Convergence analysis of a numerical scheme for a tumour growth model

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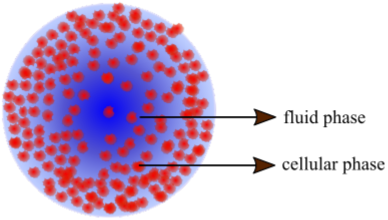
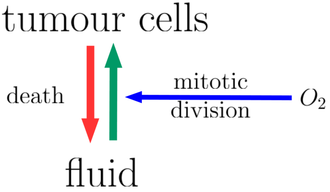
Model of tumour–growth



cross-section of tumour spheroid



Assumptions

- Cells and fluid exchange matter via the processes, cell division and cell death.
- Mass and momentum are conserved internally.
- No blood vessels. Limiting nutrient - Oxygen, follows diffusion.

- Domain – $0 < t < T$, $x \in \check{\Omega}(t) = (0, \check{\ell}(t))$.
- $\check{\ell}(t)$ – tumour length, $x = 0$ – tumour centre.
- $\check{\alpha}$ – volume fraction of tumour cells, $\check{u}$ – cell velocity, $\check{c}$ – oxygen tension.

Model of tumour growth

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cell volume fraction (hyperbolic conservation law)

$$\frac{\partial \check{\alpha}}{\partial t} + \frac{\partial}{\partial x}(\check{\alpha}\check{u}) = \underbrace{\frac{(1+s_1)\check{c}\check{\alpha}(1-\check{\alpha})}{1+s_1\check{c}}}_{\text{Birth rate}} - \underbrace{\frac{s_2+s_3\check{c}}{1+s_4\check{c}}\check{\alpha}}_{\text{Death rate}},$$

$$\alpha(0,x) = \alpha_0(x).$$

- $1+(1/s_1)$, s_2 – maximal birth and death rates, s_3/s_4 – minimal death rate.
- Set $f(\check{\alpha},\check{c}) = \frac{(1+s_1)(1-\check{\alpha})\check{c}}{1+s_1\check{c}} - \frac{s_2+s_3\check{c}}{1+s_4\check{c}}$

Model of tumour growth

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cell velocity (elliptic)

$$\frac{k\check{\alpha}\check{u}}{1-\check{\alpha}} - \mu \frac{\partial}{\partial x}\left(\alpha \frac{\partial \check{u}}{\partial x}\right) = -\frac{\partial}{\partial x}\left(\check{\alpha}\mathscr{H}(\check{\alpha})\right),$$

$$\check{u}(t,0) = 0, \quad \mu \frac{\partial \check{u}}{\partial x}(t, \ell(t)) = \mathscr{H}\left(\check{\alpha}(t, \ell(t))\right).$$

- μ – coefficient of viscosity of cell phase. k – interfacial drag coefficient.
- Set $\mathscr{H}(\check{\alpha}) = (\check{\alpha} - \alpha^*)^+/(1-\check{\alpha})^2$, $a^+ = \max(a, 0)$.

Model of tumour growth

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Oxygen tension (parabolic)

$$\frac{\partial \check{c}}{\partial t} - \frac{\partial^2 \check{c}}{\partial x^2} = \underbrace{-Q\check{\alpha}\check{c},}_{\text{Ox. consumption rate}}$$

$$\check{c}(0,x) = c_0(x), \quad \frac{\partial \check{c}}{\partial x}(t,0) = 0, \quad \check{c}(t,\ell(t)) = 1.$$

- Q – Maximum oxygen consumption rate.

Model of tumour growth

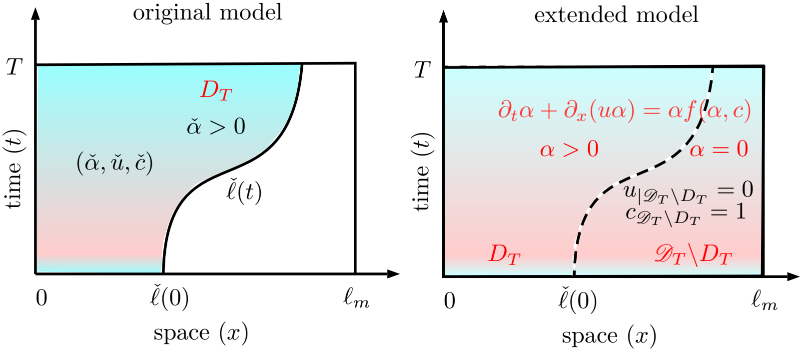
- Domain – $0 < t < T$, $x \in \check{\Omega}(t) = (0, \check{\ell}(t))$.
- $\check{\ell}(t)$ – tumour length, $x = 0$ – tumour centre.
- $\check{\alpha}$ – volume fraction of tumour cells, $\check{u}$ – cell velocity, $\check{c}$ – oxygen tension.

