Mathematical Modeling and Applications

Fatma Zohra Nouri

Mathematical Modeling & Numerical Simulation Lab
Badji Mokhtar University-Annaba (ALGERIA)

Mathematics in Colors (MiC), January 28, 2026

Outline

- Mathematical Modeling : Motivation
  - Some Proposed Models
    - Cellular Systems Modeling and Tumor Growth
      - Theoretical and Numerical Results
        - Concluding Remarks

Mathematical Modeling

Why are models required ?

- Cost
- Data : Absence/Not enough
- Measurement Errors
- Prediction of Solutions
- Prevention

Necessary Ingredients

- Nature of the Medium
- Physical Laws
- Parameters, Variables, Data
- Conditions from Data

Methods for Modeling

- Equation Setting

  ODEs/PDEs, Deterministic/Stochastic

- Mathematical Analysis

  Well posedness in strong and weak sense, Regularisation

- Numerical Analysis & Simulation

  Suitable & Efficient schemes, Stability-Consistency-convergence

- Validation or Calibration

Pollution in Surfacic Water

Today the world is facing a great environmental pollution problem, causing serious and irreparable damage to human society. Pollution can take many forms : the air we breathe, the water we drink, the soil we use to grow our food,...

Water & Soil pollution happens when chemicals or dangerous substances are introduced (sewage, pesticides, fertilizers).
Air pollution originates from both human and natural sources, primarily involving the release of harmful gases (vehicles, power plants, industry)

The central element of such problems is the oxygen. The main tracers currently used are the "BOD" the amount of oxygen per unit volume necessary for the micro-organisms & aerobic bacteria to break down the organic matter contained in the water and the "DO" the oxygen concentration housed in a unit volume of water.

Proposed Model : PDEs

Streeter,Phelps (1925), Bernardi,Nouri (2010,2013), Lachache,Nouri (2023, 2025)

In a bounded open Ω of $\mathbb{R}^d$, $d = 2$ or 3,

$$\begin{aligned} -\mathrm{div}\,(d\,\nabla b) + r\,b &= f && \text{in } \Omega, \\ -\mathrm{div}\,(d\,\nabla c) + r^*\,c + r\,b &= g && \text{in } \Omega, \\ c &= \alpha && \text{on } \partial\Omega, \\ d\,\partial_n c &= \beta && \text{on } \partial\Omega. \end{aligned}$$

The unknows are :

- The density of the Biochemical Oxygen Demand b
- The concentration of the diluated oxygen c

In practice, measurements on c are easy while those on b require a strict chemical protocol and take longer.

The dispersion coefficient d and the reaction parameters r and r^* are positive but depend on the the space variable. The coupling term $r\,b$ is the depletion of oxygen due to elevated BOD.
The data f is the source of the pollution, while g describes the uptake oxygen from the atmosphere to reduce its deficit caused by the biodegradation of the pollutants.

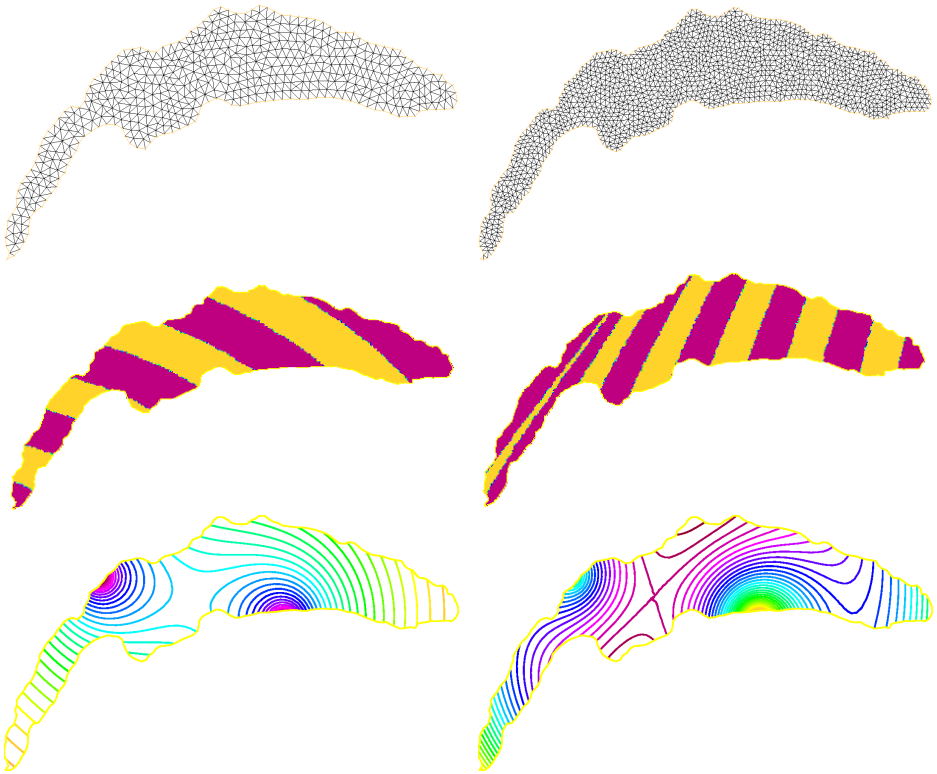
Need to determine $\partial_n b$ on the boundary, for given values of f, g, α and β.

Even if the model is linear, its analysis still not evident !

Reconstructed Geometry from satellite's photos and discrete solutions

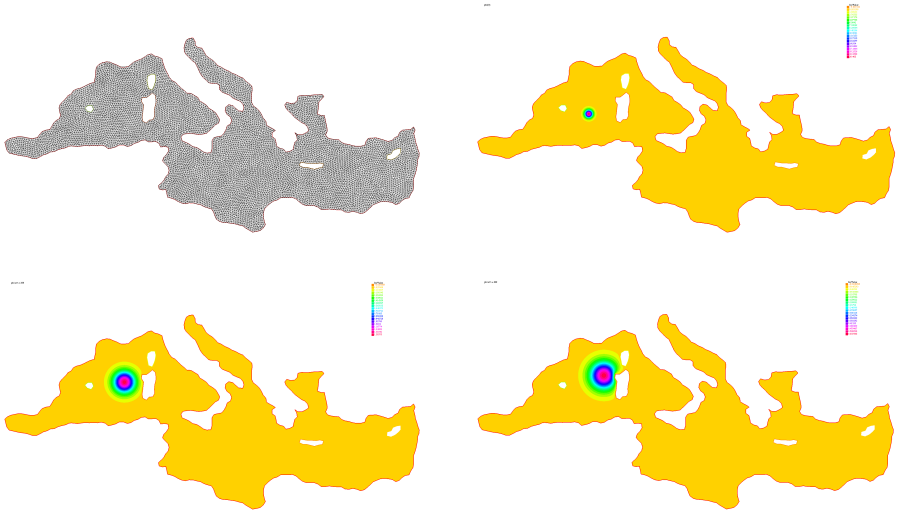
Tests on a Lake : FEM

r, r^* and (b_h, c_h) for $\neq$ meshing,



Pollutant Transport in Mediterranean sea

$$\frac{\partial C}{\partial t} + \vec{u}.\nabla C - \nu \Delta C = -a_0 C + \sum_{j=1}^{n} f_j(t)\delta_{P_j} \qquad Q = (0,\ T) \times \Omega,$$



