Optimality of contraction-driven crawling

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We study a model of cell motility where the condition of optimal trade-off between performance and metabolic cost can be made precise. In this model a steadily crawling fragment is represented by a layer of active gel placed on a frictional surface and driven by contraction only. We find analytically the distribution of contractile elements (pullers) ensuring that the efficiency of self-propulsion is maximal. We then show that natural assumptions about advection and diffusion of pullers produce a distribution that is remarkably close to the optimal one and is qualitatively similar to the one observed in experiments on fish keratocytes.

Although the idea of optimal trade-offs in biology is rather natural, the examples supporting optimality at the quantitative level are few. A prominent case is the demonstration that the structure of transport networks minimizes energy consumption at a fixed material cost [1]. Each validation of this type is of considerable interest as a step towards the general understanding of homeostasis [2–4]. In this Letter we present a new example of cost-performance trade-off associated with contraction-driven cell motility. We show that the observed distribution of molecular motors in crawling fish keratocytes [5] is close to the optimal one and explain the mechanism behind this optimality.

The efficiency of self-propulsion in viscous environments has been a subject of intense studies since the pioneering work of G.I. Taylor [6]. Optimal strategies for various Stokes swimmers were identified under a tacit assumption that the organism is able to perform the desired shape changes [7, 8]. Similar reasoning has been applied to crawling on frictional surfaces where the optimal propulsion can be induced by actuators prescribing spatially and temporarily correlated compression and stretch [9]. Such approach, however, does not reveal the physical mechanisms ensuring optimal actuation and it remains unclear whether actual crawling cells can follow the optimal strategy.

To address these questions we choose the simplest case of keratocytes whose motility initiation is largely contraction driven. Experiments show that contractile elements (‘pullers’) are narrowly localized at the trailing edge [5, 10, 11] and our goal will be to check whether such configuration is optimal in terms of the trade-off between the Stokes performance and the energetic cost of active force generation and whether it is compatible with the physical model of motor redistribution. In our analysis we neglect the presence of ‘pushers’ because active treadmilling does not play an important role at the stage of motility initiation [12, 13]. Several comprehensive computational studies of crawling taking treadmilling into account but not addressing the question of optimality are available in the literature [14].

We model a steadily crawling cell fragment using a one-dimensional version of the active gel theory [10, 15–17]. The cytoskeleton is interpreted as an infinitely compressible viscous fluid, adhesion is represented by a frictional interaction with a rigid substrate and the cortex is assumed to impose a fixed size on the moving cell. Using these simplifying assumptions and choosing parameters in the biological range we show that the stationary distribution of motors is close to the optimal one.

Consider a one-dimensional layer of active gel placed on a frictional rigid background [15, 16]. The balance of forces takes the form

\[ \partial_x \sigma = \xi v, \]

where \( \sigma(x,t) \) is the stress, \( v(x,t) \) is the velocity and \( \xi \) is the friction coefficient. We model the gel as a viscous fluid subject to active contractile stresses \( \tau \geq 0 \). We can then write

\[ \sigma = \eta \partial_x v + \tau, \]

where \( \eta \) denotes viscosity.

The regime of interest is when the cell moves with a constant velocity \( V \) while maintaining a length \( L \) fixed by the cortex. We therefore look for the configuration \( \sigma(y) \) and \( v(y) \) depending on the moving coordinate \( y = (x - Vt)/L \) and satisfying the boundary conditions \( v(\pm1/2) = V \) and \( \sigma(\pm1/2) = \sigma_0 \), where \( \sigma_0 \) is the reaction stress due to the length constraint. Without loss of generality, we assume \( V \geq 0 \).

The task is to find the distribution of active stresses \( \tau(y) \) ensuring optimal efficiency

\[ \Lambda = P/H, \]

where \( P \) is the functional power and \( H \) is the metabolic cost per unit time. In the absence of an explicit cargo, we assume that the useful work is the translocation of the cell as a whole against frictional resistance. Therefore we write

\[ P = \xi V^2 L \]

as in the theory of Stokes swimmers [18]. The rate of free energy consumption can be written as a sum \( H = H^* + H^{**} \) where

\[ H^* = -\int_{-1/2}^{1/2} \tau \partial_y v dy \]

and
is the power exerted by the active stress \( \tau(y) \) on the environment and \( H^{**} \) is the cost of the maintenance of the force generating machinery [19].

First we suppose that the physical mechanism of force generation is unknown and pose the problem of finding the function \( \tau(y) \geq 0 \) maximizing \( \lambda \) at a given value of \( H^{**} \). We also prescribe average value of the contractile stress

\[
\bar{\tau} = \frac{1}{2} \int_{-1/2}^{1/2} \tau(y)dy,
\]

which is equivalent to fixing the total number of motors at constant cell length. It will be convenient to use non-dimensional variables \( \sigma/\bar{\tau}, x/\sqrt{\eta/\xi} \) and \( t/(\eta/\bar{\tau}) \) without changing the notations. In dimensionless variables the stress distribution can be written as

\[
\sigma(y) = \sigma_0 \frac{\cosh((L \bar{\tau})y)}{\cosh(L \bar{\tau}/2)} + L \int_{-1/2}^{1/2} \Psi(z,y)\tau(z)dz,
\]

where

\[
\Psi = \frac{\sinh(L(1/2 - y))\sinh(L(1/2 + z))}{\sinh(L)} - \theta(z-y)\sinh(L(z-y)),
\]

