Mathematical modelling of cell aggregation under the impact of a chemotactic signal

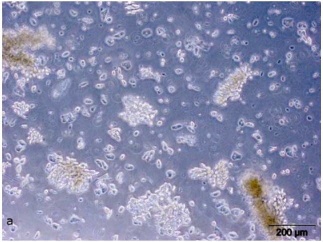
Angela Xu

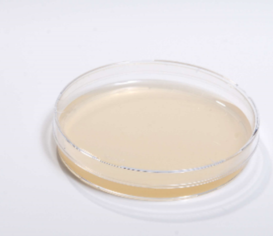
Supervisor: Anotida Madzvamuse

2024.7.10

Definitions

- **Chemotaxis**: Directed movement of cells in response to chemical stimuli.
  Chemical stimuli can either attract or expel cells.
- **Cell Aggregation**: Binding of cells of the same type.
  Cells attract and stick to each other to form clusters.
  Mechanism for tissue formation.

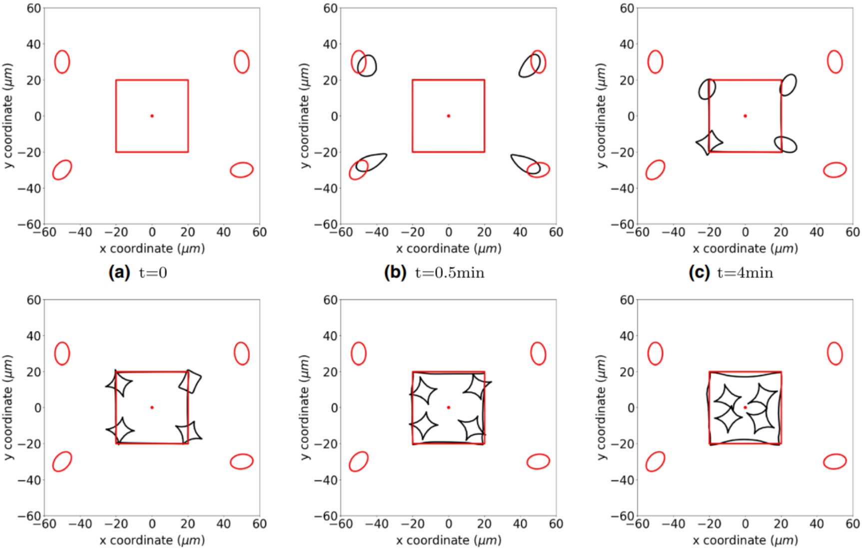




Motivation

- Peng et al.(2021)'s work on chemotaxis and cell differentiation.
- Use elasticity to control the extent of cell membrane deformation.
- Consider repulsive force between cells only.
- We want to provide a better mechanism for cell membrane deformation and include cell aggregation.

Motivation


y coordinate (μm)
x coordinate (μm)
60
40
20
0
−20
−40
−60
(a) t=0
(b) t=0.5min
(c) t=4min

Model

Mechanisms of Displacement:

1. Chemotaxis
2. Random Walk
3. Repulsion from Domain Boundary
4. Surface Tension
5. Area Constraint
6. Lennard-Jones Potential Force

Chemotaxis

Distribution of Point Source:

$$\delta(x) = 0,\ \forall x \in \mathbb{R}^2,\ x \neq \mathbf{0}$$

$$\int_\Omega \delta(x) = 1,\ \textit{if}\ \mathbf{0} \in \Omega$$

Concentration of Chemoattractant:

$$\frac{\partial c(x,t)}{\partial t} - D\nabla^2 c(x,t) = k\delta(x(t) - x_s), x \in \Omega$$

- $c(x,t)$: Concentration of chemoattractant
- D : Diffusion rate of the chemoattractant
- k : Secretion rate of point source
- Displacement of cells depends on $\nabla c(x,t)$ and weight of chemotaxis.