Water Quality Model : Concentration of pollution
n is the number of outlets,
$f_j = q_j \rho_j^i$, where q_j is the river flow rate at outlet j and ρ_j^i the partial density of the substance i at the reject point j.
δp_j is the Dirac measure at the outlet p_j.

Problems in Medecine : Stem Cell Therapy

The majority of orthopaedics tissues have become targets for cellular therapies, with the repair of cartilage defects, tendons and intervertebral discs.
Such therapies introduce cells by :

- Direct injection
- Surgical implantation

Limitations

- Inaccessible locations and Multiple sites
- Need for repeated dosages
- Non-surgical candidates

Magnetic Stem Cells

Kyrtatos (2009), Huang et al, Riegler et al (2010) and Elhaj & Kimpton, Data (2012)
Requirements : Delivering MSCs to their intended site(s) of action
Suggestions : Magnetic Labelling to guide MSCs out of the bloodstream

Literature Review :

• Richardson et al (2000) : Poiseuille force experienced by the particles in a vessel due to fluid flow and the externally applied magnetic field.
• Grief et al (2005) : advection-diffusion model is proposed for motion of magnetic particles in the bloodstream

Questions :

1. Understanding how the forces due to the blood flow and the magnetic field compete and control the cell motion in $\neq$ vessels

2. Optimal number of Super Paramagnetic Iron Oxide particles in a cell ; predicting the proportion of SPIO- loaded cells that reach the target site

3. How long MSCs take to reach the target site

4. What length of time external magnets should be used

First Attempt

Action Fluid$\hookrightarrow$Cell : modelled by the hydrodynamic force and torque acting on its surface, used as the RH sides of Newton Euler Equations.

Action Cell $\hookrightarrow$Fluid : modelled by no-slip boundary conditions on the cell in Navier-Stokes Equations.

Inconvenience of this Model

This coupling can be numerically unstable requiring very small time steps $+$ if we choose to use FEM and since the position of the cell evolves in t, we have to remesh the computational domain at each t-step or after few t-steps.

Proposed Model : Fluid - Bubble (Bi-phasic model)

We consider 2 fluids with $\neq$ densities & viscosities, using Navier-Stokes Equations

$$\rho(\phi(x,t))\partial_t u + \rho(\phi(x,t))(u.\nabla u) - \mu(\phi(x,t))\Delta u + \nabla p = f$$

$$\rho(x,t) = \begin{cases} \rho_f & \forall x \in \Omega_f \\ \rho_b & \forall x \in \Omega_b \end{cases}, \quad \mu(x,t) = \begin{cases} \mu_f & \forall x \in \Omega_f \\ \mu_b & \forall x \in \Omega_b \end{cases}$$

$$\rho(\phi) = \rho_b + (\rho_f - \rho_b)H(\phi) \ , \quad \mu(\phi) = \mu_b + (\mu_f - \mu_b)H(\phi)$$

ϕ is the level set function solution of

$$\begin{cases} \partial_t \phi + u \ \nabla\phi = 0 \ \forall \ (x,t) \in \Omega \times (0,T) \\ \phi = \phi_{in} \quad on \quad \Sigma_{in}, \ \ \phi = \phi_0, \quad \forall x \in \Omega, \ \ t = 0 \end{cases}$$

$\Sigma_{in} = \{(x,t) \in \partial\Omega \times (0,T); u.n < 0 \ \}$

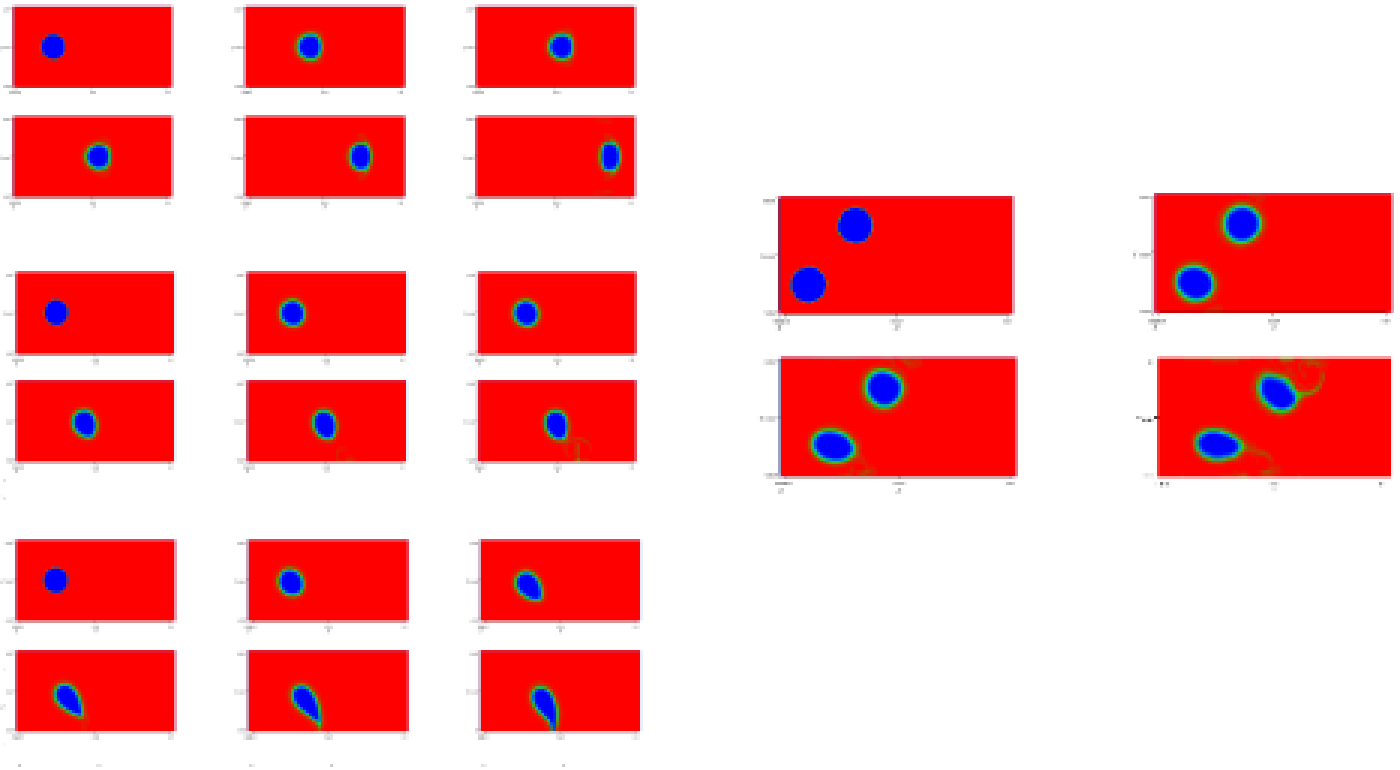
https ://mmsg.mathmos.net/uk/2012/magnetic-stem-cells/

