014).
**Figure 20:** Phase diagram for the static solutions in the parameter space \((A, B)\). \(A + B = 0\) line is the trivial (homogeneous) solution. In the bottom corner we show the blow up of the same diagram.

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11. Appendix A

Solutions of boundary value problem (29) correspond to closed trajectories on the phase plane \((s, s')\) passing through the origin \((s = 0, s' = 0)\) and different types of such trajectories are illustrated in Fig. 20.

Depending on the position of a point in the parametric plane \(A, B\), one can identify five different types of behavior:

1. If \(A + B = 0\), then equation \(W(r) = 0\) has one double root at \(r = 0\) and one single root (negative or positive) at \(r = s_\pm\) (Case 3 on Fig. 20). The only solution is then the trivial one \(s(u) = 0\) and \(L = \hat{L}_\pm\).

2. If \(A + B < 0\), then Eq. \(W(r) = 0\) has three roots: \(r = 0\), \(r = s_- < 0\) and \(r = s_+ > 0\). This case corresponds to static branches labeled in Fig. 20, Fig. 7, Fig. 9(a) and Fig. 9(b) by numbers without a prime (Case 1 on Fig. 20). In this domain, we find nontrivial static solutions with \(0 \leq s(u) \leq s_+\). Different solutions correspond to different number \((m)\) of sign changes for the function \(s'(u)\) and different values of \(L = 2m \int_0^{s_+} W(\sigma)^{-\frac{1}{2}} d\sigma\).

3. If

\[
A + B > 0
\]

\[
1 - \sqrt{A^2 - 2B + 1} < Be^{-\sqrt{A^2 - 2B + 1} + A + 1}
\]

then Eq. \(W(r) = 0\) has three roots: \(r = 0\) and \(r = s_- < 0\) and \(r = s_+ > 0\) with, \(s_+ > s_-\). This case corresponds to non motile branches labeled in Fig. 20, Fig. 7, Fig. 9(a) and Fig. 9(b) by numbers with a prime ‘ (Case 2 on Fig. 20). In this domain, we find nontrivial static solutions with \(s_- \leq s(u) \leq 0\). Again, different solutions correspond to different number of sign changes for the function \(s'(u)\) and different values of \(L = 2m \int_0^{s_-} W(\sigma)^{-\frac{1}{2}} d\sigma\).

4. If

\[
A + B > 0
\]

\[
1 - \sqrt{A^2 - 2B + 1} < Be^{-\sqrt{A^2 - 2B + 1} + A + 1}
\]

\[
A > -1
\]

\[
27
\]
then Eq. $W(r) = 0$ has three roots: $r = 0$ and $r = s_+ > 0$ and $r = s_- > 0$ with $s_+ > s_-$. and there are no static solutions since there are no closed paths in the phase plane passing through the point $(0, 0)$.

5. If $1 - \sqrt{\pi^2 - 2B + 1} > Be^{-\sqrt{\pi^2 - 2B + 1}r^2 + 1}$, then equation $W(r) = 0$ has only one non degenerate root at $u = 0$. In this case there are no static solutions since there are no closed paths in the phase plane.

Notice also that for the solutions described above the map between the two parameterizations $(A, B)$ and $(\mathcal{K}, \mathcal{P})$ is explicit

$$
\mathcal{K} = A/(2m \int_0^{r_{2+}} W(r)^{-1/2} dr - 1) = (2m \int_0^{r_{2+}} W(r)^{-1/2} dr - 1)
$$

$$
\mathcal{K}P = 2m \int_0^{r_{2+}} (r - A)W(r)^{-1/2} dr.
$$

(52)

Notice also all nontrivial static solutions bifurcate from the trivial branches in the sense that there are no detached solutions. Indeed, if a solution were detached, it would not pass through the origin (trivial solution) in the space $(s, s')$. But that would mean it cannot satisfies boundary conditions.