\( \theta \) is the Heaviside function and \( L = L_\sqrt{\eta/\xi} \) is a parameter of the problem. The constants \( V \) and \( \sigma_0 \) can be found explicitly (cf. [12])

\[
V = -\frac{\xi}{2} \int_{-1/2}^{1/2} \frac{\sinh(Ly)}{\sinh(L/2)} \Delta \tau dy,
\]

\[
\sigma_0 - \bar{\sigma}_0 = \frac{\xi}{2} \int_{-1/2}^{1/2} \frac{\cosh(Ly)}{\sinh(L/2)} \Delta \tau dy,
\]

where \( \Delta \tau = \tau(y) - 1 \) is the spatially inhomogeneous component of the distribution of active dipoles and \( \bar{\sigma}_0 = 1 \) is the pre-stress induced by its constant part. The first of these formulas states that contraction-induced crawling is due entirely to spatial asymmetry: this is an analog of the famous Scallop Theorem [20]. Since the total force dipole produced by the system is \( \mathcal{L} \int_{-1/2}^{1/2} y\nu(y)dy = \sigma_0 - \bar{\sigma}_0 \) the second formula in (3) states that the inhomogeneity of motor distribution is also at the origin of a force dipole applied by the cell to the background [21]. Using [5, 15, 16, 22] we obtain \( \bar{\tau} \sim 10^2Pa, \xi \sim 2 \times 10^6Pa\cdot m^{-2}, s, \eta \sim 10^5 Pa\cdot s \) and \( L \sim 20 \times 10^{-6}m \) which gives \( \mathcal{L} \sim 10 \).

The optimal distribution \( \tau(y) \) also depends on the parameter \( 3\mathcal{\mathcal{H}}^{**} = H^{**} \sqrt{\eta/\xi}/\bar{\tau}^2 \) which contains condensed information about the mechanism of active force generation. Optimality here implies a trade-off between maximization of velocity \( V \) and minimization of the power of active stresses \( \mathcal{H}^{**} \). It is easy to show from (3) that the maximum velocity is \( V^{\infty} = L/2 \) and that it corresponds to full localization of motors at the trailing edge. Similarly, one can reach the lower bound of the cost \( \mathcal{\mathcal{H}}^{**} = 0 \) by taking \( \tau = 1 \), however, in this case \( V = 0 \). The optimal trade-off depends on the value of \( 3\mathcal{\mathcal{H}}^{**} \) and it is clear that optimally distributed motors localize at \( 3\mathcal{\mathcal{H}}^{**} \rightarrow \infty \) and spread at \( 3\mathcal{\mathcal{H}}^{**} = 0 \).

Mathematically, we have to solve an ‘obstacle’ problem for a quadratic functional. Its general solution has the form \( \tau(y) = f(y)\theta(f(y)) \), where \( f(y) = Ay^2 + By + Cw \) and the constants \( A, B, C \) can be found from a simple algebraic minimization problem [23]. In the limit \( \mathcal{H}^{**} \rightarrow 0 \), we obtain \( \lambda \rightarrow (L/2)\cos(L/2) - 1 \) and \( \tau(y) \rightarrow 1 - 2y \). In the opposite limit \( \mathcal{H}^{**} \rightarrow \infty \) the efficiency tends to zero as \( \lambda \sim (V^{\infty})^2/\mathcal{\mathcal{H}}^{**} \) and \( \tau(y) \rightarrow \delta(y + 1/2) \) where \( \delta \) is the Dirac distribution. In Fig.1 we show the optimal efficiency \( \Lambda_{op} \) and some optimal profiles \( \tau_{op}(y) \) for the intermediate values of \( \mathcal{H}^{**} \). The regimes representing physical “designs” must be necessarily inside the admissible region bounded by the optimal curve \( \Lambda_{op}(\mathcal{H}^{**}) \). Observe that under the assumption \( \tau(y) \leq 0 \) we would have obtained exactly the same localization of ‘pushing’ elements near the front end of the moving cell.

Suppose now that the active stress is generated by motors with mass density \( \rho(x, t) \) and that \( \tau = \chi\rho \), where \( \chi \) is a positive material constant. Following [10, 24], we assume that the transport of motors is governed by the standard advection-diffusion equation which in dimensional variables takes the form

\[
\partial_t \rho + \partial_x (\rho \chi) - D \partial_{xx} \rho = 0,
\]

where \( D \) is the diffusion coefficient. After making the traveling wave ansatz, assuming no flux boundary conditions and changing to dimensionless variables we can integrate (4) to obtain the solution of this equation in the form [10]

\[
\rho(y) = \frac{e^{\lambda(\sigma(y) - V \mathcal{L}/2)}}{\int_{-1/2}^{1/2} e^{\lambda(\sigma(y) - V \mathcal{L}/2)}dy}.
\]

Here density is normalized by \( \bar{\rho} = \bar{\tau}/\chi \) and \( \lambda = \chi \bar{\rho}/(\xi D) \) is an additional parameter.

