A One-Dimensional Viscoelastic Cell Motility Model

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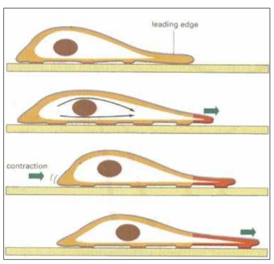
Abstract –

This project attempts to model the length, velocity, and internal stress experienced by a crawling cell as it moves on a substrate. We assume the cell's viscoelastic properties can be described by a Maxwell element. Through balance equations, we develop a Moving Boundary Problem. We solve this MBP numerically, as well as analyze its traveling wave solution. We then change our model to assume that the cell's actin concentration satisfies a second MBP and discuss our future plans for solving this new, more complicated model.

1. Introduction – Biological & Physical Background

3-Step Process of Crawling Cell Movement



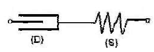
I. The leading edge protrudes and adheres to a substrate

II. The rear breaks its adhesions

III. Contraction occurs, pulling the rear forward.

Viscoelasticity – Maxwell Element

A Maxwell element is a dashpot and spring connected in series.



γ = viscoelastic stress ε = strain

E = Young's Modulus μ = viscosity constant

Stress-strain relationship of a Maxwell element:

$$\frac{\partial \varepsilon}{\partial t} = \frac{1}{E}\frac{\partial \gamma}{\partial t} + \frac{\gamma}{\mu} \quad (1)$$

1D Continuum Mechanics

Conservation of Momentum: $\rho \frac{Dv}{Dt} = \frac{\partial \sigma}{\partial x} + X$ Assume the only external force is viscous drag: $X = -\beta v$

Assume low Reynold's Number: $\frac{Dv}{Dt} = 0$ Therefore:

$$\frac{\partial \sigma}{\partial x} = \beta v \quad (2)$$

2. Model

Differential Equation

Define total stress is the sum of viscoelastic and contractile stress: $\sigma = \gamma + \tau$

u = displacement, β = drag coefficient

$$\varepsilon = u_x \qquad \varepsilon_t = \frac{1}{E}\gamma_t + \frac{\gamma}{\mu} \ (1) \qquad \sigma_x = \beta v \ (2) \qquad \text{Therefore: } \varepsilon_t = u_{xt} = \left(\frac{\sigma_x}{\beta}\right)_x$$

Model One:

$$\frac{\partial}{\partial x}\left(\frac{1}{\beta}\sigma_x\right) = \frac{1}{E}\sigma_t + \frac{\sigma - \tau}{\mu} \quad (3)$$

Boundary Conditions (4)

$r(t)$ = rear of cell, $f(t)$ = front of cell, $L(t) = f(t) - r(t)$

$$\sigma(r(t),t) = 0 \quad \sigma(f(t),t) = 0$$

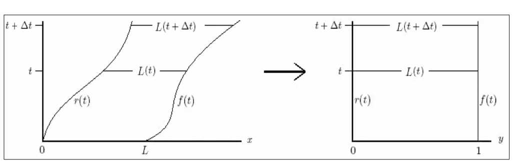
$$r_t = V_d + v(r,t) \qquad f_t = \frac{V_0 L_0}{L} + v(f,t)$$

From (2):

$$r_t = V_d + \frac{\sigma_x(r,t)}{\beta} \qquad f_t = \frac{V_0 L_0}{L} + \frac{\sigma_x(f,t)}{\beta}$$

Mapping to a Fixed Domain (5)

Let $y = \frac{x - r(t)}{L(t)}$



Moving Boundary Problem

Equation (3) and boundary conditions (4), (5) become

$$\sigma_t = \frac{E}{\beta L^2(t)}\sigma_{yy} + \left(\left(\frac{1}{\beta}\right)_y \frac{E}{L(t)} - y_t\right)\sigma_y - \frac{E}{\mu}\sigma + \frac{\tau}{\mu}$$

$$\sigma(0,t) = 0 \qquad \sigma(1,t) = 0$$

$$r_t = V_d + \left[\frac{1}{\beta L}\sigma_y\right]_{(0,t)} \qquad f_t = \left[\frac{V_0 L_0}{L} + \frac{1}{\beta L}\sigma_y\right]_{(1,t)}$$