12. Appendix B

Equation (39) has two families of solutions depending on whether $\omega$ is real or pure imaginary. In the first case, we denote $\omega_\alpha \equiv |\omega| \geq 0$ whereas $\omega_\alpha \equiv -|\omega| \leq 0$ in the second case.

$$
2[\cosh(\omega_\alpha) - 1] + (Z \omega^2/\hat{L}^2 - 1)\omega_\alpha \sinh(\omega_\alpha) = 0 \quad \text{if } \omega^2 > 0,
$$

$$
2[\cos(\omega_\alpha) - 1] + (Z \omega^2/\hat{L}^2 + 1)\omega_\alpha \sin(\omega_\alpha) = 0 \quad \text{if } \omega^2 < 0.
$$

(53)

Equations (53) have only one non degenerate root at $\omega_\alpha = 0$ originating at the trivial solution $\hat{L}_\alpha$. In Fig. 21 the eigenfunctions associated with the sub-branch $D^{+}$ bifurcating from the trivial solution $\hat{L}_\alpha$ are illustrated for $Z = 0.01$. As parameter $Z$ increases the exponential viscous boundary layers thicken. They fully disappear at $Z = \hat{L}^2/12$ where the ‘hyperbolic’ eigen-vectors become ‘trigometric’.

2. When $\omega^2_\alpha < 0$, equation (53) has two sub-families of solutions:

(a) The first family can be written explicitly: $\omega_\alpha = -2m\pi r$ with $m \geq 1$. The unstable eigen-vector has the form

$$
\left(\begin{array}{c}
\delta L \\
\delta V \\
\delta s(u)
\end{array}\right) = \left(\begin{array}{c}
0 \\
1 \\
\frac{e^{\hat{L}^2}}{Z \omega_\alpha \cosh(\omega_\alpha / 2)} \left[ \sinh(\{u - 1/2\omega_\alpha, - (2u - 1) \sinh(\omega_\alpha / 2)\right] 
\end{array}\right)
$$

Since $\delta V \neq 0$, this bifurcation leads to a motile configuration which we denote $D_1$. In Fig. 21 the eigen-functions associated with the sub-branch $D^{+}_{1}$ bifurcating from the trivial solution $\hat{L}_\alpha$ are illustrated for $Z = 0.01$. As parameter $Z$ increases the exponential viscous boundary layers thicken. They fully disappear at $Z = \hat{L}^2/12$ where the ‘hyperbolic’ eigen-vectors become ‘trigonmetic’.

(b) The second family consists of a countable set of negative roots of equation (53) given implicitly by:

$$
2\tan\left(\frac{\omega_\alpha}{2}\right) = \left(\frac{Z}{\hat{L}^2} \omega_\alpha^2 + 1\right)\omega_\alpha.
$$

(54)
13. Appendix C

Normal form in $\mathcal{K}$. In terms of the normalized stress variable $r = s/L$ the original nonlinear problem can be written as

$$-Zr''(u) + L^2r(u) = \mathcal{K}P \frac{e^{L(r(u) - V_0)}}{\int_0^1 e^{L(r(u) - V_0)} du}, \quad \text{with} \quad r(0) = r(1) = 0, \quad r'(0) = r'(1) = V. \quad (55)$$

Assume that $\epsilon$ is a small parameter and expand the solution of (55) around a bifurcation point up to third order

$$r = 0 + \epsilon r + \epsilon^2 r/2 + \epsilon^3 r/6 + o(\epsilon^3), \quad V = 0 + \epsilon V + \epsilon^2 V/2 + \epsilon^3 V/6 + o(\epsilon^3), \quad L = \hat{L} + \epsilon L + \epsilon^2 L/2 + \epsilon^3 L/6 + o(\epsilon^3).$$

Assume that the bifurcation parameter $\mathcal{K}$ and therefore

$$\mathcal{K} = \mathcal{K} + \epsilon^1 \mathcal{K} + \epsilon^2 \mathcal{K}/2 + \epsilon^3 \mathcal{K}/6 + o(\epsilon^3).$$

where $\mathcal{K}$ is the bifurcation point. These expressions are then inserted into equation (55). Separating different orders of $\epsilon$ we obtain three differential equations

$$O(1), \quad L_0(r, L, V) = 0, \quad (56)$$

$$O(2), \quad L_2(r, L, V) = \mathcal{K}P_0(r, L, V) + \mathcal{K}P_1(r, L, V), \quad (57)$$

$$O(3), \quad L_3(r, L, V) = \mathcal{K}Q_0(r, L, V) + \mathcal{K}Q_1(r, L, V) + \mathcal{K}Q_2(r, L, V) + \mathcal{K}Q_3(r, L, V) + \mathcal{K}Q_4(r, L, V) + \mathcal{K}Q_5(r, L, V), \quad (58)$$

