Modeling the Role of Collective Cell Migration in Wound Healing

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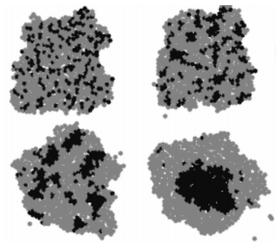
The Big Question

Can we use a simple self-propelled particle model for collective cell migration during wound healing? What can this model tell us about how cells move during this process?

Why Use a Simple Model?

We use a simple interacting self-propelled particle model with few parameters to model the system. This mitigates redundancy in curve fitting with experimental data and still allows for the observation of complex and interesting behavior.



4 time steps of self-propelled particle model used to sort cells. [1]

Building the Model

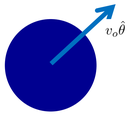
Parameters

- Initial velocity $\boldsymbol{v_0}$
- $\boldsymbol{D_r}$, the angular diffusion coefficient

Differential Equations

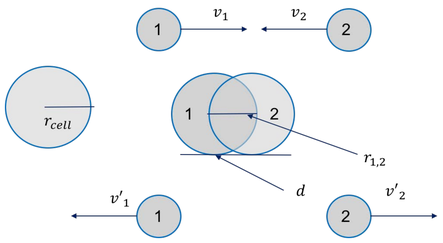
- $\frac{dr_i}{dt} = v_i\theta_i + \sum_{j=1,j\neq i}^{N} \overrightarrow{F_{i,j}}$
- $\frac{d\theta_i}{dt} = \eta_i\,(t)$
- $\theta_{i_{n+1}} = \theta_{i_n} + \sqrt{\Delta t D_r}(randn)$

Polar Self-Propelled Particle



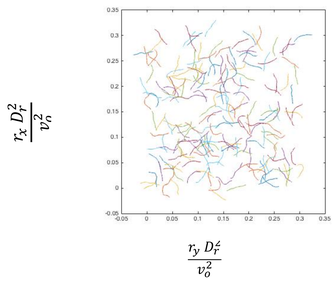
'Springy' Interactions

- $F_{1,2} = k\overrightarrow{r_{i,j}}$
  - $\overrightarrow{r_{i,j}} = (2r_{cell} - d)\hat{r}$
  - No force if $d > 2r_{cell}$

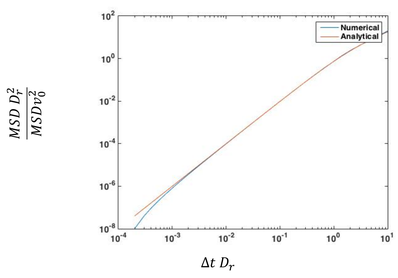


Non-Interacting Model

200 SPP Trajectories, v=0.1, D_r=.1
4000 Iterations



MSD for SPP Model, v=0.1, D_r=.1
10000 Iterations



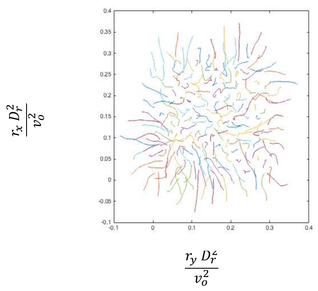
The trajectories for this model show persistent walks as expected. The mean-squared displacement shows us the MSD averaged over all 200 particles. We can see the transition from ballistic to diffusive behavior through a slope change fro m=2 to m=1. The transition happens at $\tau = \frac{1}{D_r}$, underscoring the impact of the noise term on persistence of motion. My particle fits the theoretical model:

$$MSD = 2v_0\tau[\Delta t - \tau(1 - e^{-\frac{\Delta t}{\tau}})]$$

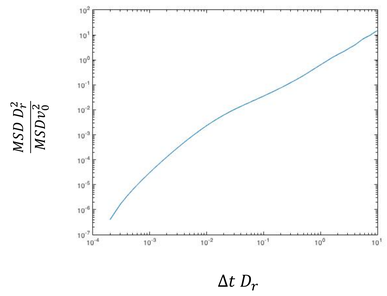
Meaning that my computational method is functioning properly.

With Interactions

200 Interacting SPP Trajectories
v=0.1, D_r=0.01 4000 Iterations

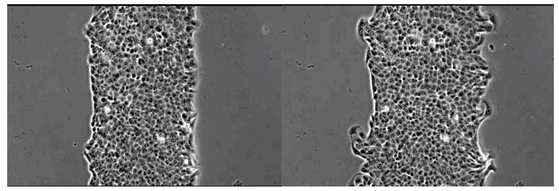


MSD for Interacting SPP Model
v=0.1, D_r=0.01 , 10000 Iterations



The above trajectories demonstrate that interacting particles cannot pass through each other as they can without interactions. There is no theoretical method to predict what an MSD graph will look like for an interacting system, but this plot shows a less steep initial slope as particles can inhibit each other's motion, but the particles will move more because the forces increase the particles' displacement at each time step.

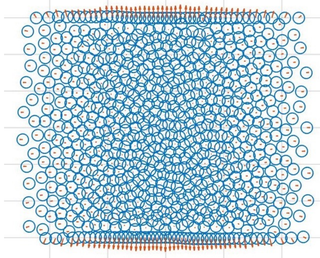
Wound Healing Strip Geometry



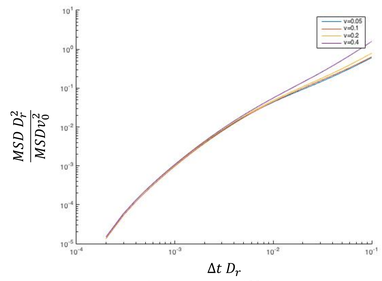
In this in vitro experiment, cells were confined in a stencil as a thin strip and then allowed to move into the empty space in order to study the role of cell confinement and motility and avoid contributions made by inflammation, for example

My Model

I packed particles into a square box due to probabilistic considerations, with a 1:1 ratio of the area of the box to the area taken up by cells. I also implemented boundary conditions that prevented cells from moving past the lower and upper vertical bounds so that they spread out horizontally.

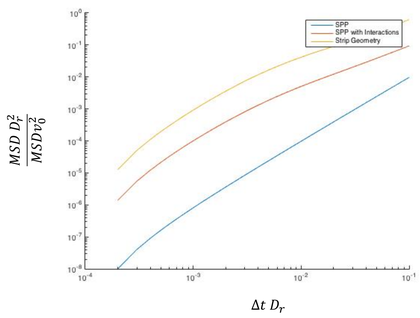


We can see some ridges like the cell strip in the experiment, but more quantitative analysis is needed. The red arrows show the magnitude and direction of the forces.



Increasing v_0 will increase MSD as time increases.

Comparing the Models at v=0.1, D_r=0.01



The MSD for the wound healing geometry is the largest perhaps because boundaries exert additional forces, increasing the MSD. The boundary conditions may be artificially changing the numerical result, these results suggest that confinement may play a role in MSD results.

Literature Cited

[1] Julio M Belmonte et al. Self-propelled particle model for cell-sorting phenomena". In: Physical Review Letters 100.24 (2008), p. 248702
[2] Xavier Serra-Picamal et al. Mechanical waves during tissue expansion". In: Nature Physics 8.8 (2012), pp. 628-634.

Acknowledgements

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