Random Walk, Repulsion from Domain Boundary

Random Walk Displacement:

$$dx = \sigma_{rw} dW(t) dt$$

- σ_{rw} : Weight of random walk
- $dW(t)$: Vector-Wiener process

Repulsion from Domain Boundary:

$$dx = \epsilon_r e^{\frac{1}{d}} n_{cb} \, dt$$

- d : Distance between cell membrane and domain boundary
- ϵ_r : Weight of repulsion
- n_{cb} : Inward unit normal vector of the cell membrane

Surface Tension, Area Constraint

$$dx = \alpha H \, dt$$

- α : Weight of surface tension
- $H = -\Delta_\tau x$: Mean curvature, solved with surface gradient of the cell membrane.

$$dx = -\lambda \, n_{cb} dt$$

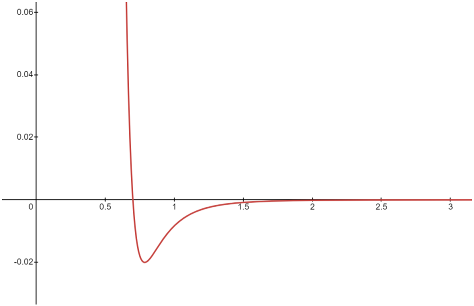
$$\frac{d\lambda}{dt} = \frac{\beta_1 \lambda (A - A_0 + \frac{dA}{dt})}{A_0(\lambda + \beta_1)} - \beta_2 \lambda$$

- λ : Lagrange multiplier that represents a uniform force over the cell membrane.

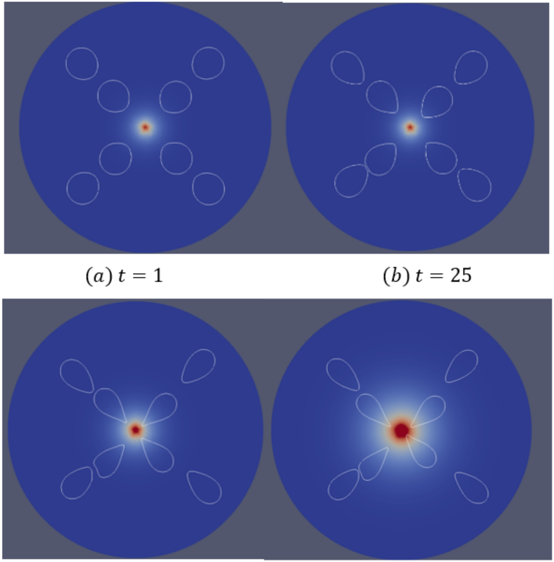
Lennard-Jones Potential Force

$$dx = 4\,\epsilon_{lj}\left(\left(\frac{\sigma}{d}\right)^{12} - \left(\frac{\sigma}{d}\right)^{6}\right)\,dt$$

- Inspired by similarity to intermolecular interaction.
- d : Distance between cell membrane.
- σ : Cutoff distance which attraction force switch to repulsion
- ϵ_{lj} : Weight of Lennard-Jones potential



Results



$(a)\ t = 1$ $(b)\ t = 25$ $(c)\ t = 50$ $(d)\ t = 75$

Future Steps

- Introduce bending energy of the cell membrane.
- Make the model more stable.
- Statistical Analysis of the variables.
- Consider different chemotaxis mechanism.
- Chemorepellent instead of Chemoattractant.

References I

[1] Q. Peng, F. J. Vermolen, and D. Weihs. "A formalism for modelling traction forces and cell shape evolution during cell migration in various biomedical processes". en. In: *Biomechanics and Modeling in Mechanobiology* 20.4 (Aug. 2021), pp. 1459–1475.

[2] Qiyao Peng, Fred J. Vermolen, and Daphne Weihs. "Physical confinement and cell proximity increase cell migration rates and invasiveness: A mathematical model of cancer cell invasion through flexible channels". en. In: *Journal of the Mechanical Behavior of Biomedical Materials* 142 (June 2023), p. 105843.

[3] Alžbeta Bohiniková, Iveta Jančigová, Ivan Cimrák, et al. "Sensitivity Analysis of Adhesion in Computational Model of Elastic Doublet". en. In: *Bioinformatics and Biomedical Engineering*. Ed. by Ignacio Rojas, Olga Valenzuela, Fernando Rojas, et al. Vol. 13347. Cham: Springer International Publishing, 2022, pp. 220–233.

[4] Charles M. Elliott, Björn Stinner, and Chandrasekhar Venkataraman. "Modelling cell motility and chemotaxis with evolving surface finite elements". en. In: *Journal of The Royal Society Interface* 9.76 (Nov. 2012), pp. 3027–3044.

References II

Pictures: Evelyn Sun. (May 2023). MICB 211 Canvas Slides.

https://www.researchgate.net/figure/
Typical-epithelial-cell-cluster-after-one-week-in-culture-a-Many-cl
fig2_260915571