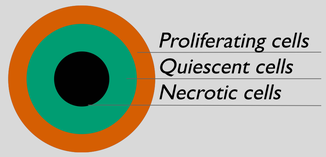
UPPSALA UNIVERSITET

Project in Computational Science
Fall semester 2020

Computational Modelling of Avascular Tumours:
Towards Multiscale Hybrid Models

Summary
A stochastic, agent-based model of an avascular tumour is used as a base model to which we make a modification and an extension. We modify the stochastic model into a deterministic, PDE-based one to enable a more efficient model. Separately, we extend the stochastic model by introducing restrictions on the cell growth by modifying and applying a more realistic boundary condition (BC).



Schematic of the growth pattern of an avascular tumour

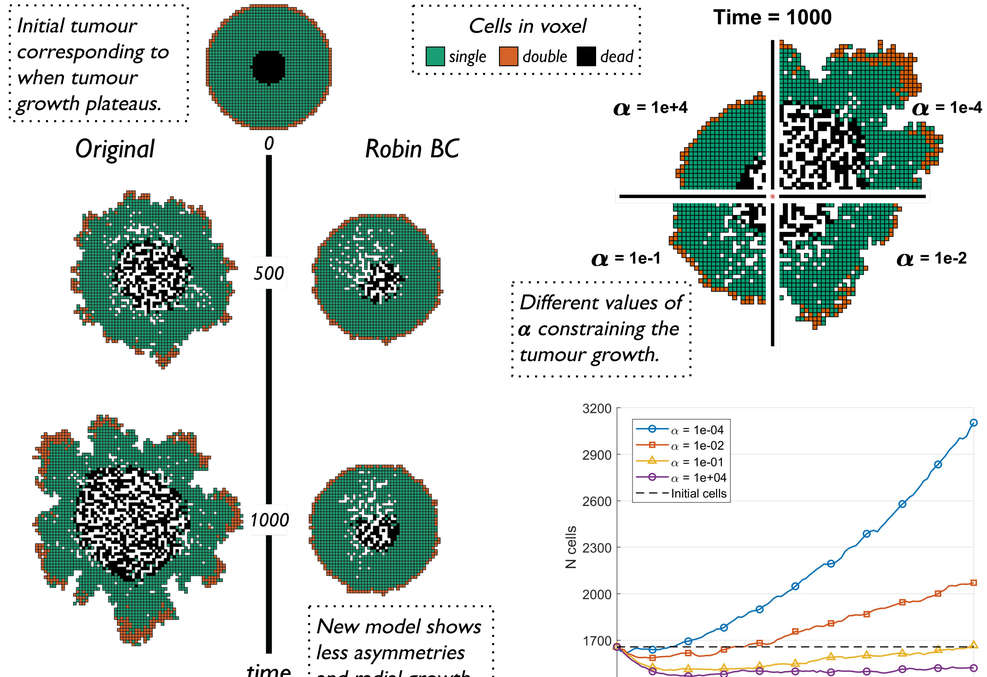
The goal of both parts is to replicate the behaviour of a growing avascular tumour, and to provide building blocks for the construction of an accurate and efficient hybrid model in a future work.

Robin Boundary Condition
A homogeneous Robin BC is applied for the pressure **p** in the tumour. For a tumour with the domain Ω and its boundary Γ, the problem is defined by

$$\begin{matrix} \textit{PDE} \\ \textit{Robin BC} \end{matrix} \begin{cases} -\Delta p = s(u), & p \in \Omega \\ p + \alpha \left(\frac{\partial p}{\partial n}\right) = 0, & p \in \Gamma \end{cases}$$

where **Δ** is the Laplacian operator, **s** is the pressure source depending on the number of cells **u** in a voxel and $\alpha \geq 0$ is a scaling parameter determining the weighting towards Dirichlet or Neumann properties.

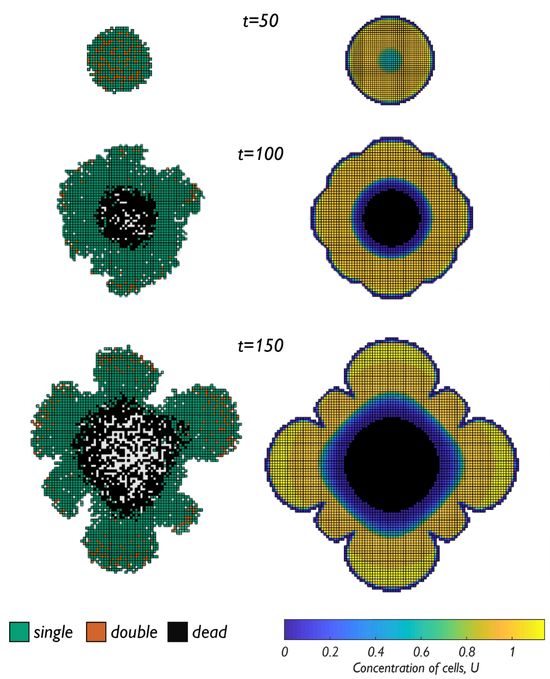
As α grows, the flux on the boundary decreases, making the boundary harder to penetrate, constraining the tumour growth. This can be desirable as real tumour growth follows a sigmoidal curve where the radial growth ultimately plateaus, ending in a mostly circular structure.



PDE Formulation
The model clearly emulates the growth pattern of an avascular tumour, with three distinct layers forming. A comparison of the stochastic agent-based model and the deterministic PDE-model can be seen for times t = 50,100 and 150 the figure.

Asymmetries in the agent-based model stems from the stochasticity, and without a constraining boundary condition they eventually lead to protrusions forming and break-up occuring.

Oxygen is released to the tumour in a circular shape in both models, while the domain that the tumours grow in is a rectangle. For the deterministic model, the geometrical discrepancy causes a slow loss of radial symmetry, resulting in the flower-like shape of the tumour.



The four governing equations:

$$-\Delta p = s(u-1)$$
$$-\Delta c = -\lambda \cdot u$$
$$u_t = -\nabla p \cdot \nabla u - k_d(c) \cdot u + k_b(c) \cdot u$$
$$u_{dead,t} = -r_d \cdot u_{dead} + k_d(c) \cdot u$$

where **p** is for pressure and **s(u-1)** are source terms, **c** is the concentration of oxygen and λ is the consumption of oxygen, **u** and $\mathbf{u_{dead}}$ are concentrations of alive and dead cells, $\mathbf{k_d(c)}$ is the rate of death, $\mathbf{k_b(c)}$ is the rate of birth and $\mathbf{r_d}$ is the rate of degradation.

Working on the same grid as the agent-based model, made up of discrete sites in 2D, PDEs are used for computations of the grid physics, i.e. the oxygen diffusing into the tumour and the pressure exerted by crowded sites. In this model though, cell movement, death and proliferation is also modelled with PDEs, instead of voxel-to-voxel interactions.

Conclusions
A multiscale hybrid model of an avascular tumour may utilise the models created in this project. The deterministic PDE-model has potential to be more efficient than the stochastic, agent-based one. A hybrid model might use it for the bulk of the computations in order to save time, but adapt so that agent-based modelling is used where granular precision is required.

Further, the model may use the Robin BC to more realistically model tumour growth. With the help of our Robin BC, functionalities as, e.g., setting a maximum radius for the tumour could readily be developed.

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