Figure 21: Solution branches of the characteristic equation (53) as functions of $Z$ for the trivial static solution $\hat{L}$ ($P = 0.01$). From (36), the locus of the bifurcation points are recovered and shown of Fig. 8. We refer to Fig. 9(a) for the label of bifurcation points. We represent in inserts Figure 21: Solution branches of the characteristic equation (53) as functions of $Z$ for $\epsilon = 0.15$ and the eigenfunction $\delta_s$ related to $D_1^+$ for $Z = 0.01$. The eigenfunctions are normalized to 1; solid and dashed lines correspond to the two possible directions of the pitchfork bifurcation.

The unstable eigen-vector is

$$\begin{pmatrix} \delta L \\ \delta V \\ \delta s(u) \end{pmatrix} \approx \begin{pmatrix} 0 \\ \frac{i \omega}{\omega_{\epsilon}} \sin(\omega_{\epsilon}/2) \{ -2(u - 1/2) \sin(\omega_{\epsilon}/2) \} \end{pmatrix}$$

It corresponds to motile branches because $\delta V \neq 0$. We denote this family by $D_m$. In Fig. 21 the eigen-functions associated with a subbranch $D_m^+$ originating at trivial solutions $\hat{L}_+$ are illustrated for $Z = 0.01$. 

where $L$ is the linear operator already introduced in the stability analysis, see (34):

$$L(r, L, V) := r''(u) - \omega^2 r(u) + \left(\frac{u - \frac{1}{a}}{Z}\right)(\omega^2 Z - \hat{L}^2)V + \frac{(2L - 1)\omega^2(\omega^2 Z - \hat{L}^2)L}{(L - 1)\hat{L}^2}$$

and $P_0, P_1, Q_0, Q_1$ and $Q_2$ are known non linear operators. The boundary conditions remain the same at all orders $i$:

$$r(0) = r(1) = 0, \quad r'(0) = r'(1) = V$$

In the leading order, we obtain the results already reported in Section 5 including the eigenvalue $\mathcal{K}$ and the eigenfunction $r(u), L, V$. To have a nontrivial solution in the next order, the right-hand side of equation (57) must be orthogonal to the kernel of the dual of $L$ (for the $L^2$ scalar product). In the $(C_1, C_2, \delta L, \delta V)$ space, see Section 5, this means orthogonality to the kernel of the transpose of matrix (38). The resulting linear scalar equation determines the value of $\hat{K}$. When this value vanishes, higher orders must be considered in a similar way. We summarize below the main results obtained by implementing this procedure.

1. **Static branches** result from transcritical bifurcations. For the $m^{th}$ branch we have

$$\hat{K} = (L^2 - 4m^2\pi^2 Z)/[L(\hat{L} - 1)]$$

2. **Motile branches** all correspond to pitchfork bifurcations with $\mathcal{K} = 0$. They can be either subcritical or supercritical depending on the sign of

$$\hat{K} = \{(2L - 1)\hat{L}^4(3a^2 + 770) + 2L^{12}(3(8 - 11L)a^4 + 1415(1 - 2L)a^2 + 4620(1 - 2L)) + 3L^{10}a^2Z^2(40L(a^4 + 61a^2 + 374) - 31a^4 - 1340a^2 - 7480) + 2L^7a^2Z^3(4L(6a^4 + 89a^2 - 3150) - 9a^4 + 50a^2 + 7380) + L^5a^2Z^4(-2L(165a^4 + 6502a^2 + 195a^4 + 6574a^2 + 22440) + 6L^3a^2Z^5((61L - 34)a^4 + (2622L - 1339)a^2 + 7072(2L - 1)) + L^2a^2Z^6(3(31 - 60L)a^4 + 4264(1 - 2L)a^2 - 28224(2L - 1)) + 2(2L - 1)a^2Z^7(9a^4 + 472a^2 + 3456)Z^3) (144L(\hat{L} - 1)(2L - 1)\omega^4Z^2(L^2 - \omega^4Z)((L^2 - 2L^2 (\omega^2 + 6) Z + \omega^4Z^2))^{-1}$$

