Review of the paper:

Mathematical modelling of cancer cell invasion of tissue: Local and non-local models and the effect of adhesion

(by A. Gerisch, M.A.J. Chaplain)

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Motivation
(and previous work done)

- Cancer spread depends on a multitude of factors such as type of cancer (e.g. after a mutation)
- Invasion rate facilitated by enzymes that destroy the surrounding tissue
- Previous papers (such as by Anderson et al. (2000)) have modelled the migration of cancer cells by haptotaxis
- Armstrong et al. (2006) has introduced cell motility by inclusion of non-local terms
- Authors choose non-motile ECM population (**only** changes due to degradation by enzymes) and a cancer population driven by adhesive effects
- Researchers of this paper take the (so-called local) model and modify it and compare it to a non-local model with more parameters (adhesion interactions between cells and cells and the matrix)
- Look at how rate of migration is affected via numerical simulations

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- Use the following notation for the PDEs:
  * $c(t,x)$ - the cancer cell density
  * $v(t,x)$ - extra-cellular matrix density
  * $m(t,x)$ - matrix-degrading enzyme density
- After non-dimensionalizing the equations (for both models) we have the following systems:
- Some changes to the local model: the $(1-c-v)$ terms ensures no overcrowding (**volume filling term**)
- Note the similarities and differences: main change is the flux for the cancer density equation $\chi_{12}(1-c-v)$ replaced by $\mathscr{A}$ and in the left model we have slightly different expressions to previous papers (underlined in orange)

Models

The local and non-local models

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$$\frac{\partial v}{\partial t} = -\gamma m v + \mu_2(1-c-v), \quad (2b)$$

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Model parameters

The functions $g(u)$ and $\Omega(r)$

- In the non-local model, $\mathscr{A}$ (adhesion velocity) is an integral of a sum of a product between a function $g(u)$ and $\Omega(r)$ defined as:

$$\mathscr{A}\{\underline{u}(t,\cdot)\}(\underline{x}) := \frac{1}{R}\int_0^R \sum_{k=0}^{1} \underline{\eta}(k)\cdot\Omega(r)g(\underline{u}(t,\underline{x}+r\,\underline{\eta}(k)))\,\mathrm{d}r,$$

  where $\eta(k) = (-1)^k$

- The $g(u)$ equation is defined as

  where S_{cc} and S_{cv} are adhesion parameters

- The second bracket $(.)^+$ ensures that densely packet areas do not influence in direction of invasion (to avoid aggregation)

- Two types of Ω:
  - Ω_1: all points in sensing disk have equal share in direction of movements
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Numerical Results

Travelling wave cluster

- Researchers show results for the two coefficients (non-local model)
- Also switch on MDE degradation term to avoid build-up of the enzyme concentration ($\mu_2 > 0$)
- Choose Ω_2 (more realistic), $R = 0.1$ (larger R leads to slower invasion) and $S_{cv} = S_{cc} = 0.1$ (same value):
- True detachment of cells travelling in wave-like manner along matrix edge
- Also have a population around $x = 0$

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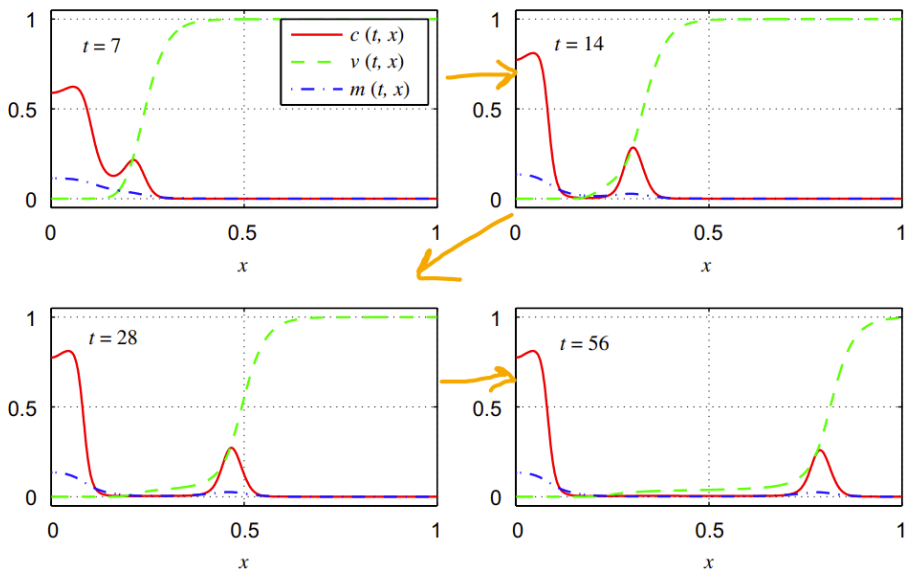

