A structure preserving scheme for a tissue growth model of porous medium type

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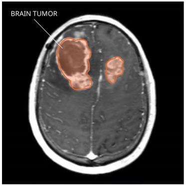
Overview

Outline

Tissue growth

Spatial organization of tissue is of great interest.

- Factors influencing tissue growth:
  nutrient, space availability, etc.
- A mechanistic view assumes the cells driven by *pressure* and considers the *contact inhibition effect*.



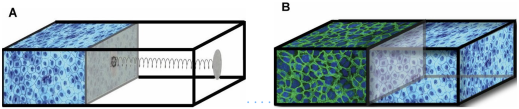


Figure: Measurement of "homeostatic pressure" p_H *

*M. Basan, T. Risler, J.-F. Joanny, X. Sastre-Garau, J. Prost (2009)

A compressible model of tissue growth

Assumptions from a mechanistic view:

- The cells move down pressure gradients, $\mathbf{v} = -\nabla p$, where $p = n^\gamma$ is the internal pressure of the tumor.
- The pressure also controls the cell proliferation through an inhibitory effect, $G'(p) \leq -\alpha$, for $p < p_H$ and $G(p_H) = 0$.

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With the assumptions:

$$\frac{\partial n}{\partial t} - \nabla \cdot (n \nabla p) = nG(p) \tag{1}$$

where $(\mathbf{x}, t) \in Q_T := \mathbb{R}^d \times (0, T)$.

Main theoretical results (B. Perthame etc., 2014, 2021)

Theorem (*A priori* estimates)

Given (n_γ, p_γ) a weak solution for $\gamma > 1$ and $T > 0$, there exists a constant $C(T)$, independent of γ, such that
(1) $0 \leq n_\gamma \leq n_H$, $0 \leq p_\gamma \leq p_H$,
(2) $\|n_\gamma(t)\|_{L^1(\mathbb{R}^d)} \leq C(T)$, $\|p_\gamma(t)\|_{L^1(\mathbb{R}^d)} \leq C(T)$,
(3) $\|\partial_t n_\gamma\|_{L^1(Q_T)} \leq C(T)$, $\|\partial_t p_\gamma\|_{L^1(Q_T)} \leq C(T)$
(4) $\|\nabla p_\gamma\|_{L^2(Q_T)} \leq C(T)$.

Theorem(Incompressible limit - complementarity relation)

With the same assumptions, the limit pressure p_∞ as $\gamma \to \infty$ satisfies

$$p_\infty(\Delta p_\infty + G(p_\infty)) = 0, \text{ in } D'(Q).$$

Question: Can we propose a scheme which preserves exactly the a priori estimates and the asymptotic structure?

Literature review: numerical study

- Finite difference scheme: J.L. Graveleau and P. Jamet (1971), E.D. Benedetto and D. Hoff (1984), L. Monsaingeon (2016), $\cdots$
- WENO scheme: Y. Liu, C.-W. Shu and M. Zhang (2011), $\cdots$
- Finite volume method: M. Bessemoulin-Chatard and F. Filbet (2012), R. Eymard, T. Gallouet, R. Herbin and A. Michel (2002), $\cdots$
- Finite element methods: M.E. Rose(1983), Q. Zhang and Z.-L. Wu (2009), M.J. Baines, M.E. Hubbard and P.K. Jimack, etc (2005, 2006), C. Ngo and W. Huang (2017), $\cdots$
- The relaxation scheme: G. Naldi, L. Pareschi and G. Toscani (2002), F. Cavalli, G. Naldi, G. Puppo and M. Semplice (2007), $\cdots$

The algorithm preserving the free boundary limit is rarely studied. One recent work is by J.-G. Liu, M. Tang, L. Wang and Z. Zhou (2018).

