Modeling Dorsal Closure

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Introduction

- During Drosophila morphogenesis, dorsal closure occurs, when an eye-shaped opening on the surface of the embryo (the amnioserosa) reduces in area by the joining of two flanks of epidermal tissue.
- A model of dorsal closure offers insights in understanding wound healing and the mechanism of morphogenesis[1].
- Force-producing biological elements (sarcomeres) drive the closure.
- The understanding of various phenomena e.g. oscillation of the amnioserosa cells observed on the onset of dorsal closure plays a major role in understanding the phenomenon.

Biology

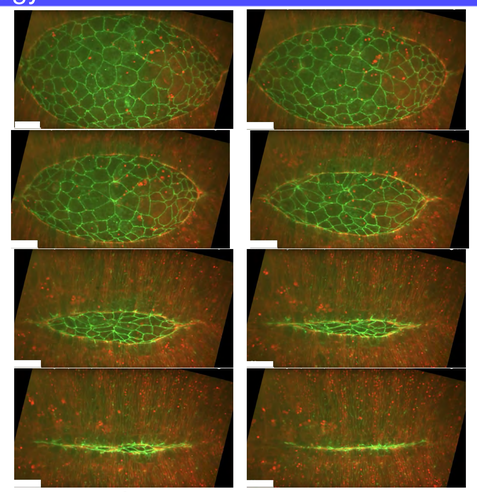

Figure 1: The figure[4] shows a real amnioserosa undergoing dorsal closure. The process takes approximately 2.5- 3 hours.

Early Phase (approx. 0-50 minutes)

- Zero net area contraction[2]
- Cell oscillations

Slow Phase (approx. 50-130 minutes)

- Internal ratcheting - rest length of each edge decreases after each period of oscillations
- External ratcheting - actin cable forms along leading edge of epidermis with decreasing rest length
- Zippering - a zipping mechanism has been considered to act along the dorsal midline at the canthi
- Oscillations are significantly damped

Fast Phase (approx. 130-180 minutes)

- Amnioserosa area contraction accelerates

Research Goals

- Analyze the dynamics of the biological system through the use of mathematical modeling
- Test different model equations and geometric structures and compare results with experimental data
- Implement tests similar to ones done in experiments
- Study mechanisms of dorsal closure that are not easily analyzed in the lab or produce simulation results that may drive new experiments

Geometry

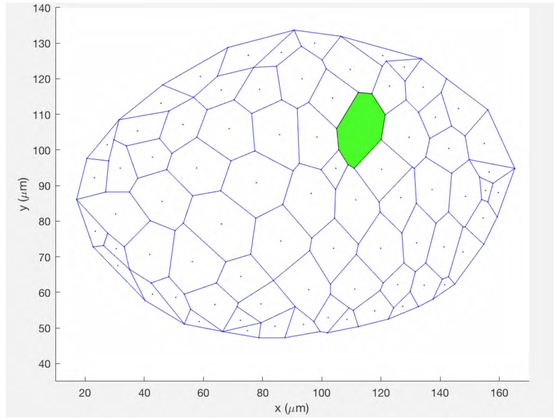

Figure 2: The figure shows a representation of an amnioserosa. The data for the plot was found using image processing on a real amnioserosa.

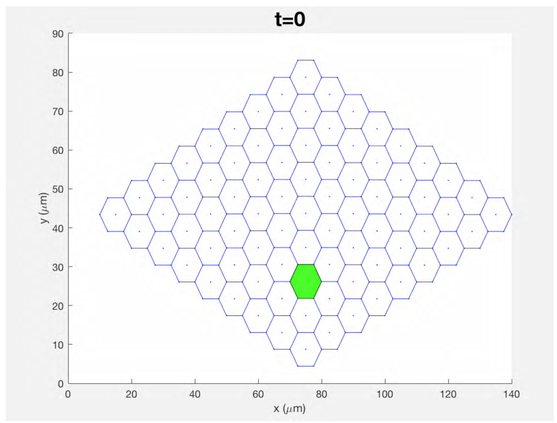

Figure 3: The figure shows a simplified representation of an amnioserosa as a network of 81 regular hexagonal cells. With this geometry, we can more easily predict outcomes to test and validate our model. Once we are confident that we have implemented the equations correctly, we will test on a more realistic geometry.

Implementation

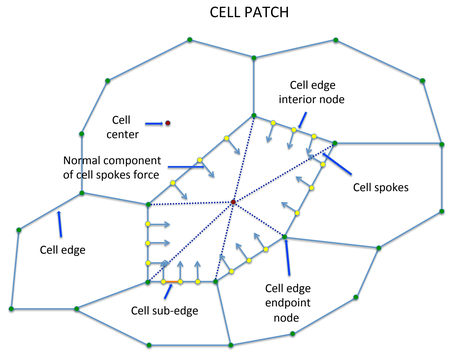

Figure 4: The figure shows the various geometric structures relevant to the implementation of the model.

