THE INFLUENCE OF FIBER ALIGNEMENT ON CELL MIGRATION PATTERNS AND MORPHOLOGY

Jordan Moreno, Jia Gou
Department of Mathematics, Interdisciplinary Center for Quantitative Modeling in Biology
University of California, Riverside, 92521

UC RIVERSIDE Research in Science & Engineering (RISE)

STEM CONNECT

Introduction

Cell migration is a fundamental biological process present in embryonic development, wound healing, and cancer metastasis, and understanding its properties is crucial. Our research focuses on understanding how a substrate's structural organization can influence cell migration/morphology.

Past experimental observations have shown that tendon cells can align themselves with fibers in their surroundings. [2] Cells in microchanneled hydrogels can also develop aligned internal structures (F-actin stress fibers) and show increased elongation compared to cells on plain hydrogels with most cell nuclei oriented within 20° of the channel direction. [3]

Background

Our study uses computational modeling of cell migration using a motor-clutch framework, which simulates the complex interactions between a cell and its extracellular environment.

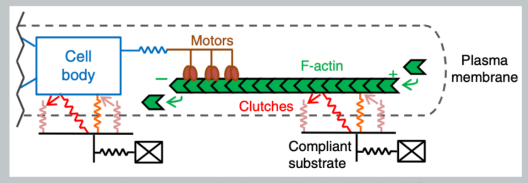


Fig. 1: Motor-Clutch Model Visualization [1]

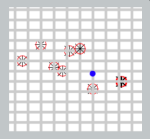


Fig. 2: Grid Fibers

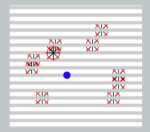


Fig. 3: Horizontal Fibers

Components of the motor-clutch model:

Motors: Generate forces within the cell
Clutches: Form connections between the cell and the extracellular matrix (ECM)
F-actin: Transmits forces from motors to clutches
Substrate: Represents the ECM with defined stiffness

The substrate was set up with two fiber alignments: one with a grid structure and one with only horizontal fibers. (Fig.2 & 3)

Results

Trajectory of the Cell on Grid vs Horizontal fibers

*Simulations ranging from 20-60 minutes with fiber spacing between 502-2564 nm and Spring constant between 15-150 pN/nm

Fig. 4: Trajectory on a Grid Fiber Layout

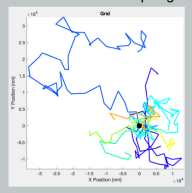
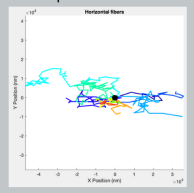


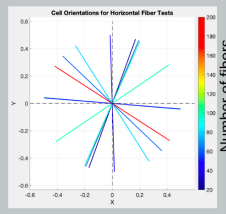
Fig. 5: Trajectory on a Horizontal Fiber Layout



Cell trajectory analysis shows longer path lengths and increased displacement in the direction of fiber alignment for the cell in a horizontal fiber layout compared to those in a grid fiber layout

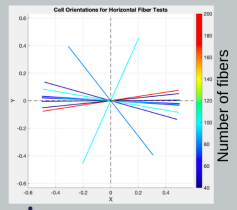
Cell Orientation on Grid vs Horizontal fibers

Fig. 6: Cell Orientations on Grid Fibers



The Grid Fiber layout yields no preference to cell orientation at the end of the simulation. There appears to be a random distribution.

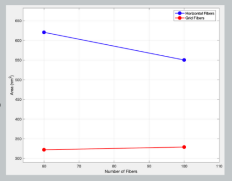
Fig. 7: Cell Orientations on Horizontal Fibers



Here we see that when cells are in a horizontally aligned fiber network, they are much more likely to orient parallel to fiber direction.

Cell Area vs Fiber Spacing

Fig. 8: Cell Area for Substrate Stiffness 25 pN/nm



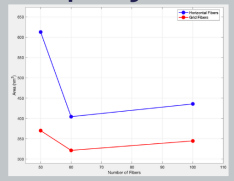
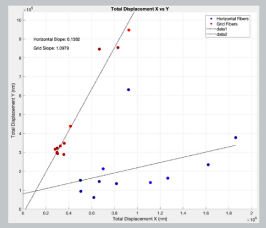


Fig. 9: Cell Area for Substrate Stiffness 50 pN/nm

Cells simulated on horizontally oriented fiber networks exhibited larger average cell areas compared to those on grid-patterned substrates, contradicting previous experimental results [2].

Conclusions

Fig. 10: Cell Displacement in X vs Y Direction.



Points with similar shading share spring constant and fiber spacing parameters.
Grid slope: 1.0979
Horizontal slope: 0.1382

The results demonstrate that the physical structure of the cellular environment significantly influences cell behavior.

-Fiber alignment correlates with displacement, trajectory, and cell orientation.
-Substrate stiffness impacts cell area inversely in this model, indicating that a recalibration to experimental data may be needed.

Future Work

-Calibrate the motor clutch model with experimental data and compare for better results.
-Develop more complex 3D models that better mimic real life conditions and incorporate multiple cell types/matrix components.
-Experiment using perturbed fiber alignment with variations in slope and average fiber density/spacing to study its impact on cell migration.
-Modify the model to have fibers change/react to the forces from cell migration and study how cell fiber interactions affects cell migration.

References

1 - Bangasser, B. L., Shamsan, G. A., Chan, C. E., Opoku, K. N., Tüzel, E., Schlichtmann, B. W., Kasim, J. A., Fuller, B. J., McCullough, B. R., Rosenfeld, S. S., & Odde, D. J. (2017). Shifting the optimal stiffness for cell migration. Nature Communications, 8, 15313.
2 - Hiraki HL, Matera DL, Rose MJ, Kent RN, Todd CW, Stout ME, Wank AE, Schiavone MC, DePalma SJ, Zarouk AA and Baker BM (2021) Magnetic Alignment of Electrospun Fiber Segments Within a Hydrogel Composite Guides Cell Spreading and Migration Phenotype Switching. Front. Bioeng. Biotechnol. 9:679165. doi: 10.3389/fbioe.2021.679165
3 - Ajay Tijore et al 2018 Biofabrication 10 025003
4 - Chan, C. E., & Odde, D. J. (2008). Traction dynamics of filopodia on compliant substrates. Science, 322(5908), 1687-1691.

Acknowledgements
UCR RISE, CNAS, STEM Connect, Noel Salunga, Liz Jimenez, Alexis Acosta, Dr. Virginia White, Luis Molina