Outline

Semi-discretization

Notations: $n_i(t) \approx n(t, x_i)$, $p_i(t) = n_i^\gamma(t)$

Semi-discrete scheme:

$$\frac{dn_i}{dt} = \frac{n_{i+\frac{1}{2}} q_{i+\frac{1}{2}} - n_{i-\frac{1}{2}} q_{i-\frac{1}{2}}}{\Delta x} + n_i G_i \tag{2}$$

where $q_{i+\frac{1}{2}} = \frac{p_{i+1} - p_i}{\Delta x}$, $G_i = G(p_i)$ and

$$n_{i+\frac{1}{2}} = \begin{cases} n_i, & \text{if } q_{i+\frac{1}{2}} \leq 0, \\ n_{i+1}, & \text{if } q_{i+\frac{1}{2}} > 0. \end{cases} \tag{3}$$

Stability results

Theorem (*A priori* estimates)

Let $T > 0$ and $n_H := p_H^{\frac{1}{\gamma}}$, $\gamma > 1$. Then, for all $0 \le t \le T$ and i, it holds
(1) $0 \le n_i(t) \le n_H$, $0 \le p_i(t) \le p_H$,
(2) $\|n(t)\|_{l^1} \le C(T)$, $\|p(t)\|_{l^1} \le C(T)$,
(3) $\|\delta_x n(t)\|_{l^1} \le C(T)$,
(4) $\int_0^T \|\frac{dn(t)}{dt}\|_{l^1} \le C(T)$, $\int_0^T \|\frac{dp(t)}{dt}\|_{l^1}\, dt \le C(T)$
(5) $\int_0^T \|\delta_x p(t)\|_{l^2}^2 \, dt \le C(T)$.

The proof follows almost the same idea as in the continuous case (N. David and B. Perthame, 2021).

Proof of (3)

Multiplying $\frac{d}{dt}(\delta_x n_{i+\frac{1}{2}})$ with $\text{sign}(\delta_x n_{i+\frac{1}{2}})$, we get

$$\frac{d}{dt}|\delta_x n_{i+\frac{1}{2}}| \leq \delta_x^2(n_{i+\frac{1}{2}}|q_{i+\frac{1}{2}}|) + \delta_x(n_{i+\frac{1}{2}}G_{i+\frac{1}{2}})\text{sign}(\delta_x n_{i+\frac{1}{2}})$$
$$\leq \delta_x^2(n_{i+\frac{1}{2}}|q_{i+\frac{1}{2}}|) + |\delta_x n_{i+\frac{1}{2}}|G_i$$

where

$$\delta_x^2(n_{i+\frac{1}{2}}|q_{i+\frac{1}{2}}|) = \frac{n_{i+\frac{3}{2}}|q_{i+\frac{3}{2}}| - 2n_{i+\frac{1}{2}}|q_{i+\frac{1}{2}}| + n_{i-\frac{1}{2}}|q_{i-\frac{1}{2}}|}{(\Delta x)^2},$$
$$\delta_x(n_{i+\frac{1}{2}}G_{i+\frac{1}{2}}) = \frac{n_{i+1}G_{i+1} - n_i G_i}{\Delta x}.$$

Summing over i and noticing the fact that $\sum_i \delta_x^2(n_{i+\frac{1}{2}}|q_{i+\frac{1}{2}}|) = 0$ and $G_i \leq G(0)$, we have

$$\frac{d}{dt}\|\delta_x n(t)\|_{l^1} \leq G(0)\|\delta_x n(t)\|_{l^1}.$$

Proof of (5)

We consider the reformulated form

$$\frac{d}{dt}n_i = \frac{n_{i+\frac{1}{2}} - n_i}{\Delta x}q_{i+\frac{1}{2}} + \frac{n_i - n_{i-\frac{1}{2}}}{\Delta x}q_{i-\frac{1}{2}} + n_i(\delta_x^2 p_i + G_i)$$

Multiplying both sides by $\gamma n_i^{\gamma-1}$, we get

$$\begin{aligned}\frac{d}{dt}p_i &= \gamma n_i^{\gamma-1}\left(\frac{n_{i+\frac{1}{2}} - n_i}{\Delta x}q_{i+\frac{1}{2}} + \frac{n_i - n_{i-\frac{1}{2}}}{\Delta x}q_{i-\frac{1}{2}}\right) + \gamma p_i(\delta_x^2 p_i + G_i) \\ &\leq |q_{i+\frac{1}{2}}|_+^2 + |q_{i-\frac{1}{2}}|_-^2 + \gamma p_i(\delta_x^2 p_i + G_i).\end{aligned}$$