Regularisation : using the heavyside function

$$H(\phi) = \begin{cases} 0, & if \ \frac{\phi}{|\nabla\phi|} < -\varepsilon \\ \frac{1}{2}(1 + \frac{1}{\varepsilon}\frac{\phi}{|\nabla\phi|} + \frac{1}{\pi}\sin(\frac{\pi}{\varepsilon}\frac{\phi}{|\nabla\phi|})), & if \ -\varepsilon \leq \frac{\phi}{|\nabla\phi|} \leq \varepsilon \\ 1, & if \ \frac{\phi}{|\nabla\phi|} > \varepsilon \end{cases}$$

$[-\varepsilon, \varepsilon]$ **is the thickness of the interface between the fluid and the cell.**

$$u = \lambda u_f + (1 - \lambda) u_b$$



Understanding polypharmacology of antibodies

Background :

- **Antibodies (ABs)** are widely recognized for their therapeutic potential, lots of interest in their development and application.

- Progress in antibody engineering led to many $\neq$ **ABs** that differ in size and shape, including **bispecific ABs.**

- **Bispecific ABs** are artificially designed molecules, capable of simultaneously binding $2 \neq$ **antigens**, and can be applied to redirect effector cells to tumor cells.

Goal of Bispecific Antibodies :

Bispecific ABs are capable of binding $2 \neq$ **targets** concurrently

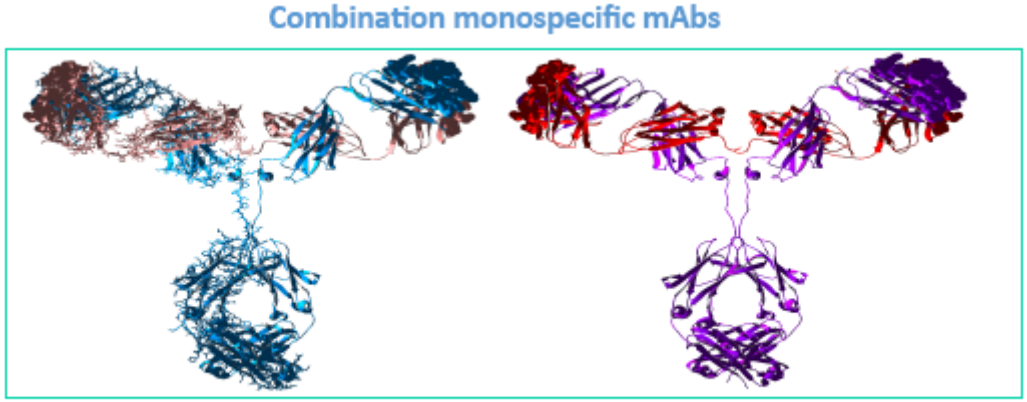
1. Targeting therapeutics to specific disease processes

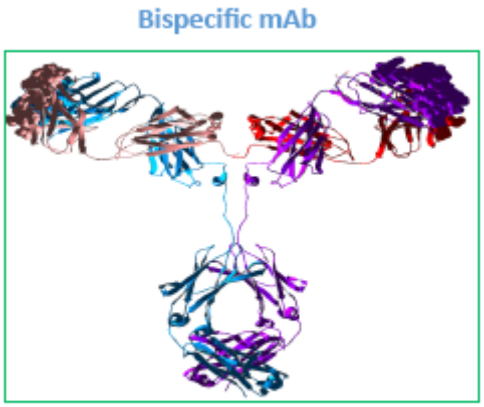
2. Mobilising additional arms of the immune system to fight cancer or infection

