# Finite-volume approximation of cross-diffusion systems for tumor growth

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ongoing work with Ansgar Jüngel

## Model

We present an implicit Euler finite volume scheme for the mechanical tumor growth model proposed by Jackson and Byrne in [1], which is a system of nonlinear cross-diffusion equations for the volume fractions of tumor cells, $u_1$, and the extracellular matrix, $u_2$, written in terms of $u = (u_1, u_2)^T$:

$$\partial_t u - \nabla\cdot(A(u)\nabla u) = f(u) \quad \text{in } \Omega, \quad t > 0. \tag{1}$$

Here $\Omega = (0,1)^2$, the diffusion matrix $A$ is given by

$$A(u_1,u_2) = \begin{pmatrix} 2u_1(1-u_1) - \beta\theta u_1 u_2^2 & -2\beta u_1 u_2(1+\theta u_1) \\ -2u_1u_2 + \beta\theta(1-u_2)u_2^2 & 2\beta u_2(1-u_2)(1+\theta u_1) \end{pmatrix},$$

and the reaction term

$$f(u_1,u_2) = \begin{pmatrix} \gamma u_1(1-u_1-u_2) - \lambda u_1 \\ \alpha u_1 u_2 (1-u_1-u_2) \end{pmatrix}.$$

The equations are subjected to Neumann boundary and initial conditions

$$(A(u)\nabla u)\cdot\nu = 0 \quad \text{on } \partial\Omega,\ t>0, \quad u(0) = u^0 \quad \text{in } \Omega. \tag{2}$$

The nonnegative parameters describe:

- $\gamma$: water fraction rate;
- $\alpha$: ECM production rate;
- $\lambda$: tumor cell death rate;
- $\beta, \theta$: pressure coefficients.

## Discrete Boundedness-by-Entropy Method

The entropy of the model is defined by

$$H(u) = \int_\Omega h(u)dx = \int_\Omega \sum_{i=0}^{2} u_i(\log u_i - 1),$$

where $h(u)$ is the entropy density, as in [2].
In order to apply the Discrete Boundedness-by-Entropy Method the inequality

$$z^\top h''(u)A(u)z \ge c_A \sum_{i=1}^{n} u_i^{2(s-1)} z_i^2 \tag{3}$$

should be satisfied, for some $0 < c_A$ and $0 < s < 1$. However the matrix $A(u_1,u_2)$ only fulfills (3) for $s = 1$, see [2].
This can be overcome by adding an artificial diffusion term of the form $\delta\Delta u_i$ with $\delta > 0$ in both equations. Then (3) is satisfied with $s = 1/2$ and, formally,

$$\frac{dH}{dt} \ge \sum_{i=1}^{2} c\int_\Omega |\nabla u|^2 + \delta|\nabla\sqrt{u}|^2 + f(u)\cdot h'(u).$$

## Numerical Scheme

The implicit Euler finite-volume scheme is given by

$$\mathrm{m}(K)\frac{u_{i,K}^k - u_{i,K}^{k-1}}{\Delta t} + \sum_{\sigma\in\mathcal{E}_K} \mathcal{F}_{i,K,\sigma}^\delta = \mathrm{m}(K) f_i\left(u_K^k\right),$$

where the fluxes $\mathcal{F}_{i,K,\sigma}^\delta$ are defined as

$$\mathcal{F}_{i,K,\sigma}^\delta = -\sum_{j=1}^{n} \tau_\sigma (A_{ij}(u_\sigma^k) + \delta u_j^k)\mathrm{D}_{K,\sigma} u_j^k \quad \text{for } K\in\mathcal{T}, \sigma\in\mathcal{E}_K,$$

and $\mathcal{T}$ is a family of open polygonal control volumes, $\mathcal{E}_K$ is the set of edges of $K$. Moreover $\tau_\sigma$ is the transmissibility coefficient and $\mathrm{D}_{K,\sigma}v := v_{K,\sigma} - v_K$.