Summing over i and integrating over $[0, T]$, a detailed computation shows that

$$\int_0^T \|\delta_x p(t)\|_{l^2}^2 \, dt \leq \frac{\|p(0)\|_{l^1} - \|p(T)\|_{l^1}}{\gamma - 1} + \frac{\gamma}{\gamma - 1}\int_0^T \|p(t)G(t)\|_{l^1} dt.$$

Full-discretization

NOTATIONS: $N_i^n \approx n(t_n, x_i)$, $P_i^n = (N_i^n)^\gamma$, $G_i^n = G(P_i^n)$

FULLY IMPLICIT SCHEME:

$$\delta_t^+ N_i^n = \frac{N_{i+\frac{1}{2}}^{n+1} Q_{i+\frac{1}{2}}^{n+1} - N_{i-\frac{1}{2}}^{n+1} Q_{i-\frac{1}{2}}^{n+1}}{\Delta x} + N_i^{n+1} G_i^{n+1}$$

where

$$Q_{i+\frac{1}{2}}^n = \frac{P_{i+1}^n - P_i^n}{\Delta x}, \quad N_{i+\frac{1}{2}}^n = \begin{cases} N_i^n, & \text{if } Q_{i+\frac{1}{2}}^n \leq 0, \\ N_{i+1}^n, & \text{if } Q_{i+\frac{1}{2}}^n > 0. \end{cases}$$

Reformulation of the fully discrete scheme

To numerically analyze the scheme, it is more convenient to rewrite it as

$$L(N_{i-1}^{n+1}, N_i^{n+1}, N_{i+1}^{n+1}) = N_i^n,$$

where $\nu = \Delta t/\Delta x$, $\Delta t < 1/G(0)$ and

$$L(N_{i-1}^{n+1}, N_i^{n+1}, N_{i+1}^{n+1}) = \\ (1 - \Delta t G_i^{n+1}) N_i^{n+1} - \nu \left(A(N_i^{n+1}, N_{i+1}^{n+1}) - A(N_{i-1}^{n+1}, N_i^{n+1}) \right)$$

with $A(U_l, U_r) = U_r v(U_l, U_r)_+ - U_l v(U_l, U_r)_-$, $v(U_l, U_r) = \frac{(U_r)^\gamma - (U_l)^\gamma}{\Delta x}$.

Monotone scheme

The scheme is monotone since

$$\partial_1 A(U_l, U_r) \leq 0, \quad \partial_2 A(U_l, U_r) \geq 0.$$

Solvability

Lemma

Consider the evolution equation

$$\frac{dn_i(t)}{dt} + L(n_{i-1}(t), n_i(t), n_{i+1}(t)) = N_i^n$$

Take the sub- and super-initial data $\underline{n}_i(0) \equiv 0$ and $\overline{n}_i(0) \equiv n_H$, then $\frac{d}{dt}\underline{n}_i(t) \geq 0$, $\frac{d}{dt}\overline{n}_i(t) \leq 0$, $\underline{n}_i(t) \leq \overline{n}_i(t)$ for all $t > 0$. and

$$\lim_{t\to\infty} \underline{n}_i(t) = \lim_{t\to\infty} \overline{n}_i(t).$$

Theorem (Solvability)

The scheme with a general initial data $0 \leq N_i^0 \leq n_H$ is uniquely solvable, which can be determined by

$$N_i^{n+1} = \lim_{t\to\infty} \underline{n}_i(t) = \lim_{t\to\infty} \overline{n}_i(t).$$

Stability results

Theorem (*A priori* estimates)

Let $T > 0$, $\gamma > 1$, $\Delta t < 1/G(0)$ and $n(T) = \lfloor n/\Delta t \rfloor$, it holds
(1) $0 \leq N_i^n \leq n_H$, $0 \leq P_i^n \leq p_H$, $\forall i, n$,
(2) $\sum_i N_i^n \leq C(T)$, $\sum_i P_i^n \leq C(T)$,
(3) $\sum_i |\delta_x N_{i+\frac{1}{2}}^n| \leq C(T)$,
(4) $\sum_i |\delta_t^+ N_i^n| \leq C(T)$, $\sum_i |\delta_t^+ P_i^n| \leq C(T)$
(5) $\Delta t \sum_{k=0}^{n(T)} \sum_i \left| \delta_x P_{i+\frac{1}{2}}^n \right|^2 dt \leq C(T)$.

