# A PHYSICS INFORMED NEURAL NETWORK TO SIMULATE THE FREE BOUNDARY PROBLEM OF CELL MIGRATION

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## Introduction

Single fish keratocyte crawling in a two dimensional substrate is driven by actin polymerization forming protrusions at the leading edge and a dense actomyosin network known as lamellipodium; adhesion to substrate at the front; actomyosin retraction and finally detachment of the trailing edge. During this phenomenon, the centripetal flow of actin networks occur inside the cell powered by myosin motors. Here, a free boundary computational model has been developed considering momentum balance of actin flow, free and bound myosin dynamics, and actin dynamics. With an objective of quantitative understanding of complex dynamics during cell crawling and comparison with the experimental observations, we focus on the one dimensional "traveling-wave" solutions of the model. Later, these solutions are used to train a Physics-Informed-Neural Network (PINN) model in order to reproduce the solutions for any new one-dimensional domain with given specific boundary conditions.

## Methods

The model developed is the viscoelastic flow model used in [1] with the incorporation of free boundary conditions. The governing equations are coupled nonlinear Partial Differential Equations (PDEs) which in general are difficult to solve analytically. To understand the spatial variation of actin velocity, actin density and myosin densities, we remove the complexity of time-dependence from the model and convert the system of PDEs to a set of Ordinary Differential Equations using a "traveling-wave" ansatz as discussed in [2]. The solution from this method is used to validate the prediction obtained by training a PINN model [3]. The free boundary model of cell crawling has four PDEs which are given below. Using Newton's second law, the one-dimensional governing equation for the actin flow is of the form

$$\frac{\partial u}{\partial t} + \xi u = \frac{\partial}{\partial x}\left(2\eta \frac{\partial u}{\partial x} + \sigma m_1\right)$$

The mass conservation equation for actin network, free myosin and bound myosin are of the form

$$\frac{\partial \rho}{\partial t} + \frac{\partial(\rho u)}{\partial x} + \gamma \rho = 0;$$

$$\frac{\partial m}{\partial t} = -k_1 m_1 + k_0 m_0 - \frac{\partial(u m_1)}{\partial x};$$

$$\frac{\partial m_0}{\partial t} = k_1 m_1 - k_0 m_0 - D\frac{\partial^2 m_0}{\partial x^2}$$

and the boundary conditions are given by

$$2\eta \frac{\partial u}{\partial x} + \sigma m_1 \Big|_{A(t),B(t)} = 0; \ \rho\big|_{B(t)} = \rho_0; \ m_1\big|_{B(t)} = 0;$$

$$D\frac{\partial m_0}{\partial x} + m_0\left(V_p + u\right)\Big|_{B(t)} = 0;$$

$$D\frac{\partial m_0}{\partial x} + m_0(u)\Big|_{A(t)} = 0$$

Free boundary conditions are given through boundary velocities

$$V_{f+} = V_p + (u)\big|_{B(t)} ; \ V_{f-} = (u)\big|_{A(t)}$$

Here, A(t) and B(t) are the positions of the rear and front boundaries of the one dimensional cell, respectively. $V_p$ is the growth velocity at front, while all other variables and parameters have the same meaning as given in [1].

## Results

By training a PINN we obtain a one dimensional "traveling-wave" solution for the actin flow velocity and the densities of F-Actin and myosin. They coincide well with the experimental observations as well as with the solution which was given in [1] and computed using classical methods of numerical analysis.
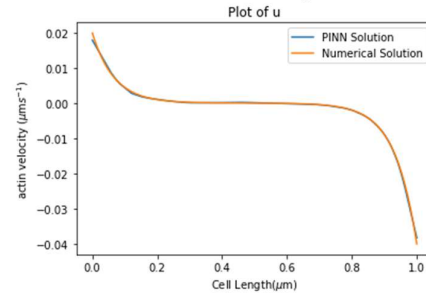


*Figure 1: Spatial variation of actin flow velocity inside the cell crawling with a constant velocity.*

## Discussion

This project serves as a proof of concept which we intend to extended to two dimensions with temporal dynamics. Our goal is to combine data and physics to develop a deep learning-based simulation framework to analyze cell migration and validate the simulation results with experimental observations.

## References

1. Rubinstein et al, Biophys J, 97(7): 1853-1863, 2009.
2. Edelstein-Keshet, Mathematical models in biology, SIAM, 436-495, 2005.
3. Raissi, et al, J Comput Phys, 378: 686-707, 2019.