At small values of \( \lambda \), the system of two equations (5), (2) has only a trivial solution \( \sigma(y) = \sigma_0 = 1 \) and \( V = 0 \). This solution becomes unstable at \( \lambda_c = 1 - \omega^2/\mathcal{L}^2 \) where \( \omega \) is the...
smallest root of the algebraic equation $2 \tanh(\omega/2) = \lambda_c \omega$. Through the pitchfork bifurcation shown in Fig. 2 the cell becomes polarized and starts to move [10]. As $\lambda$ increases the motors progressively concentrate at the trailing edge. For keratoctyes we use [22, 25] to find that $D \sim 10^{-13} m^2 \cdot s^{-1}$ which gives $\lambda_c \sim 0.5$. We then obtain an estimate $V_c = 0.08 \mu m \cdot s^{-1}$ which is very close to the value measured in [5]. Interestingly, for $L \sim 10$ we get $\lambda_c \sim 0.23$ which implies that keratoctyes operate rather close to the bifurcation point. This near-criticality may carry considerable biological advantages since a cell can easily switch from static to motile state or change the direction of the already initiated motion.

The next step is to find the link between the value of the non-dimensional parameter $\lambda$ fully characterizing the transportation problem and the cost parameter $H_{\sigma}$ from the optimization problem. For simplicity, we assume that the system is in contact with a thermal reservoir imposing a constant temperature $T$. To introduce the thermodynamic model (see [23] for more detail) we temporarily bring back the dimensional variables.

Following the general theory of active gels [15] we describe the acto-myosin network as a two-phase mixture with the total mass density $\rho(x, t)$. It satisfies the conservation equation

$$\partial_t \rho + \partial_x (\rho v) = 0,$$

which decouples from the force balance problem due to the assumption of infinite compressibility: if the velocity field $v(y)$ is known, $\rho(y)$ can be reconstructed by standard methods [10, 13].

The total free energy can be written as

$$F = \int_{-L/2}^{L/2} \rho f dx,$$

where $f(\phi, \zeta)$ is the energy density, which depends on the mass fraction (concentration) of motors in the mixture $\phi(x, t) = \rho/\hat{\rho}$ and on a variable $\zeta(x, t)$ characterizing the progress of a non-equilibrium chemical reaction (ATP hydrolysis) supplying energy to the motors. We can then write

$$H = -\dot{F},$$

where the dot denotes the full time derivative. To compute the right hand side we need to introduce the driving force of the reaction $A = -\partial_\zeta f > 0$ which we assume to be fixed by an external "chemostat". We also need to define the chemical potential of motor molecules $\mu = \partial_\phi f$ whose nonzero gradient is a crucial part of the motility mechanism. We can then write

$$\dot{F} = \int_{-L/2}^{L/2} \rho (A \dot{\zeta} + \mu \dot{\phi}) dx.$$

To show thermodynamic consistency of (4) and to derive an additional equation for the variable $\zeta(x, t)$ we observe that the dissipation rate $\dot{R}$ can be written in the form

$$R = W - \dot{F},$$

where $W = \int_{-L/2}^{L/2} \sigma \partial_x v dx$ is the external power. If there are no sources of motors we can write

$$\dot{\rho} \phi = \partial_x J,$$

where $J$ is the diffusion flux. Hence

$$R = \int_{-L/2}^{L/2} \left( \sigma \partial_x v + \dot{\rho} \phi A + J \partial_x \mu \right) dx.$$

We postulate linear relations between fluxes and forces: $\sigma = \sigma_{11} \partial_x v + \sigma_{12} A$, $\dot{\rho} \phi = -\sigma_{21} \partial_x v + \sigma_{22} A$ and $J = \chi \partial_x \mu$, where for simplicity we omitted the couplings between diffusion and reaction and between diffusion and viscosity.

Since motors are enzymes catalyzing the ATP reaction we must deviate from the Onsager scheme and assume that the coefficients $\sigma_{12}$ and $\sigma_{22}$ are functions of the motor density $\rho$. To make the thermodynamic theory consistent with our postulate $\tau = \sigma_{12} A = \chi \rho$ we need to further assume that these functions are linear. The other coefficients are assumed to be Onsagerian, for instance, $\sigma_{11} = \eta$. To compute the diffusion coefficient in (4) we notice that for dilute mixtures $\partial_\rho \mu = k_B T/\phi$ where $k_B$ is Boltzmann’s constant. If we make additional assumptions that the variation of the total density is small $\partial_x \rho/\rho >> \partial_x \hat{\rho}/\hat{\rho}$ and the diffusion coefficient is concentration independent, we recover (4) with $D = \sigma_{33} k_B T/\rho$ where $\sigma_{33}$ is the mobility per unit volume. These assumptions clearly fail near the singularities of $\rho$ where the theory has to be appropriately modified.

An important outcome of our constitutive assumptions is an equation governing the reaction progress

$$\dot{\zeta} = \phi (bA - \frac{\chi}{A} \partial_x v),$$

where $b = \sigma_{22}/\rho$ is a constant parameter. Since the value of $A$ is controlled from outside, (7) decouples from the rest of the
system with ζ easily recoverable once the fields v and φ are known.

