Modeling Tissue Changes During Limb Regeneration

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Abstract

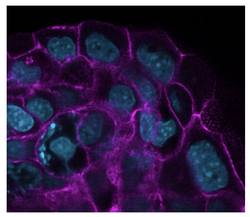
Humans cannot **regenerate limbs,** while animals such as **axolotl salamanders** can regenerate completely functional limbs. In this project, we use computational modeling in **Morpheus** to study how epithelial cells organize during the early stages of limb regeneration. By testing different cell properties, including shape, adhesion, and movement, we compare simulated tissues with biological observations and scientific literature. We also use studies focused on the Wnt signaling pathway to better understand how this pathway regulates regeneration. This work contributes to building a **computational model** that can be used to study the **cellular mechanisms involved in limb regeneration**. As high school researchers, our personal objective is to gain hands-on research experience and develop skills that will prepare us for future studies in science and medicine.

Background

- **Humans have limited regenerative abilities**, while axolotls can regenerate entire limbs.
- **Studying axolotl regeneration** helps scientists better understand tissue repair mechanisms.
- **Findings may contribute** to future advances in regenerative medicine.
- **Traditional laboratory experiments** are essential but can be time-consuming and expensive.
- **Computational modeling** provides a faster and more flexible way to study regeneration.
- **Models can simulate tissue growth & organization**, test different conditions, and predict outcomes.
- **These predictions** can help guide and improve future laboratory experiments.

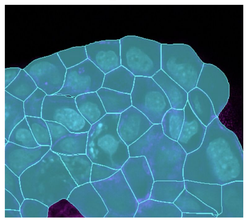
Experimental & Computational Methods

1. Microscopy



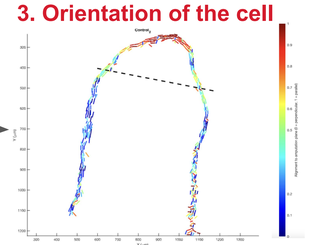
Blue: DAPI (nuclei - DNA)
Magenta: Membrane marker

2. Cell Segmentation



Software was used to segment cells and analyze their organization.

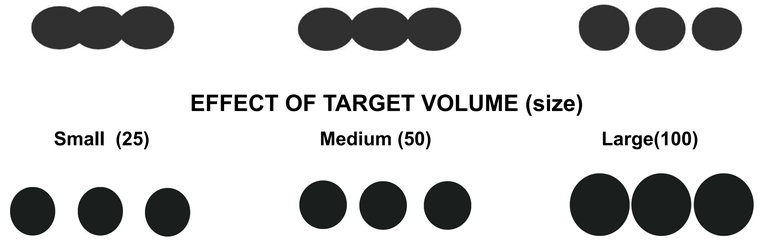
3. Orientation of the cell



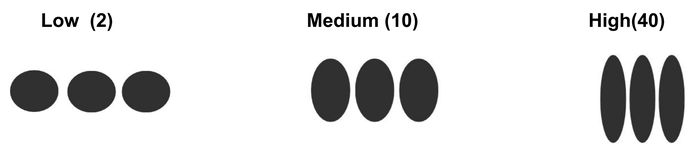
1 is parallel to amputation plane and 0 is perpendicular to amputation plane

EFFECT OF CONTACT ENERGY

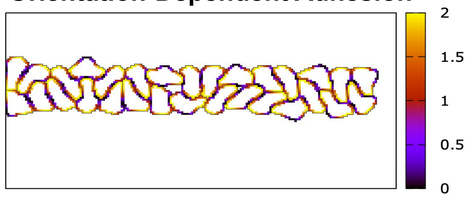
EFFECT OF TARGET VOLUME (size)



EFFECT OF CELL SHAPE CONSTRAINT (length constraint)



Orientation-Dependent Adhesion

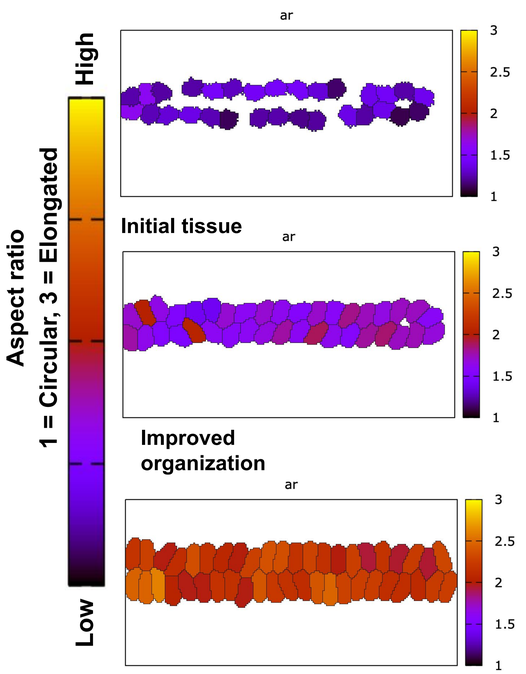


Adhesion varies around the cell membrane according to cell orientation, allowing the model to simulate directional interactions between neighboring cells.

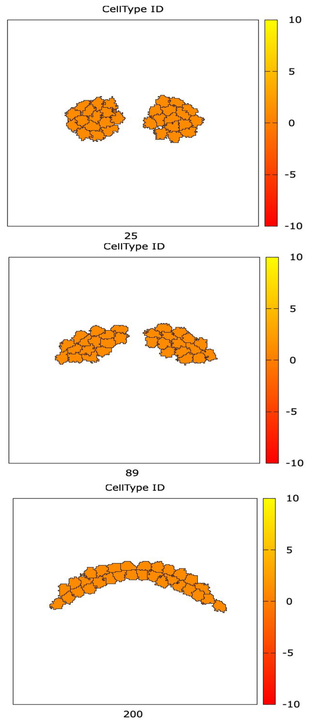
Morpheus was used for the computational modeling

Results

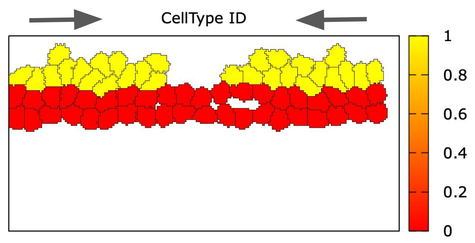
Tissue organisation



Wound closure



Combined



Cell migration during wound healing. Cells from both sides move toward the center in response to a chemical signal (chemotaxis), demonstrating the early stages of wound closure.

Conclusion and Future Steps

By adjusting cell shape, adhesion, and movement parameters, we produced more organized epithelial tissues that better resembled biological observations. These results demonstrate that computational modeling can complement laboratory experiments by providing a flexible way to investigate how individual cellular behaviors contribute to tissue regeneration. This model serves as a foundation for future studies incorporating additional biological mechanisms, including Wnt pathway, to better understand the regenerative process.

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