In Fig. 22(b) we illustrate the function $\hat{K}(P)$ for the first motile branches $D_1^+$ and $D_1^-$. As $\hat{K} \geq 0$ for all values of the activity parameter $P$, the motile branch $D_1^+$ always bifurcates from the static branch in a supercritical (pitchfork)
manner. In contrast, the motile branch $D_1^-$ can bifurcate either supercritically or subcritically depending on the value of $\mathcal{P}$. When $\mathcal{P}$ is larger than a threshold value $\mathcal{P}_s$, the coefficient $2K$ changes sign and becomes negative indicating a subcritical character of the bifurcation on the $\hat{L}$-static branch.

**Normal form in $\mathcal{P}$.** We now consider $\mathcal{P}$ as the bifurcational parameter. The derivation of the normal form in this case is more complex because the homogeneous static solution $\hat{L}(\mathcal{P})$ is a multivalued function of $\mathcal{P}$ (see Fig. 6). One can circumvent the difficulty by introducing a new variable

$$J = \mathcal{L}(L-1) + \mathcal{P},$$

(60)

whence the trivial solution is $(J, V, r) = (0, 0, 0)$. In this formulation $J$, $V$ and $r(u)$ are unknowns while the length $L$ is the bifurcation parameter. The regular expansions near the homogeneous state give

$$r = \epsilon^1 r + \epsilon^2 r/2 + \epsilon^3 r/6 + o(\epsilon^4),$$

$$V = \epsilon^1 V + \epsilon^2 V/2 + \epsilon^3 V/6 + o(\epsilon^4),$$

$$J = \epsilon^1 J + \epsilon^2 J/2 + \epsilon^3 J/6 + o(\epsilon^4),$$

$$L = L + \epsilon^1 L + \epsilon^2 L/2 + \epsilon^3 L/6 + o(\epsilon^4).$$

Distinguishing the static and motile branches as before, we obtain the following results:

1. **Static branches** are all found to be transcritical bifurcation. For the $n^{th}$ branch, we have $\mathcal{P} = \mathcal{P} + \epsilon^1 \mathcal{P} + o(\epsilon)$ where

$$0 \mathcal{P} = -L(L-1), \quad \hat{\mathcal{P}} = 1 - (2L - 1)L.$$

and $L$ is a solution of the cubic equation

$$-\mathcal{K}(L)^3(L-1) = \mathcal{Z}4\pi^2 m^2 + (L)^2.$$

In this equation only two roots corresponding to $S_m^+$ (the smaller) and to $S_m^{**}$ (the larger) are in the range $[0, 1]$. In Fig. 23(a), we illustrate the behavior of of the function $\mathcal{P}(\mathcal{K})$ for the branches $S_1^+$ and $S_1^{**}$.
2. **Motile branches** result from pitchfork bifurcations that can be either supercritical or subcritical with

\[ \mathcal{P} = \mathcal{P} + \epsilon^2 \mathcal{P}/2 + o(\epsilon^2). \]

The coefficients in this expansion can be written in the form

\[ \mathcal{P} = L(L - 1) \quad \text{and} \quad \mathcal{P} = -2J = (2L - 1)\tilde{L}, \]

where

\[ 2 = \frac{60 L Z - K(L - 1)(L)^2(K(L - 1) - 4)}{24 K(K(L - 1) + 1)^2}. \]

The length \( \tilde{L} \) can be found from the system of equations

\[ -K(L)^2(L - 1) = -Z^2 + (L)^2 \]

\[ \tanh(\omega/2) = (\omega/2)(1 - Z^2)/L^2) \]

Again, two roots are in the interval \([0, 1]\): the smaller one belongs to the branch \( D_n^m \) and the larger one to the branch \( D_n^m \). In Fig. 23(b), we illustrate the function \( \hat{\mathcal{P}}(\mathcal{K}) \) for \( m = 1 \). The bifurcation from the static homogeneous solution with longer length is always supercritical as \( \hat{\mathcal{P}}(D_1^1) > 0 \). Instead, the bifurcation from the static homogeneous solution with smaller length can change from subcritical (\( \mathcal{P} \leq 0 \)) to supercritical (\( \mathcal{P} \geq 0 \)).