3. Has **dual specificity** and a much higher affinity than that of **monoclonal ABs** by **dual antigenbinding**

4. Crosslinking **cell–surface receptors** to invoke novel biology with powerful therapeutic potential

What are the benefits of using a bispecific vs combination of monospecifics





Proposed Model : ODEs

*A- Amount of AB in solution

*B- Amount of blue target on surface

*R- Amount of red target on surface

*AB- Amount of AB bound to blue target

*AR- Amount of AB bound to red target

*ARB- Amount of AB bound to B & R targets

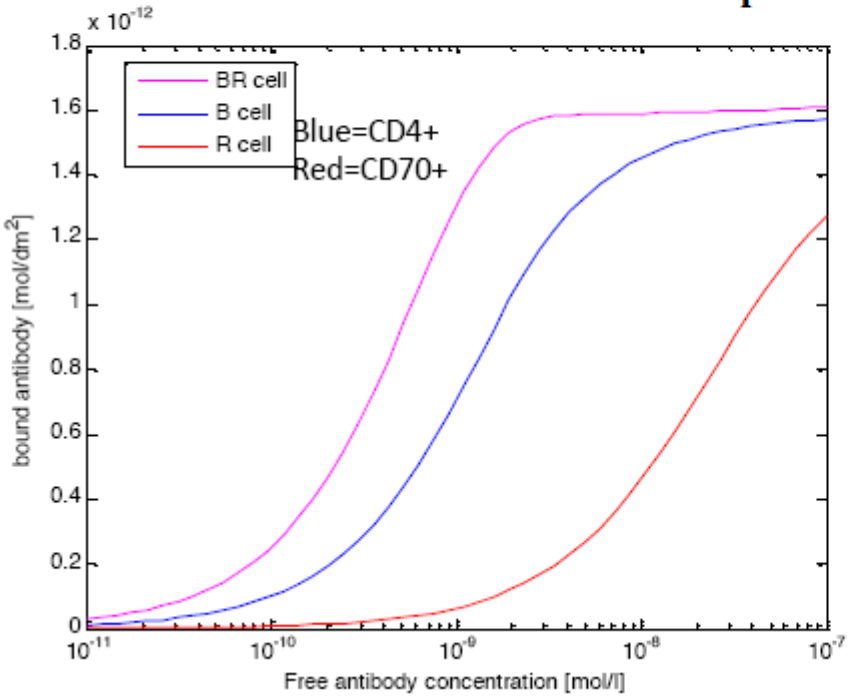
$$
\begin{aligned}
\frac{dA}{dt} &= -k_1(A)(B) + k_1^-(AB) - k_2(A)(R) + k_2^-(AR) \\
\frac{dAB}{dt} &= k_1(A)(B) - k_1^-(AB) - k_3(AB)(R) + k_3^-(ABR) \\
\frac{dAR}{dt} &= k_2(A)(R) - k_2^-(AR) - k_4(AR)(B) + k_4^-(ABR) \\
\frac{dARB}{dt} &= k_3(AB)(R) - k_3^-(ABR) + k_4(AR)(B) - k_4^-(ABR) \\
R &= R_0 - AR - ARB \\
B &= B_0 - AB - ARB \\
A(0) &= A_0, \quad R(0) = R_0, \quad B(0) = B_0, \quad AB(0) = 0, \quad AR(0) = 0,
\end{aligned}
$$

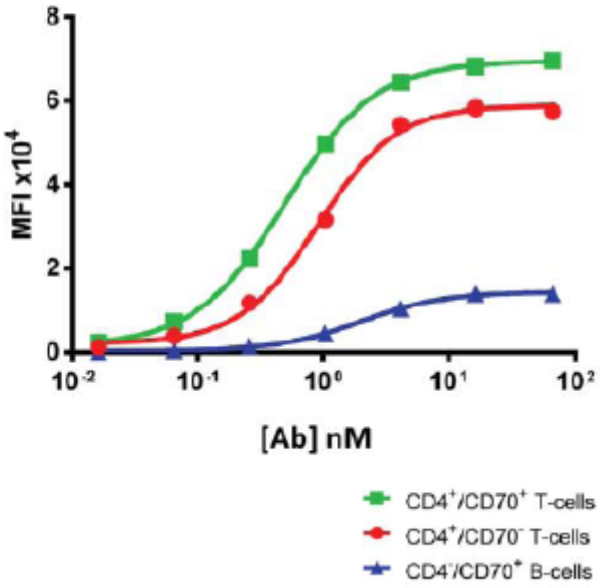
http ://www.maths-in-medicine.org/qsp-uk/2015/

Bram G. Sengers, Sean McGinty, Fatma Z. Nouri, Maryam Argungu, Emma Hawkins, Aymen Hadji, Andrew Weber, Adam Taylor & Armin Sepp (2016). Modeling bispecific monoclonal antibody interaction with two cell membrane targets indicates the importance of surface diffusion, Francis & Taylor mAbs, **8**(5): 905-915

Literature data **from**
Mazor, Y., A. Hansen, et al. (2015). "Insights into the molecular basis of a bispecific antibody's target selectivity." mAbs **7**(3): 461-469.

Comparison with Experiments





Cellular Systems Modeling and Tumor Growth

- Theoretical and Numerical Study
  - Results and Concluding Remarks

Clinical Data and Mathematical Modeling

We are interested in studying a 3D-system, representing the tumor colony of alive & dead cells together with nutrient concentration

Let $\Omega \subset \mathbb{R}^d, d = 3$, be part of a tissue where the tumor grows, $u_p(x,t), u_\tau(x,t), u_f(x,t)$ be proliferating, tumorous cells and nutrient concentration with respective diffusion coefficients D_p, D_τ, D_f

- $P(u_f)$ death rate
- $k(x)$ proliferating rate of u_τ
- β proliferation of u_p
- μ a positive constant related to the absorption of O_2 by u_p
- γ a positive constant related to the natural decay rate of O_2
- θ_p and θ_τ the max caring capacities of tissue for u_p and u_τ
- θ_f the max possible concentration of u_f.

Governing equations : R-D Model

System of 3 coupled PDEs with variable diffusion coefficients :

$$
\begin{cases}
\forall (x,t) \in (\Omega \times (t_0, T)), \\
\dfrac{\partial u_p}{\partial t}(x,t) = \nabla \left(D_p(x) \nabla u_p \right) - P(u_f) u_p + \beta u_p \left(1 - \frac{u_p}{\theta_p} - \frac{u_\tau}{\theta_\tau} \right), \\
\dfrac{\partial u_\tau}{\partial t}(x,t) = \nabla \left(D_\tau(x) \nabla u_\tau \right) + k(x) u_\tau \left(1 - \frac{u_p}{\theta_p} - \frac{u_\tau}{\theta_\tau} \right), \\
\dfrac{\partial u_f}{\partial t}(x,t) = \nabla \left(D_f(x) \nabla u_f \right) - \mu u_p - \gamma u_f \left(1 - \frac{u_f}{\theta_f} \right), \\
u_p(x,t) = \widehat{u_p}, \quad u_\tau(x,t) = \widehat{u_\tau}, \quad u_f(x,t) = \widehat{u_f}, \quad \forall (x,t) \in (\partial\Omega \times (t_0, T)), \\
u_p(x,t_0) = u_{p0}, \quad u_\tau(x,t_0) = u_{\tau 0}, \quad u_f(x,t_0) = u_{f0}, \quad \forall x \in \Omega,
\end{cases}
\tag{1}
$$

where $p(u_f) = \dfrac{\lambda}{2}\left[1 - \tanh\left(\dfrac{u_f - \delta}{\varepsilon}\right)\right]$**, with** λ**,** δ**,** ϵ **positive constants, describing the max death rate, the critical concentration of** O_2 **and the characteristic deviation of** u_f **from** δ

Well-posedness :

