Chemoattractant Distribution in a Heterogeneous Tissue and its Impact on Cell Migration

UMBC REU Site: Interdisciplinary Program in High Performance Computing

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Objective

Cell migration is critical to processes as varied as embryo development, wound healing, and cancer metastasis. In this project, we mathematically modeled and computationally simulated cell migration in the egg chamber of a fruit fly. We improved and added features to an existing model[1] in order to give a more faithful representation of experimental results.

Background

Cell Cluster Migration[2]:
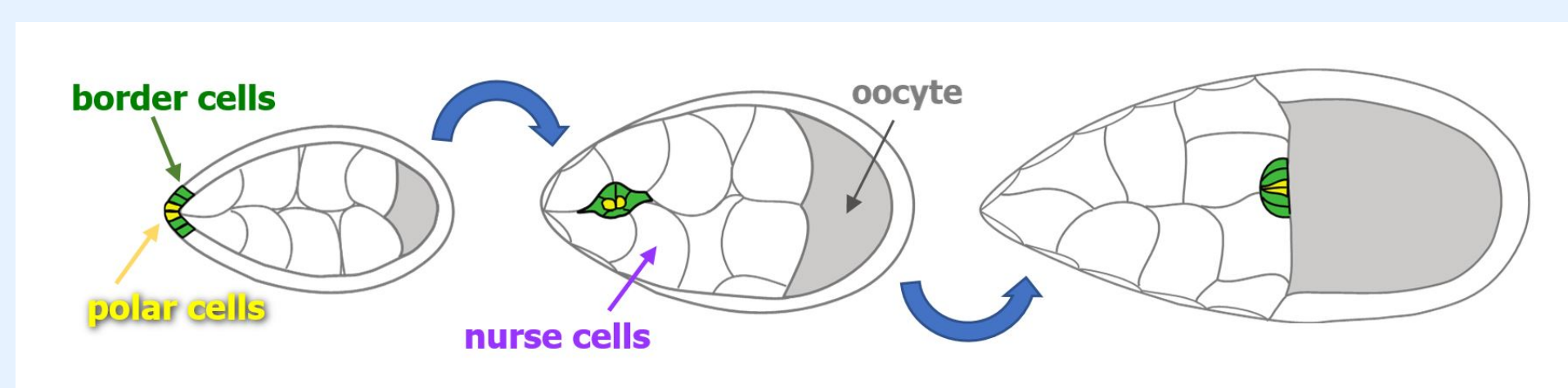
- Chemoattractants diffuse through the entire egg chamber.

- A cluster of border and polar cells responds to the chemoattractant and migrates towards the oocyte, around larger nurse cells.

- Once at the oocyte, the cluster migrates up as part of the process of fertilization.

Conclusions

- After 5hrs, the magnitude of the gradient at the oocyte is 10^9 pM times that at the apical end, so it likely does not linearly affect the migratory force.

- Secreting chemoattractant from epithelium cells causes off-center cluster migration.

- The force coefficient parameters were updated to maintain realistic migration timing after changing the migratory interactions.

Diffusion Model

The diffusion of the chemoattractant's concentration (u) through space (x, y, z), with diffusion (D) and uptake (k) constants. We use the finite element method in MATLAB to solve this equation:

$$\frac{\partial u}{\partial t} = D\left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2}\right) - ku$$
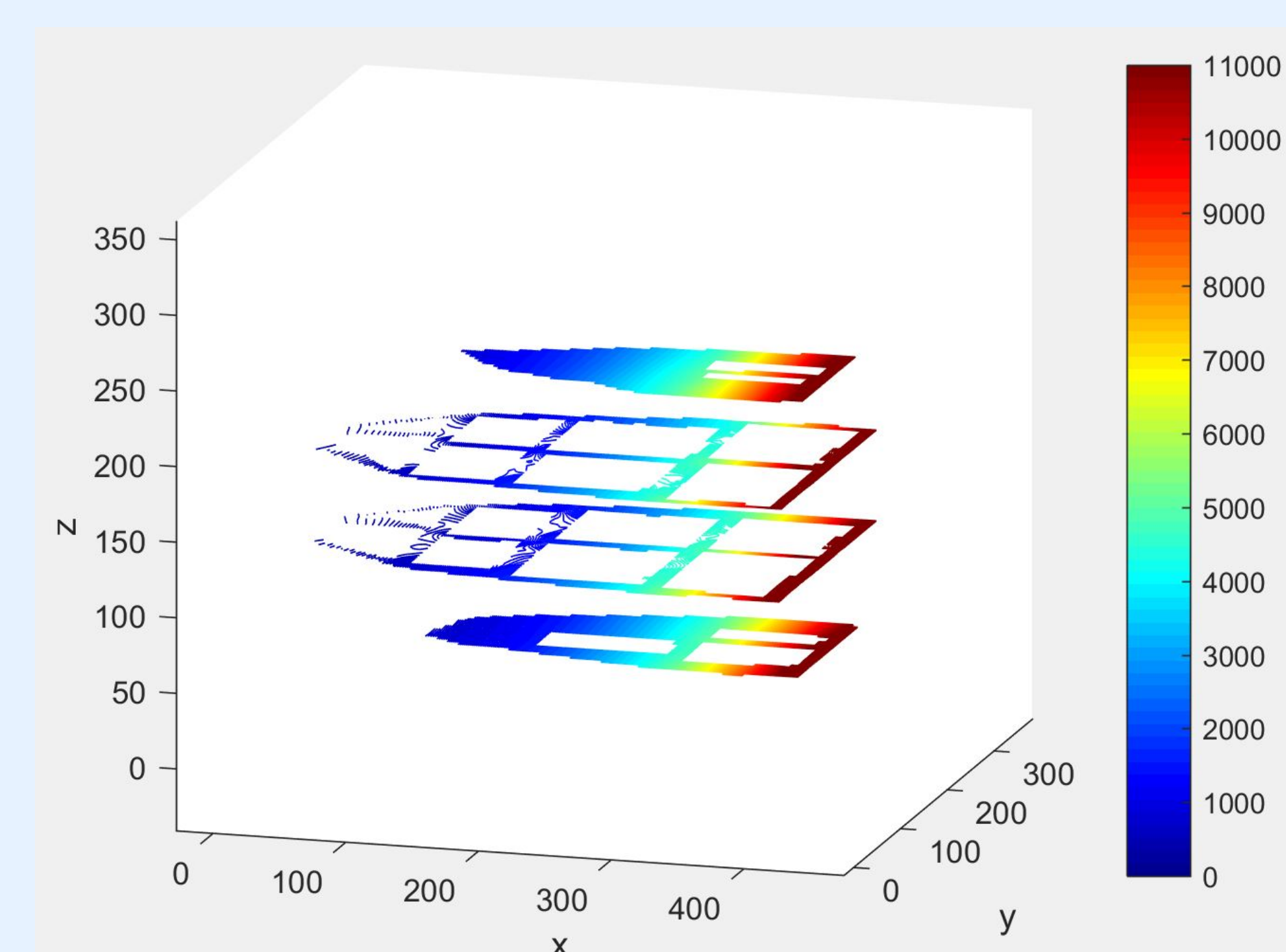
Boundary conditions: constant flux from oocyte, uptake at nurse cells, no-flux elsewhere