3. Numerical Results

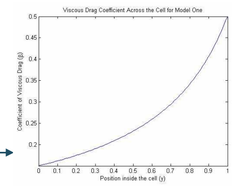
Assumptions

Elastic Modulus: $E(y) = E_o a(y)$

Contractile Stress: $\tau(y) = f_2(y) a(y)$

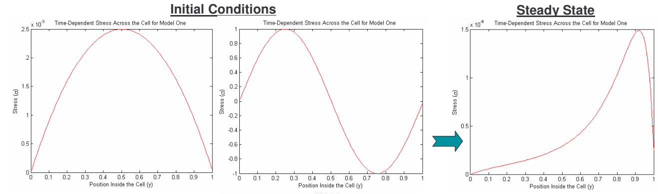
Actin Concentration: $a(y) = y$

Viscous Drag Coefficient: $\beta(y)$ = given function →

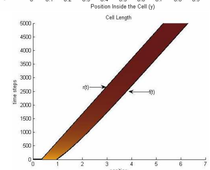


Numerical Method & Results

We use an implicit method to solve the Moving Boundary Problem (3), (4), (5)



Boundary Results



4. Traveling Wave Solutions

From the numerical results, we suspect that traveling wave solutions exist for the Model. This means there exist constants $k, L > 0$, and a function $\sigma_w(\theta)$ such that $\sigma(x,t) = \sigma_w(x - kt)$, $r(t) = kt$, $f(t) = kt + L$ satisfy the MBP.

We assume that E, β, and τ are constants.

Non-Dimensionalization

After scaling the traveling wave equation, we obtain:

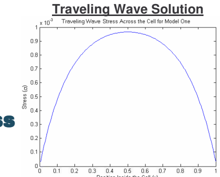
$$\begin{cases} \sigma'' = -k\sigma' + \frac{\sigma - \tau}{\mu} \\ k = V_d + \sigma'(0) \\ k = \frac{L_0}{L} + \sigma'(L) \\ \sigma(0) = \sigma(L) = 0 \end{cases}$$

We modify the implicit method from our time-dependent problem to solve the above equations.

Numerical Results

Model Constants		Results
$E = 0.21$	$\tau = 0.0010787$	$k = 0.146818 \ \mu m \cdot s^{-1}$
$\beta = 0.2588$	$\mu = 0.002$	$L = 0.518326 \ \mu m$

Traveling Wave Solution

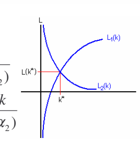


Traveling Wave: Existence & Uniqueness

There exists a solution $\sigma_w(\theta)$ to this traveling wave problem, and this solution is unique.

Proof: The problem is equivalent to showing that the graphs of the functions $L = L_1(k)$ and $L = L_2(k)$ intersect, where L_1 and L_2 are defined by the following equations:

$$\begin{cases} e^{\alpha_1 L_1} + \frac{L_0}{C_1(\alpha_1 - \alpha_2)L_1} = \frac{\alpha_2 \tau + k}{C_1(\alpha_1 - \alpha_2)} \\ e^{\alpha_2 L_2} - \frac{L_0}{C_2(\alpha_1 - \alpha_2)L_2} = \frac{-\alpha_1 \tau - k}{C_2(\alpha_1 - \alpha_2)} \end{cases}$$



5. Future Research

- Investigate the case when E is proportional to actin density.
- Prove the existence and uniqueness of traveling wave solutions for this case.
- Repeat our analysis for other viscoelastic elements (i.e. K-V, S-L, and S-S models).
- Collect laboratory data to compare the results of our model with real-life scenarios.

References

Gracheva, M.E. and Othmer, H.G., A continuum model of motility in ameboid cells, *Bull. Math. Biol.*, 66(1): 167-193, 2004.

Larippa, K. and Mogilner, A., Transport of a 1D viscoelastic actin-myosin strip of gel as a model of a crawling cell, *Physica A*, 372: 113-123, 2006.

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