## Existence of Discrete Solutions

**Theorem 1:** *[Jüngel - Xh., Work in Progress 2024]*
There exists a solution $u^k = (u_1^k, u_2^k)$ with

$$u_i^k \in \mathcal{H}_\mathcal{T} = \left\{ v:\Omega\to\mathbb{R} : \exists (v_K)_{K\in\mathcal{T}} \subset \mathbb{R}^2, v(x) = \sum_{K\in\mathcal{T}} v_K \mathbf{1}_K(x) \right\}$$

to the finite volume scheme, satisfying $u_{i,K}^k \ge 0$ for all $K\in\mathcal{T}$, $k \ge 1$, and $i = 1,2$.

*Outline of proof.*
After adding artificial diffusion, (3) is satisfied with $s = 1/2$ and we can apply the Discrete Boundedness-by-Entropy Method.
Additionally, we obtain a discrete entropy inequality:

$$(1 - C_f\Delta t)\, H[u^k] + c_A\Delta t \sum_{i=1}^{n}\sum_{\sigma\in\mathcal{E}} \tau_\sigma (\mathrm{D}_\sigma u_i^k)^2 \le H[u^{k-1}] + C_f\Delta t. \tag{4}$$

□

## Convergence of the Scheme

**Theorem 2:** *[Jüngel - Xh., Work in Progress 2024]*
Let $(\mathcal{D}_m)_{m\in\mathbb{N}}$ be a family of admissible meshes and let $(u_m)_{m\in\mathbb{N}}$ be a family of finite-volume solutions to scheme constructed in **Theorem 1**.
Then there exists a function

$$u = (u_1,u_2) \in L^2\left(0,T; H^1(\Omega;\mathbb{R}^2)\right),$$

satisfying $u(x,t) \in \overline{\mathcal{O}}$ for a.e. $(x,t)\in\Omega_T$,
where $\mathcal{O} := \left\{u = \left(u_1,u_2\right) \in (0,1)^2 : \sum_{i=1}^2 u_i < 1\right\}$ is an open simplex, such that, up to a subsequence,

$$u_{i,m} \to u_i \quad \text{strongly in } L^p(\Omega_T), \quad 1 \le p < \infty,$$
$$\nabla^m u_{i,m} \rightharpoonup \nabla u_i \quad \text{weakly in } L^2(\Omega_T),$$

for $m\to\infty$ as well as $i = 1,2$ and $u$ is a weak solution to (1) and (2).

*Outline of proof.*
We deduce uniform estimates from the entropy inequality (4) and the compactness result from [3], giving a.e. convergence of a subsequence of $(u_m)$.
In the final step, we show that the limit satisfies (1) in the weak sense, i.e.

$$\int_0^T\int_\Omega u_i\partial_t\psi_i \,dx\,dt + \int_\Omega u_i^0\psi_i(0)dx = \int_0^T\int_\Omega \sum_{j=1}^{2}(A_{ij}(u) + \delta u_j)\nabla u_j\cdot\nabla\psi_i \,dx + \int_0^T\int_\Omega f_i(u)\psi_i \,dx\,dt$$

holds for all $\psi_i \in C_0^\infty(\Omega\times[0,T))$ and $i = 1,2$. □

## Further Topics

- *Numerical Simulations*;
- *Uniqueness of Discrete Solution*: via the Relative Entropy Method;
- *Stability Analysis for system without artificial diffusion*: the approach allows for the examination of the stability of equilibrium solutions by analyzing the eigenvalues of the linearized matrix $A(u)$.

### References


[1] T. Jackson and H. Byrne, *A mechanical model of tumor encapsulation and transcapsular spread*, Math. Biosci. 180, 2002

[2] A. Jüngel, A. Zurek, *A discrete boundedness-by-entropy method for finite-volume approximations of cross-diffusion systems*, IMA Journal of Numerical Analysis (2021) 43, 560–589.

[3] T. Gallouët, J.-C. Latché, *Compactness of discrete approximate solutions to parabolic PDEs—application to a turbulence model,* Commun. Pure Appl. Anal., 2012.


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