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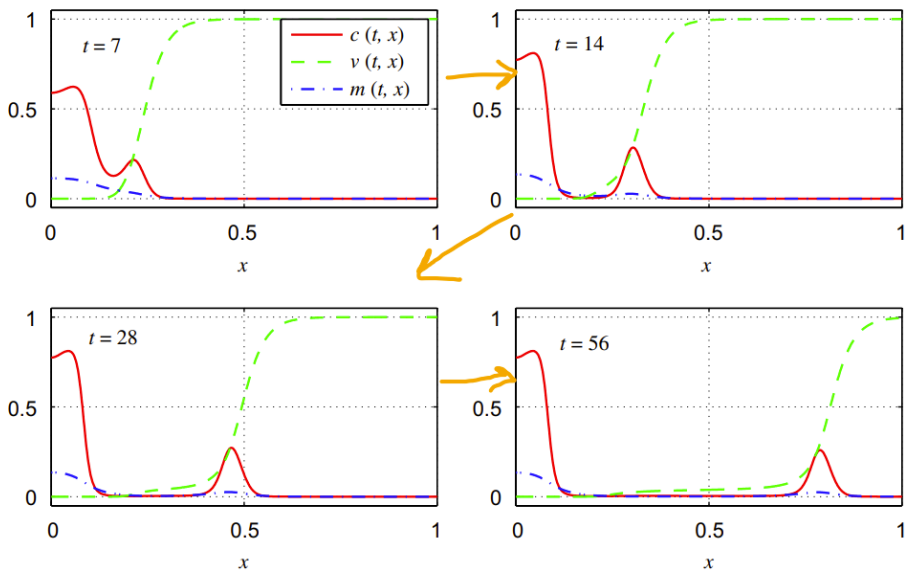

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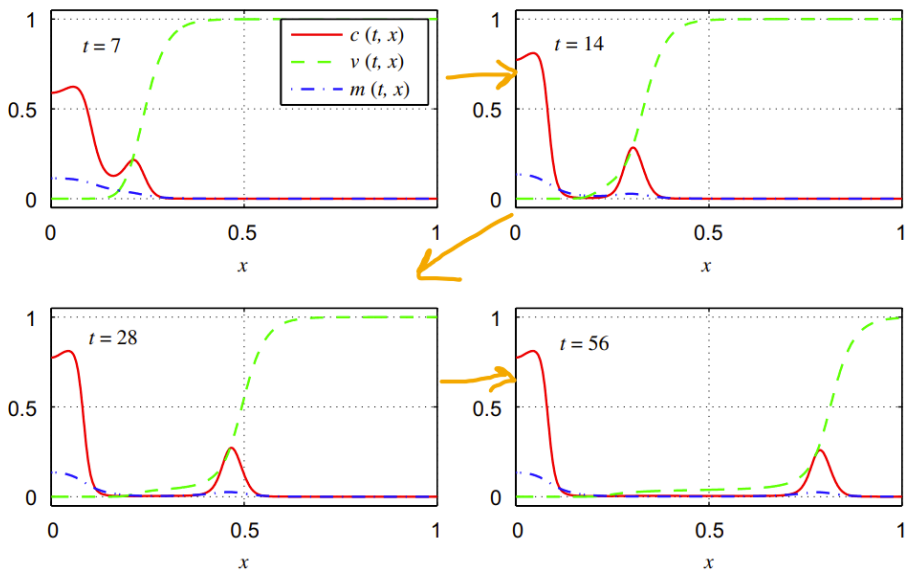

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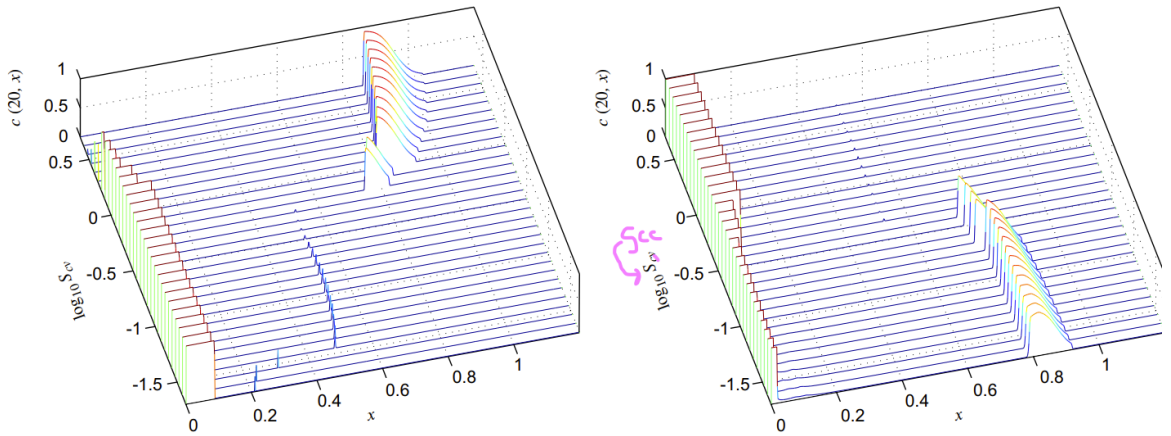
One parameter fixed, one varied

