Investigations of Tissue Growth

Project Description

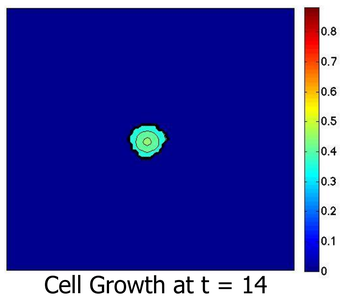
- To investigate mechanisms that control cell growth - action of the morphogen gradient, mechanical stress and equilibrium, examination of positional values
- To research background studies with respect to cell growth in Drosophila:
  - Lecuit and Brook (1996) concluded that cell growth was independent of a cells' positional value, but dependent on Dpp concentration [2]
  - Day and Lawrence (2000) concluded cell growth was directly proportional to the length of the Dpp "strip" in the wing imaginal disc, creating a morphogen gradient [3]
  - Hufnagel and Teleman (2006) concluded that the length of the Dpp strip was independent of wing imaginal disc size, that cell growth was regulated by mechanical stress within the tissue, driven by the morphogen gradient [1]
- To simulate the tissue growth model proposed by Hufnagel and Teleman [1]

Scientific Challenges

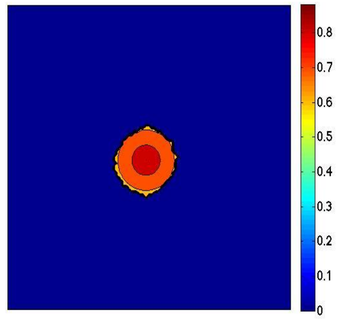
- Creating a realistic model for cell growth and development that accurately considers all of the complexities of the physical phenomena involved.

Potential Applications

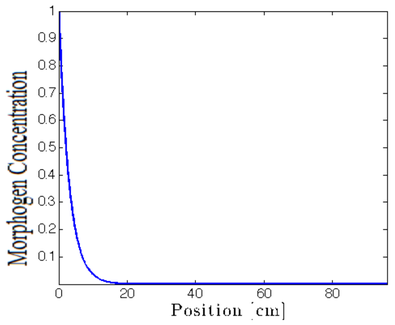
- Understanding cell and tissue growth mechanisms is beneficial towards further understanding of diseases caused by inadequacies in or excesses of cell growth and division

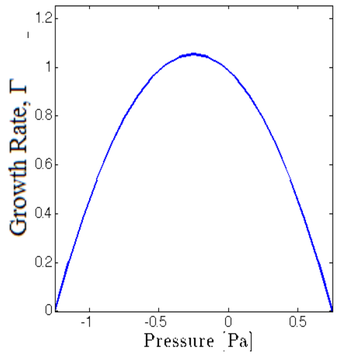


Cell Growth at t = 14



Cell Growth at t = 184





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Methodology (Tissue Growth Model coded in MATLAB)

1.) First Modeling Consideration: cell geometry is generalized as square in shape rather than hexagonal

2.) Second Modeling Consideration: maximum time for tissue growth is set to 200 time units

3.) Third Modeling Consideration: tissue perimeter (to calculate area) is modeled by a "bounding box"

4.) Fourth Modeling Consideration: cell growth is dependent on morphogen concentration and pressure

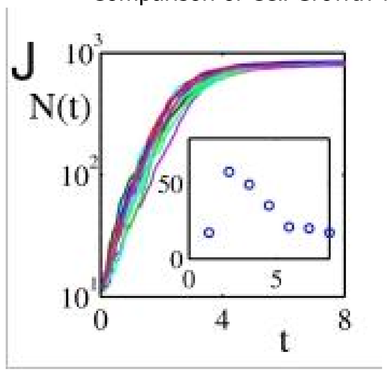
- Morphogen concentration behaves as an exponential decay
- Local pressure is linearly proportional to its distance from the center
- Pressure dependent growth rate is a quadratic
- Pressure values and morphogen concentration must fall within given threshold values for cell growth to occur

5.) Fifth Modeling Consideration: cell proliferation modeled by cells occupying the nearest empty grid position

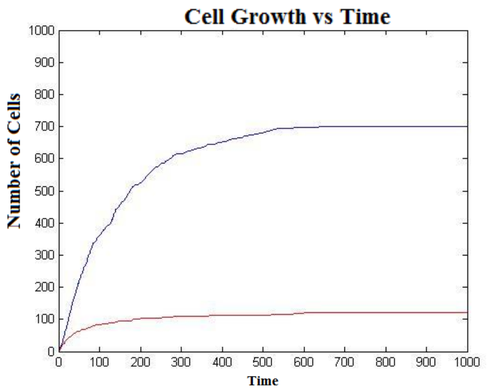
Results

Our simulation results are qualitatively similar to Hufnagel's findings.

Comparison of Cell Growth vs Time



Hufnagel simulation

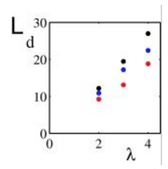


Our simulation

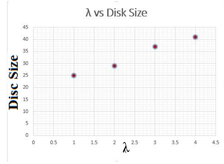
Glossary of Technical Terms

Morphogen: type of signaling molecule that acts on cells to solicit a certain response (concentration dependent)
Positional Values: a cells' spatial coordinates (dependent on cell division and rearrangement permutation)
Drosophila: a genus of small flies, also known as "fruit flies"
Dpp: decapentaplegic, a specific morphogen responsible for cell growth in the wing imaginal disc
Imaginal Disc: biological development structure within insects
Morphogen Gradient: concentration gradient that subdivides a field of cells by inducing gene expressions at specific thresholds

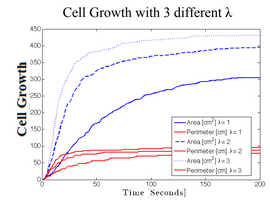
Disc size as a function of growth parameters



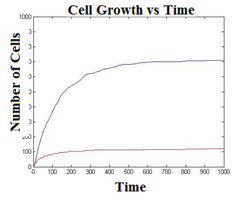
Hufnagel simulation



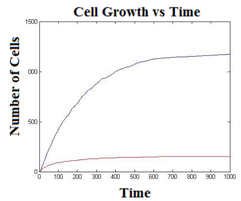
Our simulation



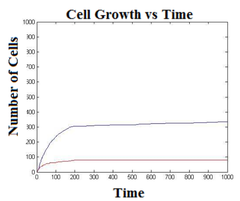
Additional Analysis: Pressure Sensitivity Graphs



Benchmark group



Insensitive group



Sensitive group

Findings: the more sensitive the cells are to pressure, the smaller the final disc size will be.

References

1. Hufnagel L, Teleman A, On the Mechanism of Wing Size Determination in Fly Development, PNAS Volume 104, 3835-3840 (2006).
2. Lecuit T, Brook WJ, Nature Volume 381, 387-393 (1996)
3. Day SJ, Lawrence PA, Development Volume 127, 2977-2987 (2000).

Acknowledgments

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