UNIVERSITY OF CAMBRIDGE

Simulation of metastasis base on the viscous fingering model

Phase-field simulation computed with FiPy

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Study Report

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Study's goal

1.1 Objectives

A tumor at the beginning of its evolution is a small sphere of infected cells. With the infection of new cells and the proliferation due to mitosis, this sphere grows larger until it begins spreading in the whole body of the infected subject by invading: this phase is called the metastasis. This is done by the creation of fingers that will grow until some infected cells detach themselves to invade an other organ of the body. The aim of this study is thanks to the analogy with viscous fingering, basing ourselves on the PhD of M. Bogdan, make a simulation of this phenomenon of fingering. New model of metastasis taking into account the activity of the tumour cells

1.2 Type of analysis

The problem is analysed as a viscous fingering problem. When a fluid of a certain viscosity is pushed against a second fluid of higher viscosity, considering the two fluids are incompressible and immiscible, you will see the formation of fingers. M. Bogdan in his PhD made an analogy of these two phenomenons, and modelled the metastasis thanks to Navier-Stokes equations ruling the viscous fingering while adding an activity to take into account the proliferation of infected cells and growing of tumors.

1.3 Method

Phase-field In this problem here we are mainly interested in the evolution of the interface between the two fluids. We have chosen the phase-field method. This ables us to have a field over the whole domain, preventing to have a discrete track of the interface.

1.4 Construction of the code

First two separate models to validate each part of the equations will be made and then, they will be assembled to form the global evolution with the right initial values.

The first model is a 1D simple phase-field code. The aim is to start with a sharp interface to a continuous one without any movement of the two fluids. This will be useful to initialize the phase-field at the beginning of the global code.

The second one is to have only one fluid (we do not take into account the interface) and if we track one cell, it advances from one end to the other end. Normally with the equations, the speed should be uniform everywhere and the cell should advance at normal speed.

Physical behaviour assumptions

2.1 Global description of the fluids

Mass conservation and incompressibility:

$$\underline{\nabla} \cdot \underline{u} = 0 \tag{2.1}$$

2.2 Constitutive properties

2.2.1 Passive fluid

Darcy's law/Equation of motion:

$$\underline{\nabla} p = -\beta_1 \underline{u} \tag{2.2}$$

with $\beta = -\frac{\mu}{k}$ with k:permeability and μ viscosity.

2.2.2 Active fluid

$$\underline{\nabla} p = \alpha \frac{\underline{v}}{\mid \underline{v} \mid} - \beta_2 \underline{u} \tag{2.3}$$

Phase-field model

3.1 Order parameter

phi = 0 for the healthy cells
phi = 1 for the tumor cells

3.2 Cahn-Hilliard equation

Order parameter: conserved
Cahn-Hilliard equation:

$$\frac{\partial \phi}{\partial t} + \underline{u} \cdot \underline{\nabla} \phi = \underline{\nabla} \cdot (M * \underline{\nabla} G) \tag{3.1}$$

The temporal evolution of the phase-field is due to a convective transport from the velocity and a diffusive transport due to the gradients of the chemical potential.
Mobility: $M = Mc * \epsilon^2$ [1]

$Mc = \frac{\mu_1}{\mu_2}$

$$\beta = \beta_1 * \phi + \beta_2 * (1 - \phi) \tag{3.2}$$

3.3 Free energy

Free energy:

$$G = \lambda * [\frac{1}{\epsilon^2}\phi(\phi - \frac{1}{2})(\phi - 1) - \nabla^2\phi] \tag{3.3}$$

After the use of this energy, the phase-field equation becomes:

$$\frac{\partial\phi}{\partial t} + \underline{u} \cdot \underline{\nabla}\phi = \underline{\nabla} \cdot (\frac{M\lambda}{\epsilon^2}(3\phi^2 - 2\phi + \frac{1}{2})\underline{\nabla}\phi) - \underline{\nabla} \cdot (M * \underline{\nabla}\lambda\nabla^2\phi) \tag{3.4}$$

Geometric Assumptions

4.1 Presentation of geometry

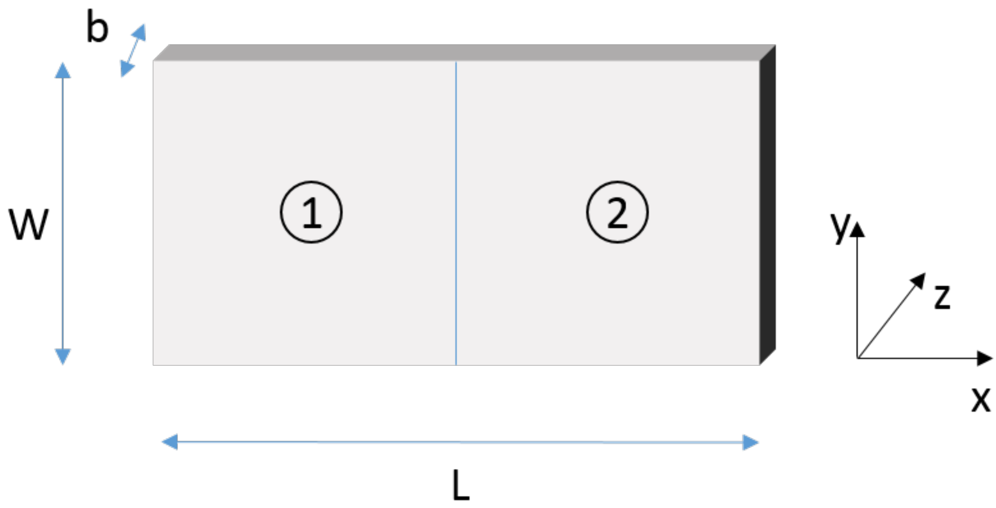

Figure 4.1: *Dispositif de simulation*

4.2 System of units used

4.3 Characteristic dimensions

Characteristic length: W
Characteristic velocity: $U_\infty = \frac{Q}{bW}$

4.4 Problem's symmetries

4.5 Boundary conditions

At the left: rate Q. At the right, U_∞. On the top and the bottom: constraints for y: the fluid stays within its boundaries.

Space Discretization Assumptions

5.1 Discretization method

Use of FiPy: Finite Volume

5.2 Numerical grid

We choose a staggered grid so that the kinetic energy is automatically conserved. Moreover it prevents the oscillations of pressure.

5.3 Size and number of elements

1D: Uniform grid, 400 elements

5.4 Mesh convergence

Time Discretization Assumptions

6.1 Numerical Scheme

Implicit by FiPy. We choose a stable time step for now.

6.2 Solution method

Resolution

7.1 Type of problem solved

Evolution of the two viscous fluids.

7.2 Initial values

Two phases.

7.3 Options of resolution

Use SIMPLE algorithm:

7.4 Results calculated

number of fingers, width

Validity of the model

8.1 Convergence

8.2 Consistency

8.3 Stability

8.4 Conservation

8.5 Boundedness

8.6 Realizability

8.7 Accuracy

Results

Analysis and Conclusions