- Paper now fixes one of the parameters to 0.5 and varies the other on [0.02, 0.5]



- The left plot has $S_{cc} = 0.5$ and varies the other, and we observe:
  - for $S_{cv} < 0.5$ most of the tumour cells remain at $x = 0$ with few migrating
  - for $S_{cv} = 0.5$ all at centre ($x = 0$)
  - for $S_{cv} > 0.5$ gives rise to only migrating cells

- The right plot has $S_{cv} = 0.5$ and varies the other, and we observe:
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- Summary: If $S_{cv} > S_{cc}$ we have an invasive tumour. If $S_{cv} < S_{cc}$ the tumour is compact (see plot)

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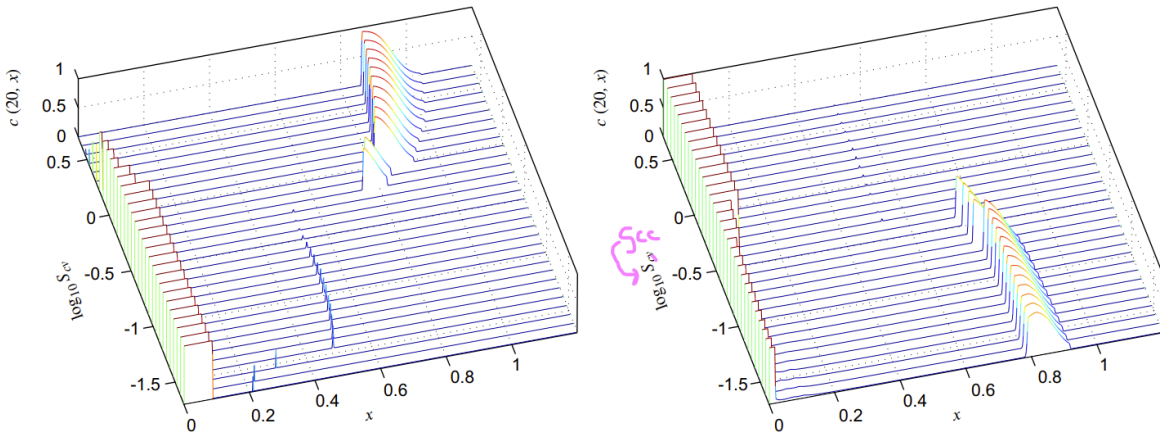

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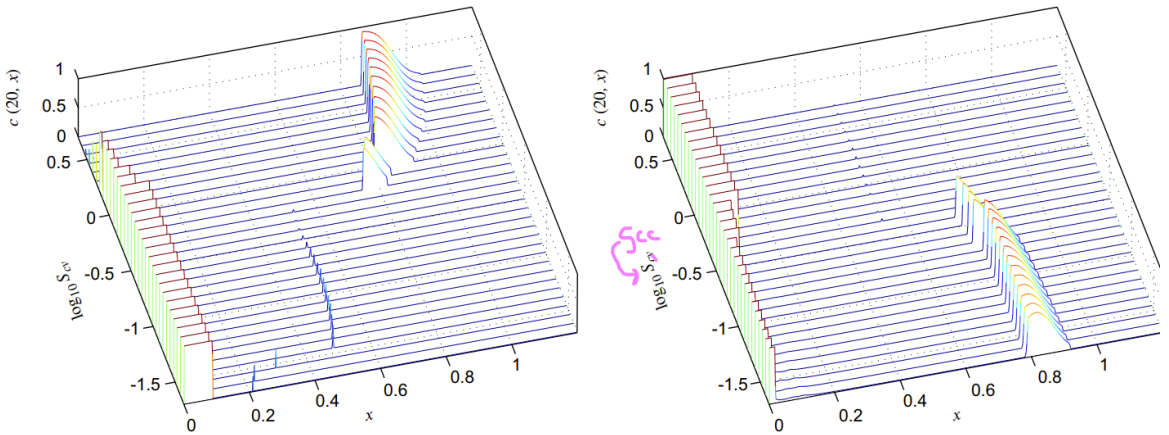