Diffusion Results

Secretion of chemoattractant from surface of oocyte; scale: μm, concentration: pM.
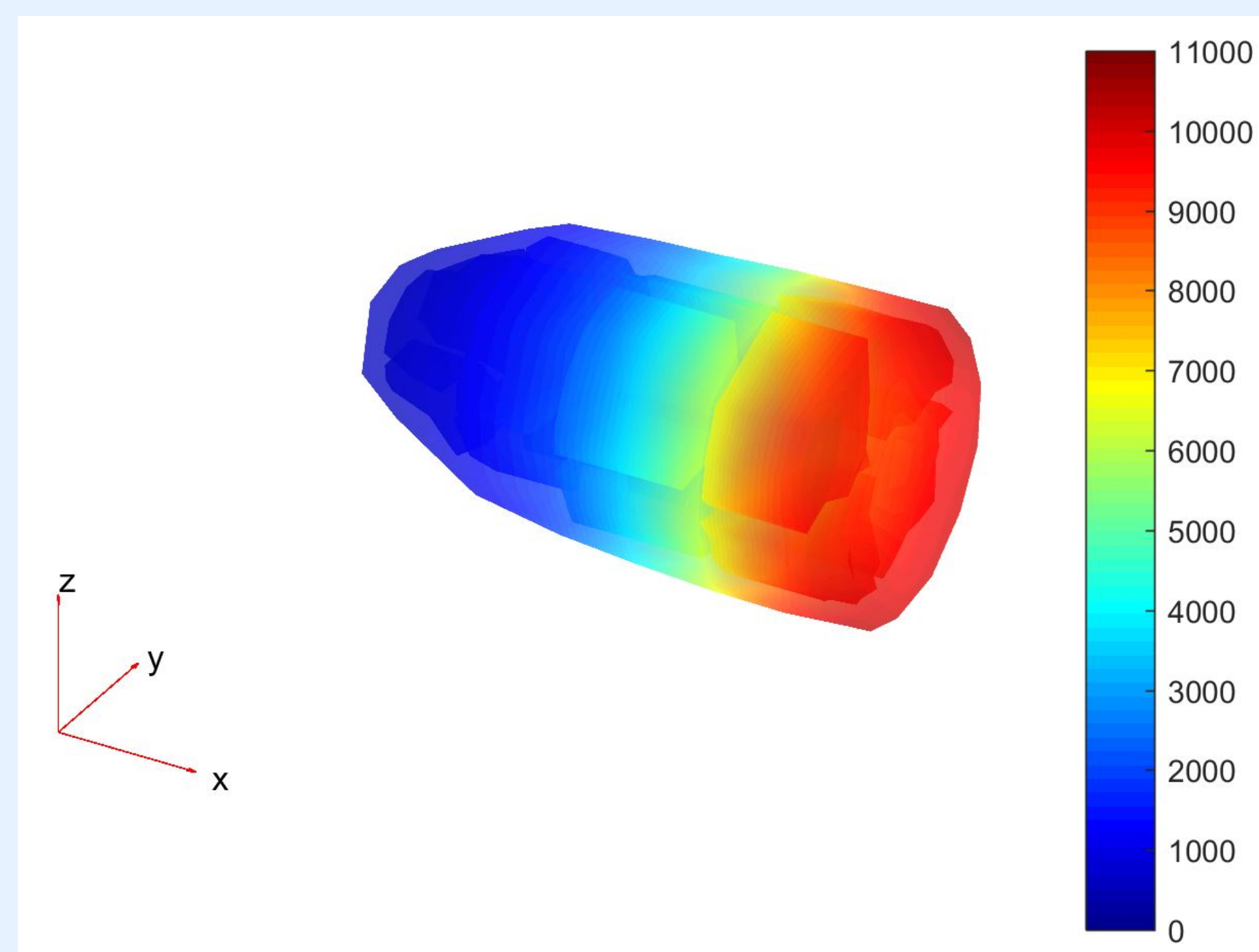
Concentration of chemoattractant on surface of egg chamber
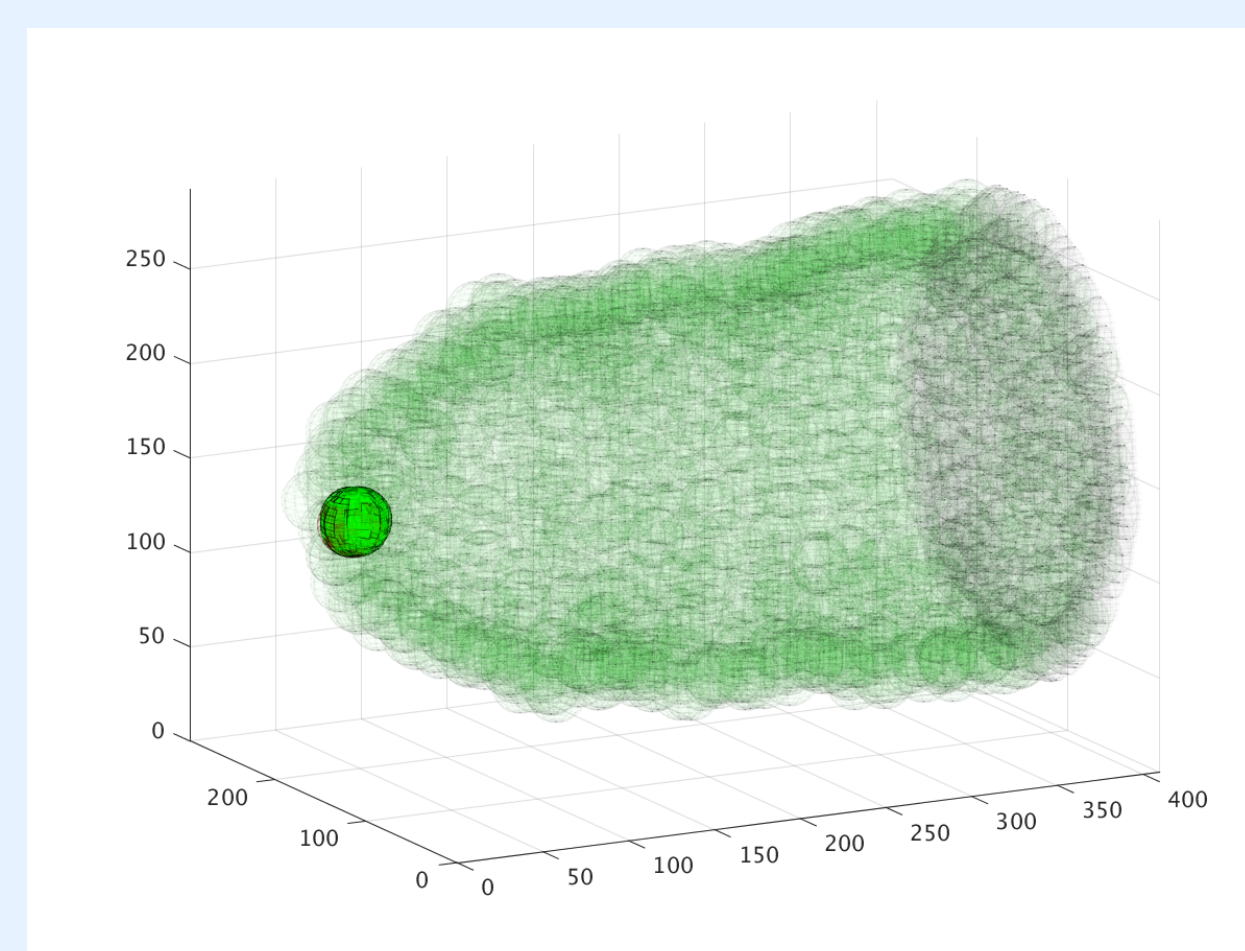