1. Strong sense : we write (1) in the form :

$$\begin{cases} \dfrac{dU}{dt} = AU + F(U), \;\; U = (u_p, u_\tau, u_f) \\ U(x, t_0) = U_0, \end{cases} \tag{2}$$

$$A = \begin{bmatrix} A_1 & 0 & 0 \\ 0 & A_2 & 0 \\ 0 & 0 & A_3 \end{bmatrix}, \qquad F(U) = \begin{bmatrix} F_1(U) \\ F_2(U) \\ F_3(U) \end{bmatrix},$$

$$A_1 = D_p(x)\Delta, \qquad F_1 = \nabla D_p(x)\nabla u_p - P(u_f)u_p + \beta u_p \left(1 - \frac{u_p}{\theta_p} - \frac{u_\tau}{\theta_\tau}\right),$$

$$A_2 = D_\tau(x)\Delta, \qquad F_2 = \nabla D_\tau(x)\nabla u_\tau + k(x)u_\tau \left(1 - \frac{u_p}{\theta_p} - \frac{u_\tau}{\theta_\tau}\right),$$

$$A_3 = D_f(x)\Delta, \qquad F_3 = \nabla D_f(x)\nabla u_f - \mu u_p - \gamma u_f \left(1 - \frac{u_f}{\theta_f}\right).$$

By semi-group (S.G.) theory and the Hille-Yosida theorem, we prove that :

A is infenitesimal generator of C_0 semigroup $(\zeta(t))_{t \geq t_0}$ on $X = (L^2(\Omega))^3$ and F is continuous in t, uniformly Lipschitz on X, leading to a unique solution of (2) S.T. :

$$U(t) = \zeta(t - t_0)U_0 + \int_{t_0}^{t} \zeta(t - s)F(s, U(s))ds. \tag{3}$$

2. Weak sense : we derive the weak formulation of (1) :

find $(u_p, u_\tau, u_f) \in V = \left\{ w \in \left(H^1(\Omega)\right)^3 \;\; S.T. \;\; \nabla w|_{\partial\Omega} = 0 \right\}$ **such that** $\forall (\psi, \phi, \varphi) \in V$

$$\int_\Omega \frac{\partial u_p}{\partial t} \psi dx = a_1(u_p, \psi) + b_1(u_p, u_\tau, \psi), \tag{4}$$

$$\int_\Omega \frac{\partial u_\tau}{\partial t} \phi dx = a_2(u_\tau, \phi) + b_2(u_\tau, u_p, \phi), \tag{5}$$

$$\int_\Omega \frac{\partial u_f}{\partial t} \varphi dx = a_3(u_f, \varphi) + b_3(u_p, \varphi), \tag{6}$$

where

$$a_1(u_p, \psi) = -\int_\Omega D_p(x) \nabla u_p \nabla \psi + P(u_f) u_p \psi dx, \tag{7}$$

$$a_2(u_\tau, \phi) = -\int_\Omega D_\tau(x) \nabla u_\tau \nabla \phi dx, \tag{8}$$

$$a_3(u_f, \varphi) = -\int_\Omega D_f(x) \nabla u_f \varphi dx - \gamma \int_\Omega u_f \left(1 - \frac{u_f}{\theta_f}\right) \varphi dx, \tag{9}$$

$$b_3(u_p, \varphi) = -\mu \int_\Omega u_p \varphi dx, \tag{10}$$

$$b_1(u_p, u_\tau, \psi) = \beta \int_\Omega u_p \left(1 - \frac{u_p}{\theta_p} - \frac{u_\tau}{\theta_\tau}\right) \psi dx, \tag{11}$$

$$b_2(u_\tau, u_p, \phi) = \int_\Omega k(x) u_\tau \left(1 - \frac{u_p}{\theta_p} - \frac{u_\tau}{\theta_\tau}\right) \phi dx. \tag{12}$$

* $a_1(.,.), a_2(.,.), a_3(.,.)$ and $b_3(.,.)$ are bilinear, continuous and coercive forms as $D_p(x), D_f(x), D_\tau(x), P(u_f) \in L^2(\Omega)$ & $0 < \left(1 - \frac{u_f}{\theta_f}\right) < 1$

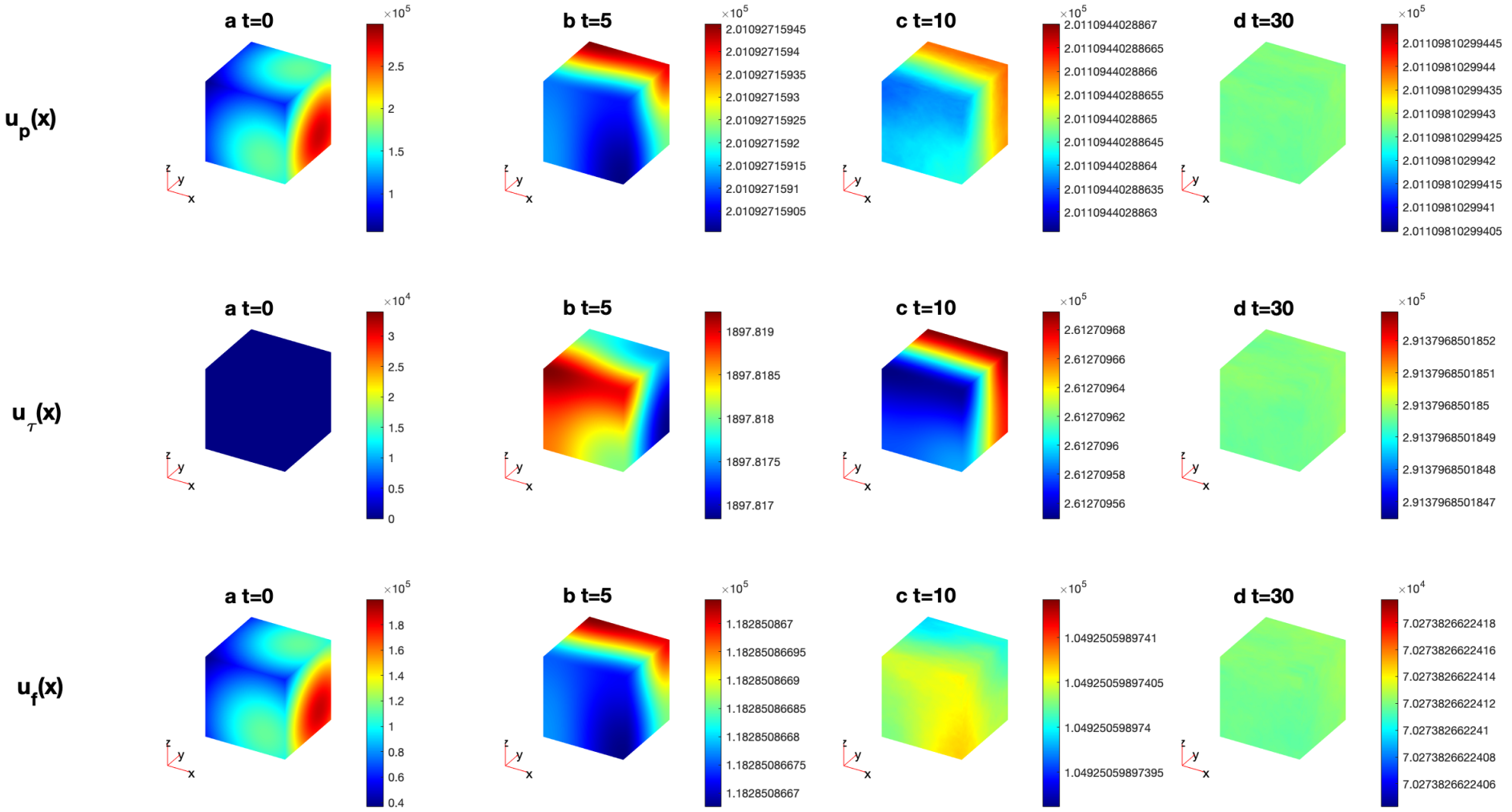
* $b_1(.,.,.), b_2(.,.,.)$ are continuous coercive forms as : $0 < \left(1 - \frac{u_p}{\theta_p} - \frac{u_\tau}{\theta_\tau}\right) < 1$ & $k(x) \in L^2(\Omega$.