We have now specified the force generation mechanism and can use (6) to obtain an explicit expression for the cost function H. First, using the force balance equation we write the mechanical cost function in the form

\[ H^* = \int_{-L/2}^{L/2} [\xi v^2 + \eta (\partial_x v)^2] \, dx \geq 0, \]

where the two entries characterize contributions due to friction and viscosity. The non-mechanical cost function can be written as

\[ H^{**} = \int_{-L/2}^{L/2} \left[ b_0 A^2 + \frac{D k_B T}{\bar{\rho}} (\partial_x \rho)^2 \right] \, dx \geq 0. \]

Here the two terms are the cost of keeping the chemical reaction out of equilibrium and the cost of supporting concentration gradients. Since the motion is driven exclusively by the "chemostat", we obtain for the physical solution that both \( H^* \rightarrow 0 \) and \( H^{**} \rightarrow 0 \) as \( A \rightarrow 0 \) [23].

To make comparison with the optimization model we need to compute the dimensionless quantity

\[ \mathcal{H}^{**} = \mathcal{M} \mathcal{L} + \frac{\mathcal{E}}{\lambda \mathcal{L}} \int_{-1/2}^{1/2} (\partial_y \rho)^2 \, dy. \] (8)

where we introduced two new parameters of the problem: \( \mathcal{M} = \eta b_0 A^2 / (\bar{\rho} \chi^2) \) and \( \mathcal{E} = k_B T / \chi \). If motors operate in stall conditions and form bipolar contractile units with size \( d \), the produced force is \( p \sim 2 \chi / d \). For myosin II we have \( d \sim 0.15 \mu m \) and \( p \sim 1.5 p N \) [26] which gives \( \chi \sim 1.1 \times 10^{-19} J \) and using \( k_B T \sim 4.3 \times 10^{-21} J \) we obtain \( \mathcal{E} \sim 0.04 \). Notice also that \( b_0 A^2 \) is the free energy consumption rate per motor and therefore that it is equal to \( k A \) where \( k \) is the rate of ATP turnover per motor. Since \( A \sim 25k_B T \) and \( k \sim 25 s^{-1} \) [26], we obtain \( \mathcal{M} \sim 0.053 \).

We can now fix the parameters \( \mathcal{E}, \mathcal{M} \) and compare physical and optimal efficiencies at different values of the remaining parameter \( \lambda \). The efficiency in the physical model is \( \Lambda_{ph}(\rho_{ph}, \mathcal{H}^{**}) \) where \( \rho_{ph}(y, \lambda) \) is the solution of (4) and \( \mathcal{H}^{**}(\lambda) \) is taken from (8). The ensuing function \( \Lambda_{ph}(\lambda) \) is to be compared with the optimal efficiency \( \Lambda_{op}(\lambda) = \Lambda_{op}(\rho_{op}, \mathcal{H}^{**}) \) where \( \rho_{op}(y, \mathcal{H}^{**}) \) is the solution of the optimization problem and \( \mathcal{H}^{**}(\lambda) \) is the same as above.

The results of the comparison are summarized in Fig.3. The function \( \Lambda_{ph}(\lambda) \) displays a single maximum at \( \lambda_o \sim 0.24 \). For all \( \lambda \geq \lambda_o \), the physical model remains close to the optimal one which is crucial since at \( \lambda \rightarrow \infty \) the rate of energy consumption diverges \( \mathcal{H}^{**} \sim \mathcal{L}^3 \lambda^3 / 3, \mathcal{H}^{**} \sim \mathcal{E} \mathcal{L}^5 \lambda^2 / 4 \). In this (high velocity) limit both physical and optimization problems generate the same profiles with motors infinitely localized at the trailing edge of the moving cell. The robust optimality in the range \( V \geq V_o(\lambda_o) \sim 1.1 \) is illustrated further in Fig. 4 where we show the ratio \( r(V) = \Lambda_{ph}/\Lambda_{op} \leq 1 \). The presence of a quasi-plateau on this graph in the biologically relevant range of velocities [5] and the fact that in this range the physical and the optimal efficiencies are close suggest that the system is tuned to optimality. In the immediate vicinity of the motility initiation point \( V = 0 \) where \( \lambda \sim \lambda_c \), the asymptotic solutions in the two models have the same general structure \( \rho(y) - 1 \sim (\lambda - \lambda_c)^{c_f} f(y) \), however, since \( \kappa_{ph} = 1/2 \) and \( \kappa_{op} = 0 \) the propulsion machinery operates sub-optimally in this regime and this may explain why small velocities have not been observed in experiments.

In conclusion, we have shown that in contraction-dominated crawling the optimal trade-off between Stokes performance and the metabolic cost is achieved by localization of contractile units at the trailing edge of the moving cell. A simple advection-diffusion model of motor redistribution based on the active gel theory performs almost optimally in the range of parameters suggested by in vivo measurements. The fact
that the near-optimal behavior is robust and extends into the
domain of parameters where sub-optimality would be par-
ticularly costly, suggests that contraction-dominated crawl-
ing presents an example of a remarkably perfected biological
mechanism.

