A Computational Model of Chemotaxis-based Cell Aggregation

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**Theoretical Model**

- Each cell emits symmetrically within the radius of influence \( R_{\text{MAX}} \). The chemical amount decays from \( C_0 \) to \( C_0/\text{cutoff} \) according to 1/r, where \( r \) is the distance from cell surface.

\[
F(r) = \begin{cases} \frac{1}{r} & r < r_{\text{cutoff}} \\ \frac{C_0}{C_0/\text{cutoff}} & r \geq r_{\text{cutoff}} \end{cases}
\]

- Single cells move in the direction of the detected gradient. The velocity of a moving cell is proportional to the magnitude of the gradient.
- All cells in an aggregate move according to the average gradient calculated for the aggregate. Velocity is divided by the mass of the aggregate in this case.
- When two cells that are not in the same aggregate touch each other they form a single aggregate.
- A cell can divide and create two daughter cells. New cells enter an inactive period where they shut down all receptors/emiters and only move randomly. If a cell remains unattached after 18 hours, it enters a dying process. It begins to shut down its receptors/emiters and eventually dies before hour 24. The probability of dying increases over the time between hours 18-24.

**Motivation & Technical Goals**

- Explore and characterize, via simulation, the biological properties and processes that affect chemotaxis-based cell aggregation.
- Provide important knowledge for tissue engineering
  - Cell-cell aggregation reflects "fundamental" biological processes occurring during tissue assembly in vivo
  - Modeling cell aggregates and their assembly/differentiation into functional tissues has implications for the mechanistic understanding of "in vitro embryology"
  - Once processes are understood, we can direct them to control and optimize cell aggregation for tissue engineering
- Define an accurate computational model that consists of the "essential" components of chemotaxis-based cell aggregation
- Determine appropriate simplifications and approximations
- Develop efficient and effective algorithms within a robust, extensible simulation environment
- Utilize model/environment to computationally investigate cell aggregation behavior

**Cell Model**

Each cell is defined by a collection of parameters and actions.

- Number and the position of CTX receptors on the cell surface
- Location of the cell
- Age
- Life cycle stage
- Chemoattractant emission rate
- Diffusion radius \( (R_{\text{MAX}}) \)
- Proliferation rate
- Number of attached cells

- Emission and sensing of chemoattractors
- Gradient following & Brownian motion
- Proliferation
- Collisions and adhesion
- Aging and cell death

**Parametric Studies**

- Perform simulations over a range of parameter values and gather statistics
- Proliferation & apoptosis rates
- Chemoattractant diffusion rate
- Upregulation factors
- Cell velocity
- Attachment/detachment probabilities

- Earth Mover's Distance (EMD) is used to compare two size distributions

The initial results of our simulations demonstrate that our model is capable of producing cell aggregation distributions similar to those found in live cell experiments.