By Lax-Miligram, $\exists$ a unique weak solution (u_p, u_τ, u_f).

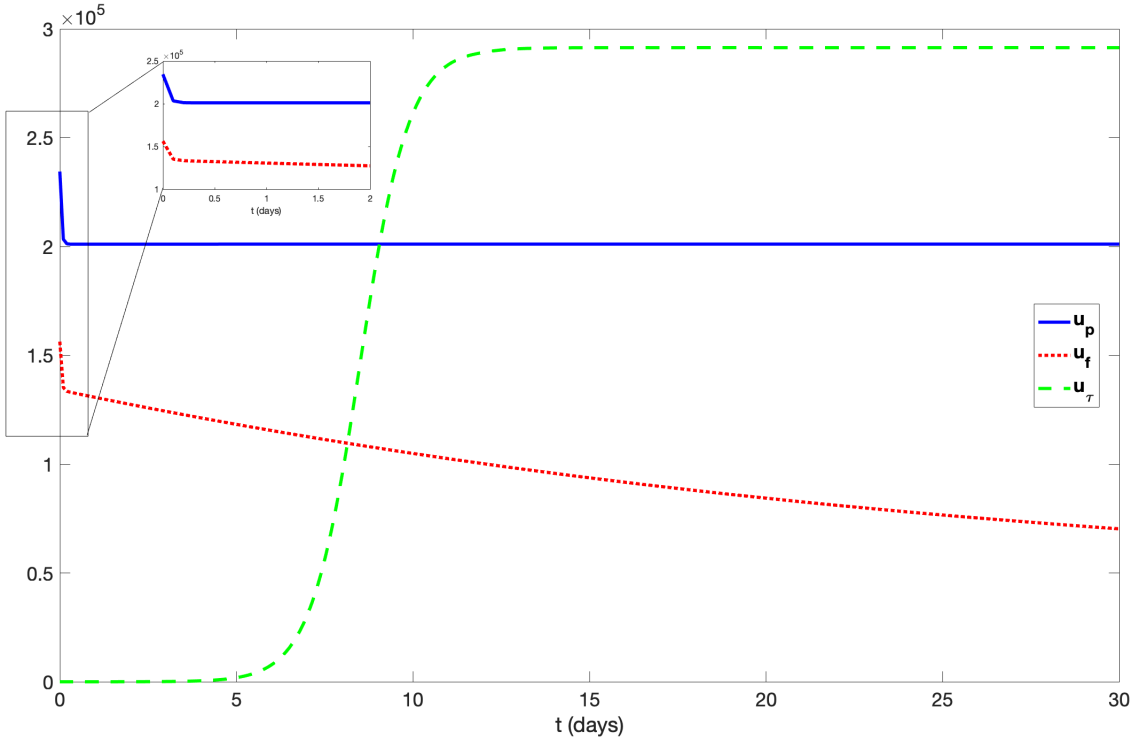
Numerical study : discrete Weak Formulation related to (4-12) on a finite-D $\Omega_h \subset \Omega$

1- Stability analysis : Energy Method

2- Numerical Discretisation : FEM in x and implicit FD scheme in t



The density of A.C. decreases with the N.C., while the T.C. increases



Variation of u_p, u_τ, u_f

These results are part of the Phd thesis work by M. Boussebha as extention of the work by Kolobov et al (2009) and Akila et al (2013) for 2D- models.

Confining Cells : In biology, cellular confinement refers to the physical limitations imposed on a cell by its surrounding microenvironment, including mechanical forces and spatial constraints. The modeling asymptions should satisfy some requirements :

1. Without proliferation and apoptosis (cell death), the number of cells has to be conserved, so migration phenomenon should be modeled by a conservation law

2. Travelling waves and sharp cell fronts are observed in biological experiments. This behaviour must be reproduced by the model

3. Sometimes cell fronts reach a steady state, i.e. the cell fronts slow down and stop in finite time. This reveals a cell region with a boundary, a behaviour to be also reproduced by the model

4. Known biochemical factors (chemoattractant/chemorepellent agents) are able to attract or repel biological cells

5. Cell motility i.e. ability to move freely, generally with a brownian motion. From the macroscopic point of view, this is a diffusive phenomenon ; for isotropic case, we have $\triangle$ diffusion operator

6. There are biological regulation factors which limit the cell density up to a certain threshold.

Keller-Segel (K-S) system

K-S system used in traffic flow modeling, was the first step toward the understanding of how, during the evolution of species, the motion from uni-cellular organisms to more complex structure was achieved

Related Recent Works

Kolobov et al (2009 : Autowaves detection

Blanchet (2010) : A Gradient flow approach to K-S Systems

Brady et al (2019) : How to predict therapies

Boussebha et al (2025) : 3D Models based on variable diffusion coefficients

However K-S can be used as a model taking into account these requirements, but cannot reproduce traveling waves or sharp cell moving fronts.