Equations

- $\boldsymbol{f_{i,j} = \mu(\ell_{i,j} - \ell_{0i,j}) + \beta m_{i,j}}$ (edge force)
- $\eta \frac{d\vec{x}_i}{dt} = \vec{f}_i$ (Newton's 2nd Law approximation)
- $\vec{f}_i = \sum_j f_{ij} \frac{\vec{x}_j - \vec{x}_i}{|\vec{x}_j - \vec{x}_i|}$ (node force)
- $\frac{df_{ij}}{dt} = \frac{1}{\eta}\left(\frac{\beta(p_0 - f_{ij})}{f_{ij} + a} + \frac{dl}{dt}\right)$ (edge force as differential equation)
- $\frac{dm_{k,j}}{dt} = k^+ s_k h_{kj} - k^- m_{k,j}$ (myosin concentration per edge)
- $k^- = k_1 e^{-k_2[\mu(\ell_{k,j} - \ell_{0k,j}) + \beta m_{k,j}]}$ (arrhenius form)
- $\frac{ds_k}{dt} = q - k_0 M_k$ (signaling)
- $M_k = \sum_j m_{k,j}$ (myosin concentration in a cell)

Results

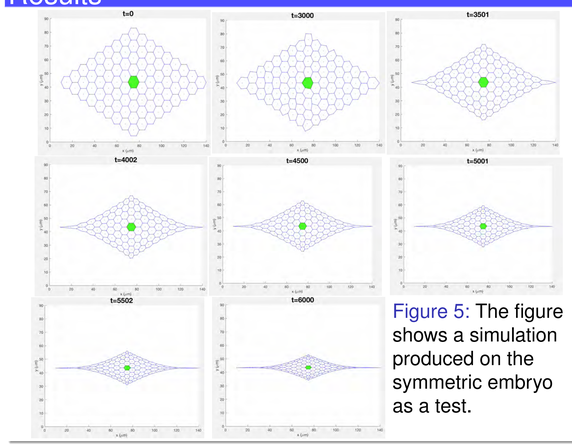

Figure 5: The figure shows a simulation produced on the symmetric embryo as a test.

Results

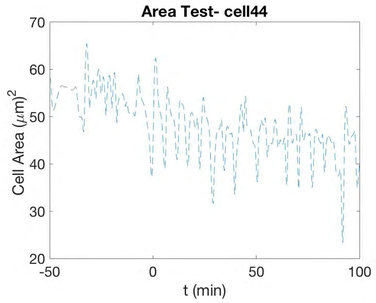

Figure 6: The figure shows a plot of the area of cell 44 over time. The oscillations are a key component in the early phase and continue after in the slow phase, since we only introduce external ratcheting.

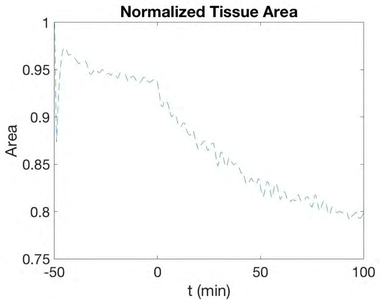

Figure 7: The figure shows a plot of the normalized tissue area vs time, again with external ratcheting only. The tissue area decreases much faster with the application of internal ratcheting.

Ongoing Work

- Incorporate internal ratcheting mechanism
- Testing on realistic embryo
- Incorporate the purse string
- Study cross-correlation of area oscillations between neighboring cells
- Perturbations

References

1. Anita T. Layton, Yusuke Toyama, Guo-Qiang Yang, Glenn S. Edwards, Daniel P. Kiehart, and Stephanos Venakides, *Drosophila morphogenesis: tissue force laws and the modeling of dorsal closure*, HFSP J. 3 (2009), 441–460.
2. Qiming Wang, James J. Feng, Len M. Pismen,*A Cell-Level Biomechanical Model of Drosophila Dorsal Closure*, Biophysical J. 103 (2012), 2265–2274.
3. Kai Dierkes, Angughali Sumi, Jerome Solon, and Guillaume Salbreux, *Spontaneous Oscillations of Elastic Contractile Materials Turnover*, Physical Review Letters. 113 (2014), 148102: 1-5.
4. cellvideoabstracts, Dorsal Closure during Drosophilia Development, "https://www.youtube.com/watch?v=332x-GxEAS0", 2015.