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Supplementary Information
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1 Solution of the optimization problem

Here we show how the infinite dimensional optimization problem formulated in the main text can be reduced to an algebraic minimization problem in two dimensions.

If we substitute the function $\sigma(y)$ from (2) into the dimensionless expression of efficiency, we obtain:

$$\Lambda = \frac{LV^2}{L \int_{-1/2}^{1/2} \tau(y)^2 dy - 2\sigma_0^2 \tanh(\frac{L}{2}) - L^2 \int_{-1/2}^{1/2} \int_{-1/2}^{1/2} \Psi(y,v)\tau(y)\tau(v)dydv + \mathcal{H}^*}. \quad (I)$$

The constants $V$ and $\sigma_0$ are defined in terms of the unknown function $\tau(y)$ in Eq.(3) of the main text (see also Eq.(III) below). Our strategy is to first fix $V$ and $\sigma_0$, optimize (I) with respect to $\tau(y)$ and then to optimize the result with respect to $V$ and $\sigma_0$.

The first problem is equivalent to minimizing the denominator in (I)

$$\min_{\tau} \left[ Q(\tau) = \int_{-1/2}^{1/2} \tau(y)^2 dy - \mathcal{L} \int_{-1/2}^{1/2} \int_{-1/2}^{1/2} \Psi(y,v)\tau(y)\tau(v)dydv \right], \quad (II)$$

under the constraints

$$\begin{cases} 2V \sinh(\frac{L}{2}) = -\mathcal{L} \int_{-1/2}^{1/2} \sinh(\mathcal{L}y)\tau(y)dy \\ 2\sigma_0 \sinh(\frac{L}{2}) = \mathcal{L} \int_{-1/2}^{1/2} \cosh(\mathcal{L}y)\tau(y)dy \\ \int_{-1/2}^{1/2} \tau(y)dy = 1. \end{cases} \quad (III)$$

An additional constraint $\tau(y) \geq 0$ states the active forces in our system are contractile.

In order to take the constraints into account, we introduce three scalar Lagrange multipliers ($\kappa_0, \kappa_1, \kappa_2$) and a non negative function $\kappa(y)$. Then the condition that the efficiency is maximal takes the form

$$(I - Q)\tau(y) = \Gamma(y) \quad (IV)$$

where

$$Q\tau = \mathcal{L} \int_{-1/2}^{1/2} \Psi(y,v)\tau(v)dv$$

and

$$\Gamma(y) = \kappa_0 - \kappa_1 \sinh(\mathcal{L}y) + \kappa_2 \cosh(\mathcal{L}y) + \kappa(y).$$
We invert the kernel of equation (IV) using an expansion in eigenfunctions [6] to obtain
\[ \tau(y) = (I - Q)^{-1}\Gamma(y) = \int_{-1/2}^{1/2} \phi(y, v)\Gamma(v)dv. \] (V)

Here
\[ \phi = \delta(y - v) + L^2 \left[ \left( \frac{1}{2} + y \right) \left( \frac{1}{2} - v \right) \theta(v - y) + \left( \frac{1}{2} + v \right) \left( \frac{1}{2} - y \right) \theta(y - v) \right], \] (VI)

\( \theta \) is the Heaviside function and \( \delta \) is the Dirac distribution. Using the expression for \( \Gamma \) we obtain
\[ \tau(y) = P(y) + \int_{-1/2}^{1/2} \phi(y, v)\kappa(v)dv. \] (VII)

The function
\[ P(y) = \kappa_0\psi_0(y) + \kappa_1\psi_1(y) + \kappa_2\psi_2(y) \] (VIII)
is a parabola since
\[ \psi_0(y) = 1 - \frac{c^2}{2}(y + \frac{1}{2})(y - \frac{1}{2}), \quad \psi_1(y) = -2y \sinh \left( \frac{c}{2} \right) \] and \( \psi_2(y) = \cosh \left( \frac{c}{2} \right) \).

The Lagrange multipliers can be found from Karush-Kuhn-Tucker conditions [1]
\[ \begin{aligned}
1 &= \kappa_0 A_0 + \kappa_2 A_2 + \int_{-1/2}^{1/2} \kappa(y)\psi_0(y)dy \\
2\gamma^2 \sinh (\frac{c}{2}) &= \kappa_1 S_1 + \int_{-1/2}^{1/2} \kappa(y)\psi_1(y)dy \\
2\sigma_0 \sinh (\frac{c}{2}) &= \kappa_0 C_0 + \kappa_2 C_2 + \int_{-1/2}^{1/2} \kappa(y)\psi_2(y)dy \\
\tau(y) &\geq 0, \quad \kappa(y) \geq 0 \quad \text{and} \quad \kappa(y)\tau(y) = 0,
\end{aligned} \] (X)

where
\[ \begin{aligned}
A_0 &= 1 + \frac{c^2}{2}, \quad A_2 = \cosh (\frac{c}{2}) \\
S_1 &= \frac{2(1 - \cosh (\frac{c}{2})) + L^2 \sinh (\frac{c}{2})}{L^2} \\
C_0 &= \cosh (\frac{c}{2}) \quad \text{and} \quad C_2 = \frac{\sinh (\frac{c}{2})}{L^2}.
\end{aligned} \]

If the function \( \kappa(y) \) is known, the Lagrange multipliers \( (\kappa_0, \kappa_1, \kappa_2) \) are readily found from the system of linear equations (X). To find \( \kappa(y) \) we first notice that the function
\[ \tau(y) = P^+(y), \] (XI)

where \( P^+(y) = \max (0, P(y)) \) satisfies the constraint \( \tau(y) \geq 0 \). The associated \( \kappa(y) \) can be obtained by inverting (VII)
\[ \kappa(y) = (I - Q)P^-(y). \] (XII)

where \( P^-(y) = \max (0, -P(y)) \).