Remark: The boundedness result, i.e. (1), comes immediately from the solvability result.

Proof of (5)

We consider the reformulated form

$$\delta_t^+ N_i^n = \frac{N_{i+\frac{1}{2}}^{n+1} - N_i^{n+1}}{\Delta x} Q_{i+\frac{1}{2}}^{n+1} + \frac{N_i^{n+1} - N_{i-\frac{1}{2}}^{n+1}}{\Delta x} Q_{i-\frac{1}{2}}^{n+1} + N_i^{n+1}(\delta_x^2 P_i^{n+1} + G_i^{n+1})$$

Multiplying both sides by $\gamma(N_i^{n+1})^{\gamma-1}$ and noticing that

$$\delta_t^+ P_i^n \leq \gamma(N_i^{n+1})^{\gamma-1} \delta_t^+ N_i^n$$

due to convexity, we get

$$\delta_t^+ P_i^n \leq |Q_{i+\frac{1}{2}}^{n+1}|_+^2 + |Q_{i-\frac{1}{2}}^{n+1}|_-^2 + \gamma P_i^{n+1}(\delta_x^2 P_i^{n+1} + G_i^{n+1}).$$

Summing over i and n, a detailed computation shows that

$$\Delta t \sum_{k=0}^{n(T)} \sum_i \left| \delta_x P_{i+\frac{1}{2}}^n \right|^2 \leq \frac{\sum_i P_i^0 - \sum_i P_i^n}{\gamma - 1} + \Delta t \frac{\gamma}{\gamma - 1} G(0) \sum_{k=0}^{n} \sum_i P_i^k \leq C(T).$$

Proof of (3) and (4)

The proof of (3) and (4) relies on the following L^1-contraction property.

Lemma (L^1-contraction)

Denote M_i^n and N_i^n to be two non-negative solutions satisfying the scheme, then we have

$$\sum_i |M_i^n - N_i^n| \leq \frac{1}{(1 - \Delta t G(0))^n} \sum_i |M_i^0 - N_i^0|.$$

- Taking $M_i^n = N_{i+1}^n$, we get the BV estimate (3).
- Taking $M_i^n = N_i^{n+1}$, we get the estimate on time derivative (4).

Asymptotic preserving property as $\gamma \to \infty$

Theorem (Convergence result)

For the limiting solution $p_{\infty,i}$, we have, in the sense of distribution, that

$$p_{\infty,i}(\delta_x^2 p_{\infty,i} + G(p_{\infty,i})) = 0.$$

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- The proof relies on *a priori* estimates as well as the following lemma.

Lemma

Given $n_{\gamma,i}$, $p_{\gamma,i}$ a solution with $\gamma > 1$, then as $\gamma \to \infty$, we have for all i

$$n_{\gamma,i} \to n_{\infty,i}, \quad p_{\gamma,i} \to p_{\infty,i}, \text{ in } L^p(0,T),$$

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- For the fully discrete scheme, similar results hold and *a priori* estimates will be enough for the proof .

Outline

A simple test: the Barenblatt solution

Consider the 1D equation

$$\frac{\partial n}{\partial t} = \frac{\partial^2 n^{\gamma+1}}{\partial x^2}$$

with the initial data the delayed Barenblatt solution $(t_0 = 0.01)$

$$n(x,0) = \frac{1}{t_0^{\beta}} \left| C - \beta \frac{\gamma}{2(\gamma+1)} \frac{x^2}{t_0^{2\beta}} \right|_+^{\frac{1}{\gamma}}.$$

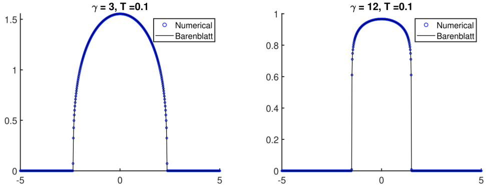

Figure: Comparison with analytical results for $\gamma = 3$ (left) and $\gamma = 12$ (right).