Hence adding a new modeling term to the equations is necessary !

Proposed model

The idea here is to replace the **K-S** convection term $\nabla(a\rho\nabla c)$, where a a constant, by $\nabla(f(\rho)\nabla c)$, where $f(\rho)$ is a nonlinear function from $[0,\infty[$ to $\mathbb{R}$ and write **K-S** in the form

$$\begin{cases} \dfrac{\partial \rho}{\partial t} - \mu\Delta\rho + \nabla.(f(\rho)\nabla c) = r\rho\,(\rho_\infty - \rho) \\ \dfrac{\partial c}{\partial t} - \Delta c = s\left(\dfrac{\rho}{\rho_\infty} - c\right), \end{cases}$$

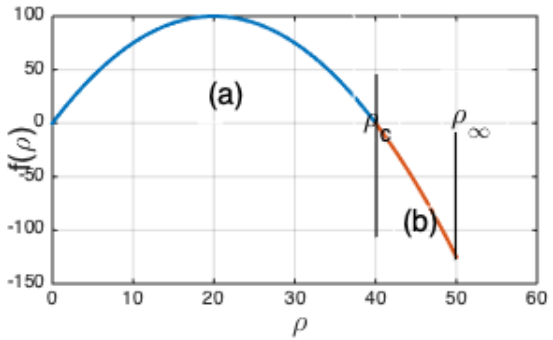
$\mu > 0$ is the diffusion rate, $\rho_\infty > 0$ the threshold cell density, c the concentration of chemoattractant (or chemorepellent) according to the sign of $f(\rho)$, $s > 0$ a reaction rate for c and $r > 0$ a proliferation rate. The convective flux for the cells is $G = f(\rho)\nabla c$.

The first constraint is no flux (i.e. no cell).
In the direction $\eta = \frac{\nabla c}{\|\nabla c\|}$, there is a flux $g = G.\eta = f(\rho)\|\nabla c\|$

The flux can be designed in order to attract cells located in low density regions toward denser regions (clustering) and to repel cells located in dense regions in order to colonize free regions (migration).

One can consider a strictly concave function $f(\rho)$ S.T $f(0) = 0$, $f(\rho_c) = 0$ ($\rho_c \in]0, \infty[$), for example a polynomial of degree 2 crossing the 2 points $(0, \rho_c)$

$$f(\rho) = \alpha\rho\left(1 - \frac{\rho}{\rho_c}\right), \alpha > 0$$



In practice, α, ρ_c and ρ_∞ should be chosen according to some biological considerations. The characteristic velocity for the convective term is $v = f'(\rho)\nabla c = \alpha\left(1 - 2\frac{\rho}{\rho_c}\right)\nabla c$ ($v = 0$ for $f'(\rho) = 0$ or $\nabla c = 0$), leading to a locally stationary wave.

Well-Posedness :

1- strong sense : use S.G. theory and the Hille-Yosida theorem

2- weak sense : use L-M theorem or its generalised version

Numerical Study :

1- Stability analysis : Energy Method

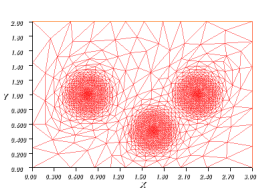
2- Numerical Discretisation : FEM in x and implicit FD scheme in t

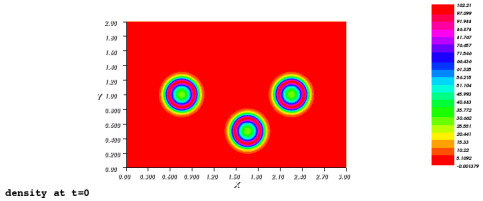
Find $(\rho_h^{k+1}, c_h^{k+1}) \in (V_h)^2$ such that $\forall (v_h, w_h) \in (V_h)^2$, $\rho_h^0 = \rho_0(x)$, $c_h^0 = c_0(x)$,

$$\int_\Omega \frac{\rho_h^{k+1} - \rho_h^k}{\Delta t} v_h \; dx = \mu \int_\Omega \left(\nabla \rho_h^{k+1} \nabla v_h \right) dx,$$

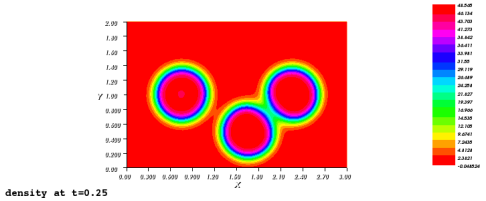
$$\int_\Omega \frac{c_h^{k+1} - c_h^k}{\Delta t} w_h dx = \int_\Omega \left(\nabla c_h^{k+1} \nabla w_h \right) dx + \int_\Omega f(\rho_h) \nabla c_h^{k+1} \nabla w_h \; dx.$$