Next we show that such \( \kappa(y) \) satisfies the last set of conditions in (X). Define the function \( \sigma_- (y) = QP^-(y) \) which solves the boundary value problem,
\[ -\mathcal{L}\sigma_-'' + \sigma_- = P^- \geq 0, \quad \sigma_- (+1/2) = 0. \] (XIII)

Maximum principle [4] ensures that \( \sigma_- (y) \leq P^-(y) \) and thus \( \kappa(y) \geq 0 \). We can also see that \( \tau(y)\kappa(y) = -P^+(y)\sigma_- (y) = 0 \), since whenever \( P^+(y) > 0 \), the
function $\sigma$ satisfies (XIII) with zero Dirichlet boundary conditions. Thus (XI) satisfies all the required conditions.

The resulting optimal distribution of active stresses is

$$\tau(y) = (Ay^2 + By + C)\theta(Ay^2 + By + C).$$  \hfill (XIV)

Notice that this function has a singularity at a point where $Ay^2 + By + C = 0$.

Instead of expressing the constants $A, B, C$ in terms of $V$ and $\sigma_0$ and then optimizing the efficiency with respect to these two variables, in our numerical code we directly minimize efficiency with respect to $A, B$. The third constant $C$ is determined by the constraint $\int_{-1/2}^{1/2} \tau(y) dy = 1$.

As an example, consider the limiting problem with $\mathcal{H}^{**} = 0$. Suppose first that there is no sign constraint on $\tau(y)$ and denote the corresponding optimal distribution $\tilde{\tau}(y)$. Then $\kappa \equiv 0$ and the system (X) is linear which allows one to find $(\kappa_0, \kappa_1, \kappa_2)$ explicitly as functions of $\sigma_0$ and $V$. We obtain

$$\tilde{\Lambda}(V, \sigma_0) = V^2 \frac{\mu(\xi)}{\mu(\xi)} + \frac{(1 - \sigma_0)^2}{\xi^2 + 1 - \frac{\xi}{\tanh\left(\frac{\xi}{\xi}\right)}}.$$  \hfill (XV)

As all terms in (XV) are positive it is clear that,

$$\tilde{\Lambda}(V, \sigma_0) \leq \mu(\xi) = \frac{L}{2} \coth\left(\frac{L}{2}\right) - 1.$$

We now get back to the initial problem with the sign constraint. Since by definition $\Lambda \leq \tilde{\Lambda}$, we can write $\Lambda \leq \mu(\xi)$. It is easy to find a non negative function $\tau$ from the family (XIV) which saturates the bound. A simple substitution shows that for $\tau(y) = 1 + \alpha y$ with $\alpha \in [-2, 2]$ one obtains $\Lambda = \mu(\xi)$. This means that the whole one parametric family is optimal. Negative (positive) values of $\alpha$ correspond to positive (negative) velocities. Therefore, the optimal velocities range is between $\pm 2\mu(\xi)/\xi$. From this set only configurations with $\alpha = \pm 2$ can be recovered in the limit $\mathcal{H}^{**} \to 0$ from the sequence of optimal configurations with $\mathcal{H}^{**} > 0$.

2 Energetic cost of maintaining a steady state

We first specialize some standard relations of continuum thermodynamics of nonequilibrium process for our problem [2, 5]. Then we introduce the crucial definition for the ‘rate of free energy consumption’ and compute its value for our traveling wave solution.

Recall, that our finite 1D layer of reacting viscous fluid is exposed to: (i) distributed (bulk) forces $-\xi v$ due to friction and (ii) surface tractions $\sigma_0$ on the boundaries $x = -L/2, L/2$ due to the cortex. The power of these external forces can be written as

$$W = -\int_{-L/2}^{L/2} \xi v^2 dx + \sigma_0 (v(L/2) - v(-L/2))$$

$$= \int_{-L/2}^{L/2} (-\xi v^2 + \partial_x(\sigma_0)) dx = \int_{-L/2}^{L/2} (-\xi v^2 + v \partial_x \sigma + \sigma \partial_x v) dx.$$
By taking into account the force balance
\[ \partial_x \sigma = \xi v, \]
we can further rewrite \( \dot{W} \) as the power of the internal forces
\[ \dot{W} = \int_{-L/2}^{L/2} \sigma \partial_x v dx. \]

The next step is to compute the rate of change of the free energy
\[ F = \int_{-L/2}^{L/2} \hat{\rho} f dx, \]
where \( \hat{\rho} \) is the total density of the mixture which is a conserved quantity
\[ \partial_t \hat{\rho} + \partial_x (\hat{\rho} v) = 0. \]

In addition to temperature, the free energy density may depend on \( \hat{\rho} \), on the mass fraction of the motor component of the mixture \( \phi = \rho / \hat{\rho} \) and on the advancement of the hydrolysis reaction per unit of mass \( \zeta \). Due to the assumption of infinite compressibility and the presence of a thermostat, we are left with only two essential variables, so
\[ f = f(\phi, \zeta). \]

Hence we can write
\[ \dot{F} = \int_{-L/2}^{L/2} \hat{\rho} (A \dot{\zeta} + \mu \dot{\phi}) dx \]
where
\[ A(\phi, \zeta) = -\partial_\xi f \]
is the affinity of the reaction and
\[ \mu(\phi, \zeta) = \partial_\phi f \]
is the chemical potential of the motors.