Accuracy test

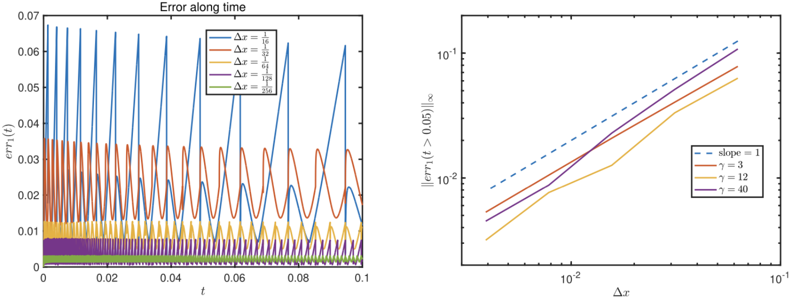

Figure: Plot of the error along time for $\gamma = 12$ (left) and plot of the error w.r.t Δx for different values of γ.

Application to 1D model with nutrient

Consider the *in vivo* model,

$$\begin{cases} \dfrac{\partial n}{\partial t} - \nabla \cdot (n \nabla p) = nG(p, c), \\ -\Delta c + \psi(n)c = (c_B - c)\mathbb{I}_{\{n=0\}}. \end{cases}$$

The exact solution in the limit $\gamma \to \infty$ can be explicitly written.

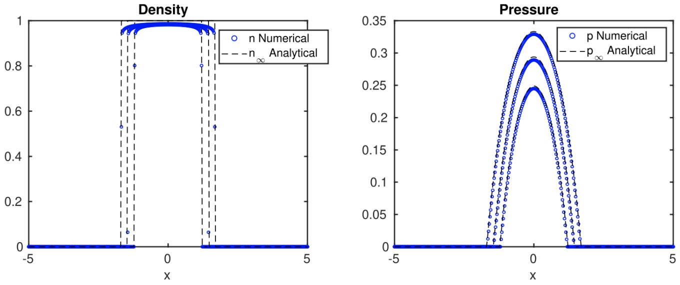

Figure: Comparison of n (left) and p (right) with the analytical solution at $t = 0.5, 1, 1.5$.

Application to a two-species model

Consider the tumor with a necrotic core,

$$\begin{cases} \dfrac{\partial n_P}{\partial t} - \dfrac{\partial}{\partial x}(n_P \dfrac{\partial p}{\partial x}) = n_P G(c), \\ \dfrac{\partial n_D}{\partial t} - \dfrac{\partial}{\partial x}(n_D \dfrac{\partial p}{\partial x}) = n_P G^{-}(c). \end{cases}$$

where n_P and n_D represent cell densities of proliferating and necrotic cells and $p = n^\gamma = (n_P + n_D)^\gamma$.

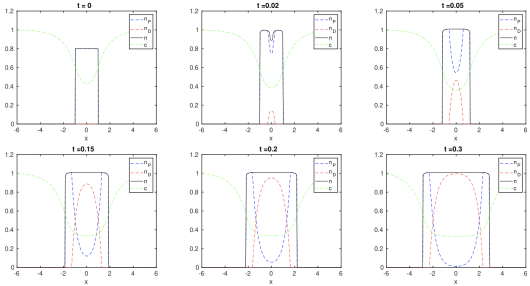

Figure: *In vivo* two-species model in 1D.

Outline

Conclusions

Conclusions: An upwind type scheme is proposed, which is proven rigorously to be asymptotic preserving and preserves the same *a priori* stability estimates.

Future work:

- To design higher-order accurate numerical schemes.
- To generalize to cross-reaction-diffusion systems of porous medium type.
- ...

Reference: An asymptotic preserving scheme for a tumor growth model of porous medium type, *N. David and X. Ruan*, ESAIM:M2AN, 2022.

Thank you all for your attention!