Numerical Results : Solution ρ_h, c_h for $t = 0, 0.25, 0.75$

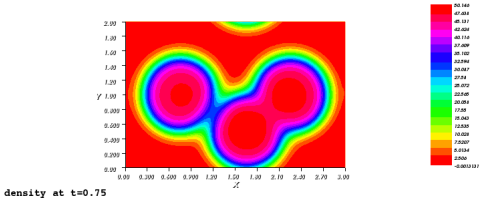




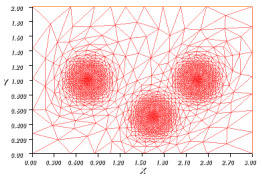
density at t=0

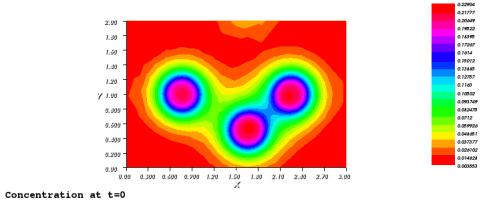


density at t=0.25

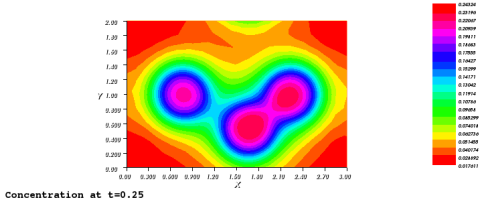


density at t=0.75

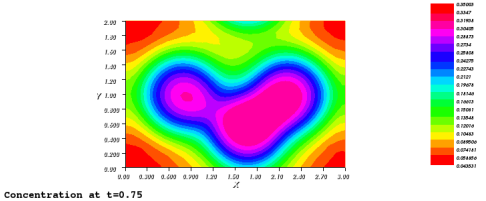




Concentration at t=0



Concentration at t=0.25

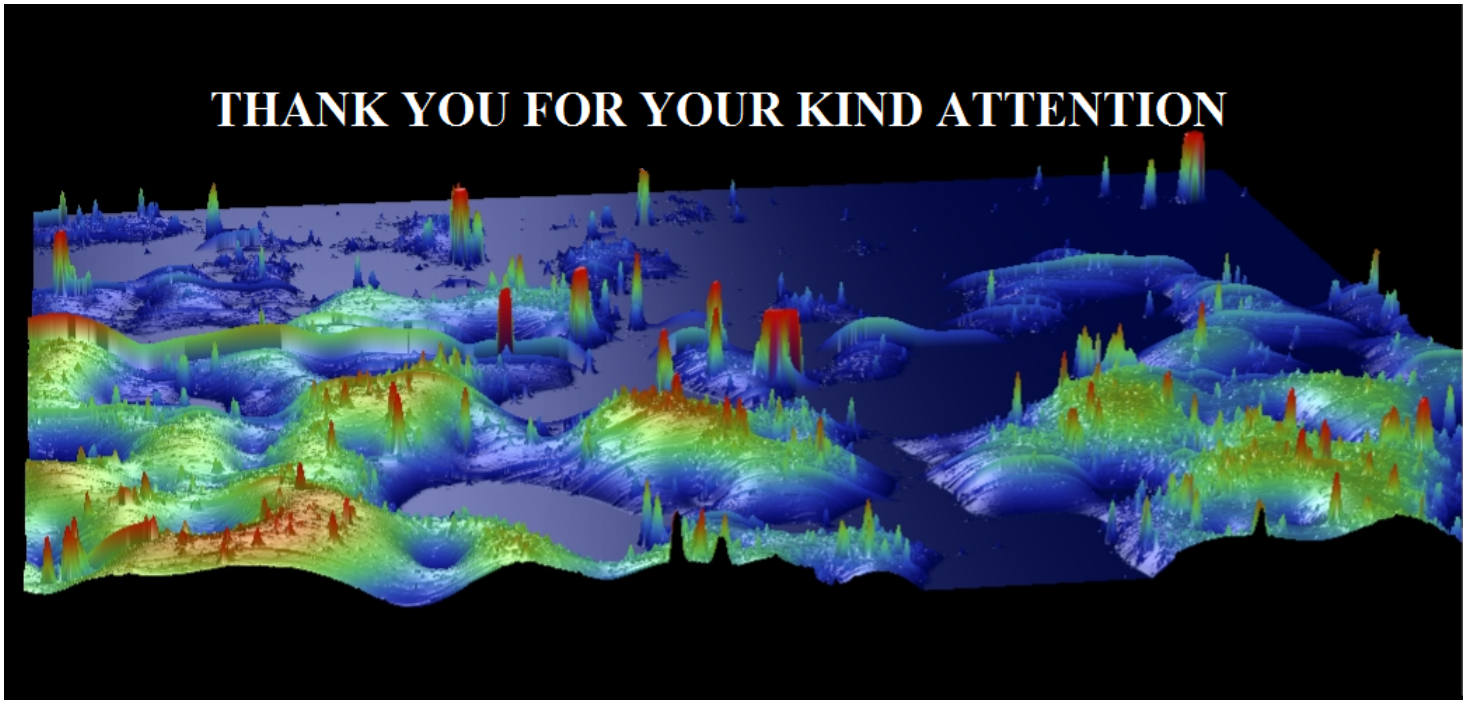


Concentration at t=0.75

Concluding Remarks

- The first model focus on the interaction between alive cells, tumorous cells and nutriments concentration

- The second model highlight a direct relationship between concentration of biochemical factors and the density of tumor cells, confirming that alive tumor cells perish in their absence , thereby promoting tumor growth.


THANK YOU FOR YOUR KIND ATTENTION

1- Blanchet, A. (2010). A Gradient flow approach to Keller-Segel Systems.
$https://www.tse-fr.eu/sites/default/files/medias/doc/by/blanchet/dec_2010/b4.pdf$

2- Brady, R., Enderling, H. (2019). Mathematical Models of Cancer : When to Predict Novel Therapies, and When Not to. Bull Math Biol, 81(12), 3722-3731.
DOI :https ://doi.org/10.1007/s11538-019-00640-x.

3- M. Boussebha and F.Z. Nouri (2025), A Mathematical and Numerical Study of a Model for an Avascular Tumor Evolution, Dynamics of Continuous, Discrete and Impulsive Systems Series B : Applications & Algorithms 32 (2025) 247-267.

4- N. Djedaidi and F.Z. Nouri (2023), Interface dynamics for a bi-phasic problem in heterogeneous porous media,Dynamics of Continuous, Discrete and Impulsive Systems Series B : Applications and Algorithms 30 (2023), pp. 21-33.

5- A. Hadji and F.Z. Nouri (2022), Mathematical and numerical study for a bioglass bioactivity degradation, International Journal of Advanced Science and Research , Vol 7, Issue 2, 2022, pp. 15-22.

6- Jones, D., Plank, M., Sleeman, B. (2009). Differential Equations and Mathematical Biology. New York : Chapman and Hall/CRC.
DOI :http ://doi.org/10.1201/9781420083583.

7-Kolobov, A.V., Gubernov, V.V., Polezhaev, A.A. (2009). Autowaves in a model of invasive tumor growth. BIOPHYSICS, 54, 232-237. DOI :https ://doi.org/10.1134/S0006350909020195.

8- Macías-Díaz, J.E., Gallegos, A. (2018). A structure-preserving computational method in the simulation of the dynamics of cancer growth with radiotherapy. J. Math Chem, 56, 1985-2000.
DOI :https ://doi.org/10.1007/s10910-017-0818-9.

9- Pazy, A. (1992). Semi-groups of Linear Operators and Applications To Partial Differential Equations, 2nd ed. Springer-Verlag, Berlin-Heidelberg New York-Tokyo.