A Stalk Cell Prediction Model Predicting Stalk Cell Trajectory Using Tip-Stalk Cell Interaction and Microscopy Data

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***Abstract*— We have built a 2D data-driven model to predict stalk cell migration based on tip-stalk cell interaction in angiogenesis. The unknown parameters in the model are inferred by Maximum Likelihood Estimation (MLE) from experimental time-lapse cell migration data. Numerical results suggest that the proposed model can accurately predict stalk cell trajectories.**

I. Introduction

Angiogenesis, the growth process of blood vessels from pre-existing vessels, is critical for growth and development, wound healing as well as cancer invasion. During angiogenesis, endothelial cells (ECs) specialize into tip cells and stalk cells. Tip cells sense and respond to the guidance cues, burrow into the extracellular matrix (ECM) and form conduits. Stalk cells trail behind tip cells along the conduits and form solid sprouts. Interactions between stalk cells and tip cells are important for creating functional vessels.

Mathematical models can be used to identify the key factors, to help optimize experimental design, to predict variables that are not experimentally accessible and to generate accurate quantitative predictions in the biological systems. The existing mathematical models for angiogenesis can be classified as continuous models, hybrid models and agent-based models. They typically focus on producing similar shape (sprout) as experimental observations through numerical simulation and the simulation process is complicated and time-consuming. As we expect a less complex model and we have time-lapse experimental microscopy data from our angiogenic experiments conducted in 'High Throughput' microfluidic devices (MFDs) [1], we proposed a simple data-driven model to predict stalk cell migration from known tip cell trajectories during angiogenesis.

II. Proposed Model

We consider two forces influencing the position and velocity of stalk cell in ECM: cell-cell interaction and drag force. ECs can interact with their neighbours through adhesive and repulsive forces. Cell-cell adhesion and cell-cell repulsion are inversely proportional to the distance between two cells as modelled in [2]. Drag forces is proportional to cell velocity, in the opposite direction. The unknown parameters in the model are inferred by Maximum Likelihood Estimation (MLE) based on data obtained from experimental time-lapse images. The numerical prediction results are obtained with the tuned parameters.

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III. Results and Conclusion

TABLE I. All the other models for comparison

Model Name	Force Component Eliminated
Approach I	Drag Force
Approach II	Cell-cell Adhesion
Approach III	Cell-cell Repulsion
Approach IV	Cell-cell Interaction
Approach V	Acceleration

Figure 1(a) compares the experimental and predicted stalk cell trajectory. We built some models (shown in Table 1) by eliminating each force component to find out its importance. Then we use k-fold cross validation to estimate all the predictive models performance quantitatively. Figure 1(b) indicates our proposed model is better than all the other approaches in Table 1 and all the forces in our proposed model are critical.

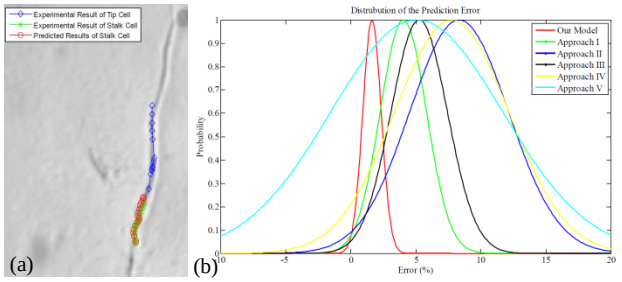

Figure 1. (a) Comparison of experimental and predicted stalk cell trajectory (b) Prediction error distribution from k-cross validation for all approaches.

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