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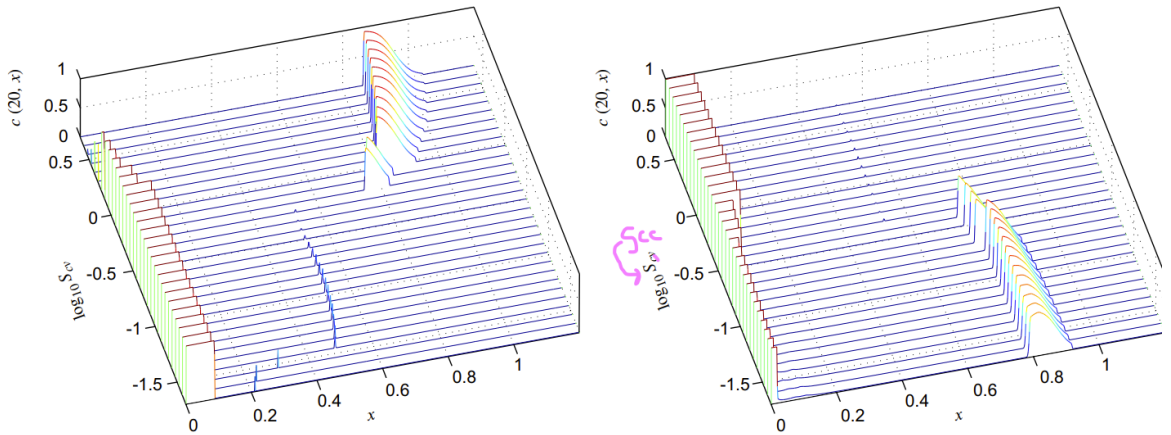

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Numerical Results in 2D

Steady-state cancer

- Now look at non-local model in 2D with a heterogeneous matrix density
- Note top row is cancer cell density, middle row is matrix density and bottom row is the enzyme concentration
- Reaches a steady-state at around $t = 30$
- Note elongation at $t = 10$ (cell-cell adhesion pulls cells together afterwards)
- Not really a lot of diffusion of the enzymes
- Remains a steady-state non-invasive tumour ... unless **key** parameters change

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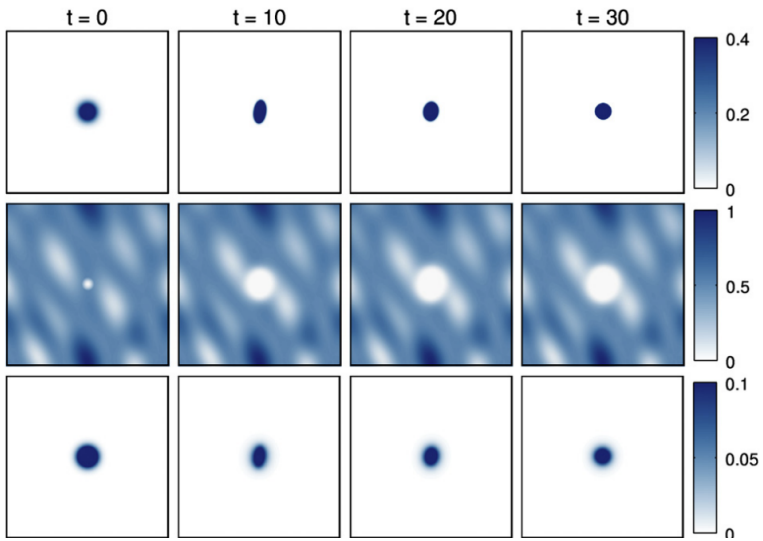

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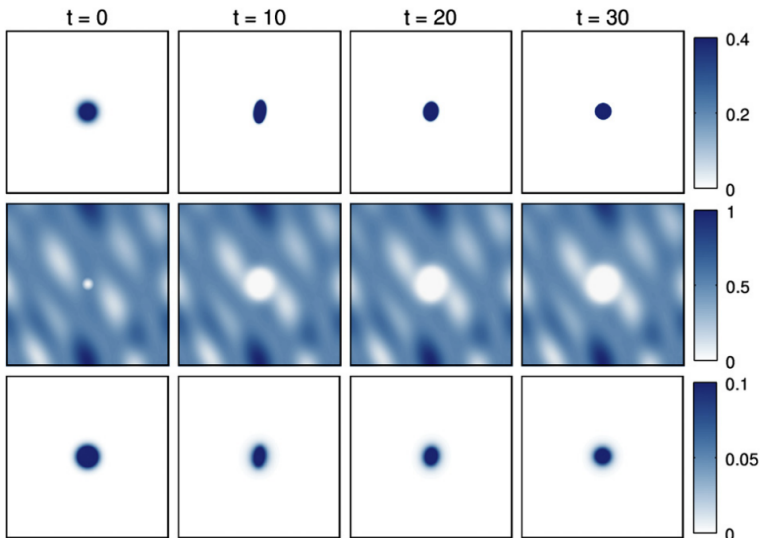