Finally, we make an assumption that motors are not created in the bulk by writing
\[ \rho_0 \dot{\phi} = \partial_x J, \quad \text{(XVI)} \]
where \( J \) is the flux of motors.

For our isothermal system the rate of irreversible entropy production can be written as
\[ T \dot{S}_i = \dot{W} - \dot{F} \geq 0. \]

Since there is no fluxes on the boundaries, we obtain
\[ T \dot{S}_i = \int_{-L/2}^{L/2} (\sigma \partial_x v + \hat{\rho} \dot{\zeta} A + J \partial_x \mu) dx \geq 0. \]

The three terms in the right hand side can be interpreted as products of the thermodynamic fluxes \( \sigma, \hat{\rho} \dot{\zeta}, J \) and the conjugate thermodynamic forces \( \partial_x v, A, \partial_x \mu \).
We make a simplifying assumption that fluxes and forces are related through Onsager type relations

\[
\begin{align*}
\sigma &= l_{11} \partial_x v + l_{12} A + l_{13} \partial_x \mu \\
\dot{\rho} \dot{\zeta} &= l_{21} \partial_x v + l_{22} A + l_{23} \partial_x \mu \\
J &= l_{31} \partial_x v + l_{32} A + l_{33} \partial_x \mu
\end{align*}
\]  

(XVII)

Here the different tensorial nature of the fluxes/forces is not an issue because the anisotropy is prescribed by our 1D ansatz.

Finally, we make another simplifying assumption that the diffusion flux \( J \) depends only on \( \partial_x \mu \) which implies that \( l_{12} = -l_{21} \). Since time inversion symmetry requires that \( l_{12} = l_{21} \), we are left with four coefficients \( l_{11}, l_{22}, l_{33}, l_{12} \).

We assume that two of these coefficients describe genuinely linear dissipative mechanisms and are therefore standard: \( l_{11} = \eta \geq 0 \) is the viscosity and \( l_{33} \geq 0 \) is a mobility per unit volume. To specify the diffusion coefficient fully we first rewrite (XVI) in the form

\[
\partial_t \rho + \partial_x (\rho v) = \partial_x (l_{33} \partial_x \mu).
\]

Assuming that the acto-myosin gel is a dilute mixture we can write

\[
f = f_0(\zeta) + k_B T \phi \log \phi
\]

where \( k_B \) is the Boltzmann constant. Therefore

\[
\mu = \mu_0 + k_B T \log \phi
\]

and

\[
\partial_x \mu = k_B T \left( \frac{\partial_x \rho}{\rho} - \frac{\partial_x \dot{\rho}}{\dot{\rho}} \right).
\]

To recover a standard diffusion equation we need to make an additional assumption that the variation of the total density is small compared to the variation of the density of motors

\[
\frac{\partial_x \rho}{\rho} \gg \frac{\partial_x \dot{\rho}}{\dot{\rho}}.
\]

Then we obtain the Einstein-Smoluchowski relation

\[
D = \nu k_B T,
\]

where \( \nu = l_{33}/\rho \) is the mobility per motor. To remain in the framework of Onsager theory we need to assume that \( \rho \sim \dot{\rho} \) and \( l_{33} = l_{33}(\dot{\rho}) \); this approximation clearly fails near the singularities of \( \rho \) where the model needs to be appropriately modified.

To finalize the model we need to specify the two remaining coefficients: \( l_{12} \), which describes chemo-mechanical coupling [3] and does not contribute to entropy production and \( l_{22} \), which describes reaction kinetics and must be nonnegative to ensure positive definiteness of the dissipation. Notice that in this model we deal with an enzymatic reaction. This is a nonlinear phenomenon because the kinetics is accelerated in the presence of motors. Therefore the straightforward linear Onsager relations do not apply and we need to replace
them with quasi-linear relations by making Onsager coefficients dependent on the fields. The simplest way to take the enzymatic activity of the motors into account is to assume that

\[ l_{12} = a \rho, \quad l_{22} = b \rho, \]

where \( a, b \) are now constants. One consequence of these assumptions is the constitutive relation for stress

\[ \sigma = \eta \partial_x v + a A \rho, \]

where the first term describes classical viscosity while the second term represents the active stress due to mechano-chemical coupling. We assume that \( a \geq 0 \) which ensures that the reaction induced stresses are contractile whenever \( A > 0 \). Another consequence of our quasi-linearity assumption is the specific form of the kinetic equation for the hydrolysis reaction

\[ \partial_t (\hat{\rho} \zeta) + \partial_x (\hat{\rho} \zeta v) = \rho (b A - a \partial_x v). \]

Observe that in this model the reaction stops completely in the absence of motors \((\rho = 0)\).

