# Mathematical Models of Cancer Cell Migration Including Cell to Cell Adhesion

Stuart Johnston
Queensland University of Technology
Supervisor: Dr Matthew Simpson

Cancer is the one of the leading causes of death in Australia, according to the National Institute of Health[1], and for a disease that has such a high mortality rate there is a lot more information that needs to be discovered about it. Throughout the course of my project I have been examining how cancer cells invade the body, with a particular focus on cancer cells that exhibit adhesive forces on other cells.

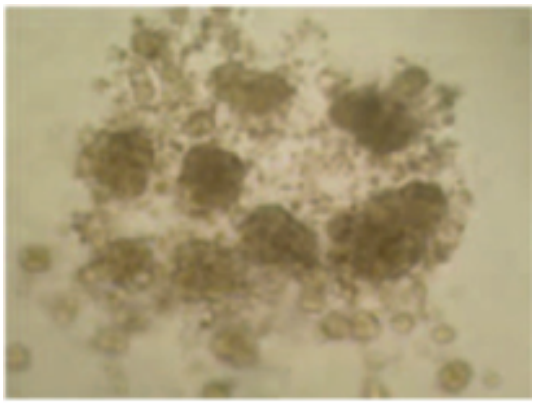

*Figure 1a: Ovarian Cancer Cells[2]*

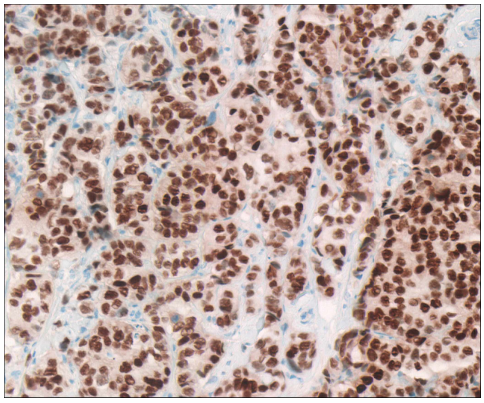

*Figure 1b: Breast Cancer Cells[3]*

The picture above of the ovarian cancer cells (Figure 1a) demonstrate pronounced clusters that form due to the adhesive properties of those cells, which the picture of the breast cancer cells (Figure 1b) shows a less obvious cluster. We are more interested in modeling the cells like the ovarian cancer cells that show higher amounts of adhesion.

To be able to model the cancer cells migrating and invading throughout the body, we used a square based lattice. Each lattice site could either be occupied or not occupied by a cell, and if a cell attempted to move into a site that was already occupied, that movement would be aborted. As each lattice site is occupied by at most one cell, this forms an exclusion process.

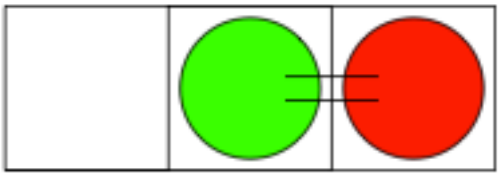

*Figure 2: An example of two cells exerting an adhesive force on each other*

In order to incorporate adhesion into our discrete lattice based model we introduce an adhesion term, σ, which modifies the probability of movement. Our value for adhesion, σ, must have an absolute value of less than one, with negative σ implying a

repulsive force and with positive σ being an adhesive force. In Figure 2, a higher value of σ would reduce the probability of the green cell jumping away from the red cell. We then used this method of describing probabilities of cells either jumping away from or occupying the same space to create a large-scale discrete simulation.

Following the discrete simulation, we were interested in creating a partial differential equation (PDE) that would replicate the data obtained in the simulation. To make this PDE we started with a conservation equation–that mass would be conserved throughout our equation as cells can move both in and out of a lattice site. We multiplied the probabilities of sites being occupied and not occupied and took the Taylor Series expansion of these terms. These equations were then simplified, and continuum limits were taken to bring them into a non-linear diffusion equation with a diffusion coefficient of

$$D(C) = 1 - \sigma C(4 - 3C)$$

We note that if σ is zero, we retain a linear diffusion equation which is an expected result based on previous work and alternate derivations.

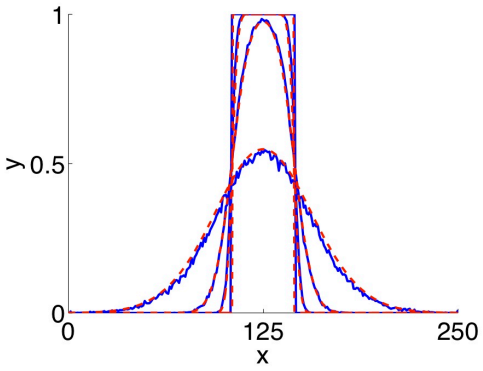


*Figure 3a: σ = 0.2*

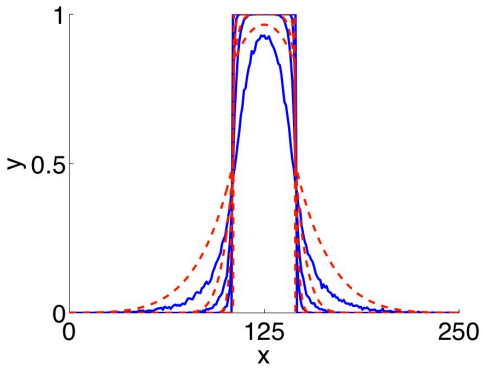


*Figure 3b: σ = 0.8*

In the above graphs, we plot both the simulation data and the numerical solution to the PDE. The numerical solution was obtained in MATLAB via the use of finite discretization and a Picard iteration to take account for the nonlinearity. The left-hand picture (Figure 3a) is for a low amount of adhesion, σ = 0.2, and the solution to the PDE matches up with our simulation data. However, when we include a large amount of adhesion, σ = 0.8, the solution to our PDE deviates away from our model data, as you can see in Figure 3b. When various values of positive σ were examined, it was found that the PDE matched the model sufficiently well for σ up to 0.6.

After thinking about the discrepancies for large values of σ, it became obvious why our PDE breaks down. When we create our PDE by multiplying probabilities together we are assuming that these probabilities are independent, which is obviously not the case. This can be fixed by introducing correlation functions[4] – equations that can be solved in order to be able to relax the probability assumption. I will be examining the use of these functions in my future work, along with other models of adhesion.

I greatly enjoyed my experience with research over the summer, and have found it to be very rewarding. I would like to thank AMSI, CSIRO and my supervisor Dr Matthew Simpson for this opportunity to explore new ideas.

**Bibliography:**


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*Postal Address:* Building 161
c/- The University of Melbourne
Victoria 3010 Australia

Email: enquiries@amsi.org.au
Phone: +61 3 8344 1777
Fax: +61 3 8344 6324
Web: www.amsi.org.au