Extracellular concentration in egg chamber, white spaces show no diffusion through nurse cells
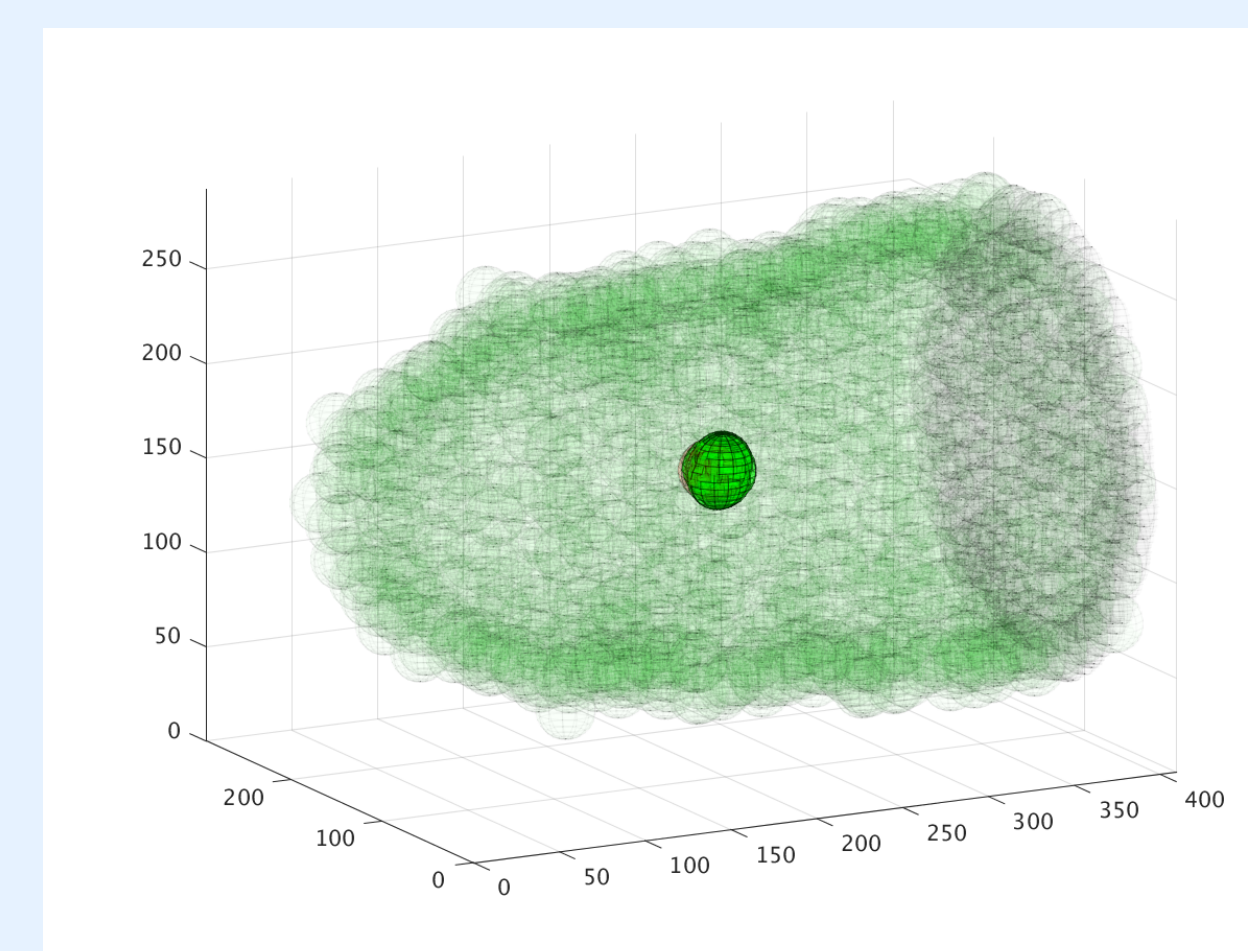
Migration Results