If the passive system described above is left isolated, it reaches equilibrium (all fluxes vanish and the entropy production stops). To maintain the non-equilibrium state, the dissipated energy must be continuously re-injected into the system. Since the temperature reservoir is in equilibrium, the system is not exchanging mass with the environment, and no directional forces conduct external work, the only way to prevent the equilibration of the system, is to keep the driving force of the reaction \( A \) away from zero.

More specifically, this means that the corresponding ratio of the concentrations of ATP, ADP and P is kept at a fixed 'distance' from its equilibrium value through incessant breaking or assembling of the associated molecular complexes. The exact microscopic mechanism of such a continuous 'fine tuning' performed by an external 'chemostat' is not fully clear, however, in our formalism such assumption of perpetual disequilibrium is tantamount to the assumption that

\[ f_0(\zeta) = -A \zeta, \]

where \( A > 0 \) is a prescribed constant. This bottomless decrease of the energy landscape mimics the continuous rebuilding of the non-equilibrium state despite the tendency of the system to reach equilibrium (where \( A = 0 \)). The crucial assumption that \( A = \text{const} \) allows one to decouple the reaction equation from the system and compute the energetic cost of maintaining disequilibrium from the knowledge of the free energy losses per unit time that must be compensated externally.

We now make the important assumption that the cost of maintaining the non-equilibrium steady state is equal to the rate of consumptions by the system of its free energy 'reserves' (that are being continuously replenished)

\[ H = H^* + H^{**} = -\dot{F}. \]
Then, using the constitutive relations we can write

\[-\dot{F} = \int_{-L/2}^{L/2} (\rho_0 \dot{\zeta} A + J \partial_x \mu) dx\]

\[= \int_{-L/2}^{L/2} (-\chi \rho \partial_x v + b A^2 \rho + \frac{D k_B T}{\rho} (\partial_x \rho)^2) dx. \quad \text{(XVIII)}\]

If we multiply the force balance equation by \(v\) and use the boundary conditions, we obtain

\[-\chi \int_{-L/2}^{L/2} \rho \partial_x v dx = \xi \int_{-L/2}^{L/2} v^2 dx + \eta \int_{-L/2}^{L/2} (\partial_x v)^2 dx.\]

By substituting this relation into (XVIII) we finally obtain

\[-\dot{F} = \int_{-L/2}^{L/2} (\xi v^2 + \eta (\partial_x v)^2 + b A^2 \rho + \frac{D k_B T}{\rho} (\partial_x \rho)^2) dx \geq 0. \quad \text{(XIX)}\]

We can now identify the terms \(H^*\) and \(H^{**}\). The mechanical cost function

\[H^* = \xi \int_{-L/2}^{L/2} v^2 dx + \eta \int_{-L/2}^{L/2} (\partial_x v)^2 dx \geq 0\]

is a sum of contributions due to frictional and viscous dissipation. The non-mechanical part

\[H^{**} = b A^2 \int_{-L/2}^{L/2} \rho dx + D k_B T \int_{-L/2}^{L/2} (\partial_x \rho)^2 dx.\]

represents the energetic cost of maintaining the finite rate of chemical reaction and the cost of keeping a nonzero concentration gradient.

To summarize, the steady state self-propulsion in the proposed model requires: (i) work against friction which is necessary for acquiring momentum, (ii) work against viscosity which is a mechanism of long range interactions in the cell providing mechanical coordination at distant points, (iii) work against diffusion to ensure optimal distribution of motors and finally, (iv) work to keep the reaction ‘burning’ which ensures mechano-chemical generation of active forces. All these processes are dissipative and the consumed free energy needs to be compensated.

As we have seen, the steady state is maintained due to the exterior chemostat which ensures that \(A \neq 0\). If \(A = 0\), the active stress is equal to zero and the velocity vanishes so the first two terms in (XIX) contributing to the cost vanish as well. The third term obviously vanishes because it is proportional to \(A^2\). In the absence of flow, the density of motors becomes homogeneous because the destabilizing advection disappears. Therefore the fourth term is also equal to zero.

To illustrate this argument, we present in Fig. I different terms entering the expression for efficiency

\[\Lambda = \frac{P}{H^* + H^{**}}\]
Figure I: Dimensionless Stokes power $P = \mathcal{L}V^2$ and metabolic costs $\mathcal{H}^*$ and $\mathcal{H}^{**}$ as functions of $\lambda$. Parameters are $\mathcal{L} = 10$, $\mathcal{M} = 0.053$, and $\varepsilon = 0.05$.

as functions of the parameter $\lambda$ which can be viewed as a dimensionless version of $A$. One can see that at $A = 0$ all three terms are equal to zero. It is also easy to show by asymptotic expansion that right above the motility initiation threshold $A = A_c$ the mechanical energy rates ($\mathcal{H}^*$ and $P$) depend linearly on $A - A_c$ while the non-mechanical cost function $\mathcal{H}^{**} \sim A_c^2$, see the inset in Fig. 1.

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