14. **Appendix D**

In the study of (40) we closely follow the procedure developed in Section 5. In essence, the results are exactly the same for fixed \( \tilde{L} = 1 \) and the product \( K \mathcal{P} \) replaced by \( \lambda \) with only one homogeneous state \( (s, v) = 0, V = 0 \) and \( s_0 = \Phi(r)/r \) and where \( \delta s \) replace \( \delta L \). As a result, there is an infinite sequence of bifurcations branching from the now unique homogeneous state. We shall only focus on the stable attractor of the problem, namely, the homogeneous solution before the \( D_1 \) bifurcation and the first motile branch after.

The critical value of the bifurcation parameter \( \lambda \) corresponding to the case when a homogeneous static solution becomes linearly unstable is given by the formula \( \lambda_c = (1 + r^2(1 - Z^2 - \epsilon^2)) \), where \( \omega_c \) is a root of the equation \( \tanh(\omega_c/2) = \omega_c(1 - Z^2)/2 \) with the smallest absolute value. We then proceed to the next order developing a regular expansions close to the bifurcation point

\[
\begin{align*}
    s &= 0 + \epsilon s + \epsilon^2 s/2 + \epsilon^3 s/6 + o(\epsilon^3) \\
    V &= 0 + \epsilon V + \epsilon^2 V/2 + \epsilon^3 V/6 + o(\epsilon^3) \\
    s_0 &= \Phi(r)/r + \epsilon s_0 + \epsilon^2 s_0/2 + \epsilon^3 s_0/6 + o(\epsilon^3),
\end{align*}
\]

Similar expansion for the bifurcation has the form

\[ \lambda = \lambda_c + \epsilon \lambda + \epsilon^2 \lambda/2 + \epsilon^3 \lambda/6 + o(\epsilon^3). \]

For the first motile branch one finds that \( \lambda = 0 \), indicating a pitchfork bifurcation.

Below we show that this bifurcation can change from supercritical to subcritical depending on the value of the dimensionless parameter \( r \). Assuming without loss of generality that \( V = \frac{1}{2} \), we obtain

\[
\lambda = \frac{(\omega^2 Z - 1)(Ar^2 + Br + C)}{144\omega^8 Z^2 (\omega^4 Z^2 - 2(\omega^2 + 6) Z + 1)}.
\]
where

\[ A = 30\omega^2Z^3 - 123\omega^4Z^4 + 6\omega^6(35 - 164Z)Z^3 + 2\omega^8Z^3(1073Z - 84) + 6\omega^4Z(1440Z^2 - 155Z + 8) + 3\omega^2(1320Z^2 - 430Z + 1) - 9240Z + 770 \]

\[ B = -2\left(21\omega^2Z^5 - 87\omega^4Z^4 + 4\omega^6(39 - 173Z)Z^3 + 2\omega^8Z^3(707Z - 66) + 3\omega^4Z(1440Z^2 - 210Z + 13) + \omega^2(2280Z^2 - 1150Z + 3) - 9240Z + 770 \right) \]

\[ C = -6\omega^2Z^3 + 21\omega^4Z^4 + 6\omega^6Z3(28Z - 5) + 2\omega^8(12 - 79Z)Z^2 + 6\omega^4Z(85Z - 2) + 3\omega^2(1320Z^2 - 430Z + 1) - 9240Z + 770 \]

these expressions show that there exists a critical value \( r_c \) of the parameter \( r \) such that the bifurcation is supercritical (i.e. \( \lambda \leq 0 \)) for \( r \leq r_c \). This regime corresponds to a state where contraction is proportional to concentration of motors.

For \( r \geq r_c \), the pitchfork bifurcation is subcritical (i.e. \( \lambda \geq 0 \)) and the regime is characterized by a contraction which saturates into the plateau. We plot on Fig. 24 the value of \( \lambda \) as a function of \( r \) for a fixed \( Z = 1 \) and in inset the value \( r_c(Z) \). When \( Z \to 0 \), \( r_c \to 2 \) and when \( Z \to \infty \), \( r_c \to (7 + \sqrt{69})/10 \).

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