We simulated the cluster's six-hour migration across the egg chamber using repulsive, adhesive, migratory, and stochastic forces; scale: μm
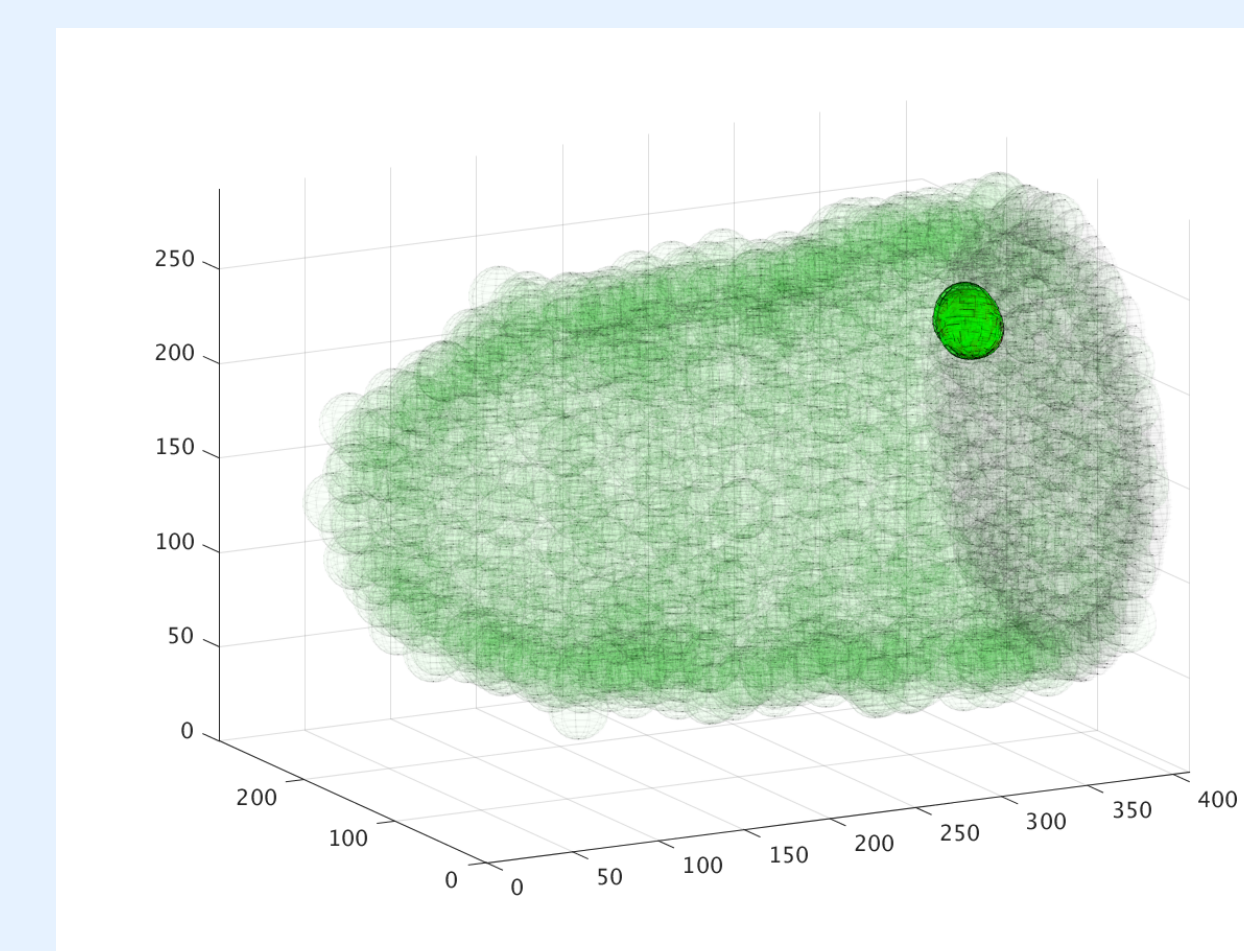
22.5 minutes

3 hours

6 hours

References

[1] Stonko et al. 2015, PLoS ONE

[2] Montell, Yoon, Starz-Gaiano. 2012

[3] Full technical report: HPCF–2017–13 hpcf.umbc.edu > Publications

Acknowledgments