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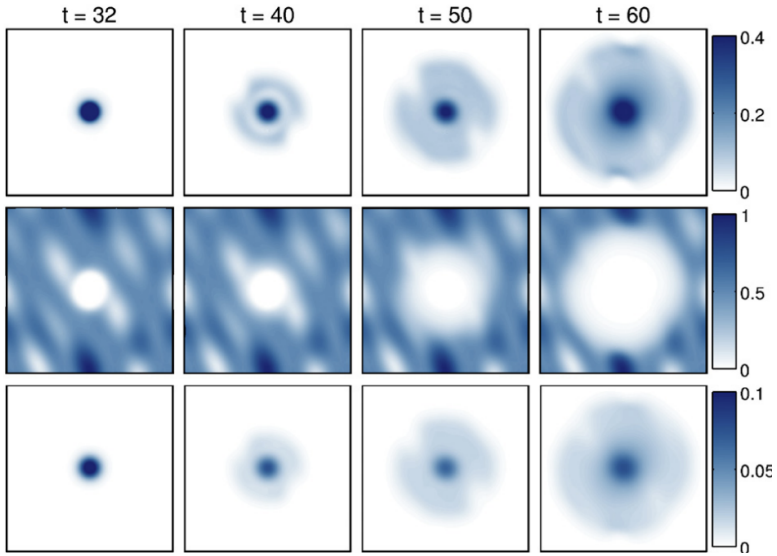
Numerical Results in 2D

Mutation: Invasion of matrix by cancer cells

- To, again, "imitate" a mutation we change the parameters for proliferation and decrease cell-cell adhesion at $t = 30$:



- Observe how the cancer, its enzymes diffuse **asymmetrically**
- At $t = 50$ see the top row, cancer does not invade low density area in matrix and at $t = 60$ it avoids high density regions
- Matrix degrades and cancer moves into it

Numerical Results in 2D

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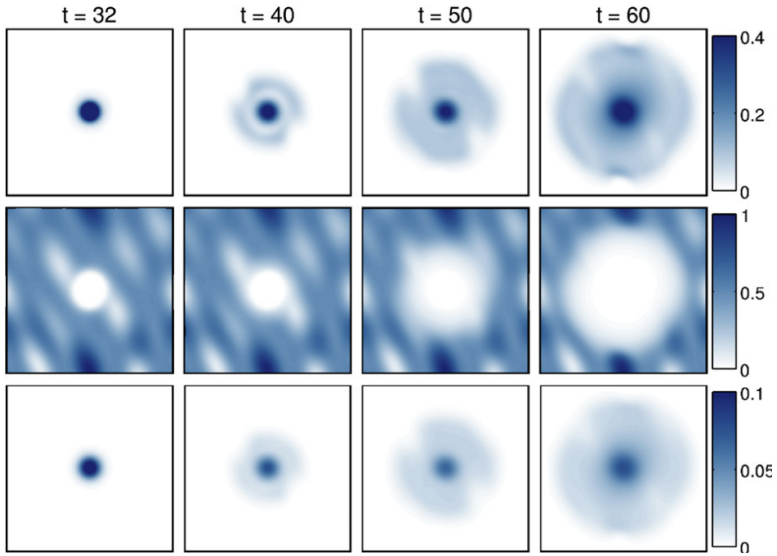

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Summary

- This paper presented a modified local model and a non-local model (with adhesion parameters and replaced haptotaxis migration by $\mathscr{A}$)
- Have briefly discussed the non-local term $\mathscr{A}$
- Non-local model gave rise to cells travelling in wave-like manner (where $S_{cc} = S_{cv}$)
- Demonstrated these are important in determining if tumour is aggressive (relative magnitudes of the adhesion parameters)
  * e.g., spreads when $S_{cv} > S_{cc}$
  * and remains compact for $S_{cv} < S_{cc}$
- Considered 2D case with an imitated mutation (parameter change)
- Conclude that adhesion terms influence both the cancer migration rate (not discussed here) and the cancer type (benign or aggressive)

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