boundary evolution

$$\check{\ell}'(t) = \check{u}(t, \check{\ell}(t)),$$

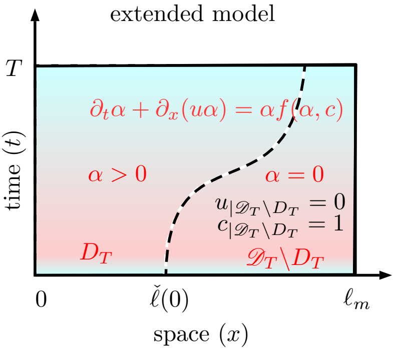
$$\check{\ell}(0) = 1.$$

Idea of extended model



- $\check{\ell}$ as the interface between $\alpha > 0$ and $\alpha = 0$.
- velocity and oxygen tension extended by 0 and 1, respectively.

Idea of threshold model



- $\check{\ell}$ as the interface between $\alpha > 0$ and $\alpha <= \alpha_{\text{thr}}$.
- velocity and oxygen tension extended by 0 and 1, resp.
- α_{thr} facilitates estimates on cell velocity and is required numerically.

Threshold solution

A threshold solution (with threshold $\alpha_{\text{thr}} \in (0,1)$) and domain D_T^{thr} of the threshold model in $\mathscr{D}_T$ is a 4-tuple (α, u, c, Ω) such that:

- $0 < m_{11} \leq \alpha_{|\Omega(t)} \leq m_{12} < 1$ for all $t \in [0,T]$,
- $m_{11} \leq m_{01}$, $m_{12} \geq m_{02}$
- $c \geq 0$,

and the following hold:

cell volume fraction

The volume fraction $\alpha \in L^\infty(\mathscr{D}_T)$ is such that $\forall \varphi \in \mathscr{C}_c^\infty([0,T) \times (0,\ell_m))$,

$$\int_{\mathscr{D}_T} (\alpha, u\alpha) \cdot \nabla_{t,x}\varphi \, \mathrm{d}t \, \mathrm{d}x + \int_{\Omega(0)} \varphi(0,x)\, \alpha_0 \, \mathrm{d}x + \int_{\mathscr{D}_T} (\alpha - \alpha_{\mathrm{thr}})^+ f(\alpha, c) \, \mathrm{d}x = 0.$$

tumour boundary

The set D_T^{thr} is of the form

$$D_T^{\text{thr}} = \cup_{0<t<T}\left(\{t\} \times \Omega(t)\right),$$

where $\Omega(t) = (0, \ell(t))$, and we have $\alpha \leq \alpha_{\text{thr}}$ on $\mathscr{D}_T \backslash D_T^{\text{thr}}$.

cell velocity

- $H^{1,u}_{\partial x}(D_T^{\text{thr}}) := \{v \in L^2(D_T^{\text{thr}}) : \partial_x v \in L^2(D_T^{\text{thr}})$ and $v(t,0) = 0 \,\forall t \in (0,T)\}$.
- $u \in H^{1,u}_{\partial x}(D_T^{\text{thr}})$ and $\forall v \in H^{1,u}_{\partial x}(D_T^{\text{thr}})$, satisfies

$$\int_0^T a^t(u(t,\cdot), v(t,\cdot))\,\mathrm{d}t = \int_0^T \mathcal{L}^t(v(t,\cdot))\,\mathrm{d}t, \tag{1}$$

where $a^t : H^1(\Omega(t)) \times H^1(\Omega(t)) \to \mathbb{R}$ is a bilinear form and $\mathcal{L}^t : H^1(\Omega(t)) \to \mathbb{R}$ is a linear form as follows:

$$a^t(u,v) = k\left(\frac{\alpha}{1-\alpha}u, v\right)_{\Omega(t)} + \mu\,(\alpha\partial_x u, \partial_x v)_{\Omega(t)} \text{ and} \tag{2}$$

$$\mathcal{L}^t(v) = (\mathscr{H}(\alpha), \partial_x v)_{\Omega(t)}. \tag{3}$$

Extend u to $\mathscr{D}_T$ by setting $u|_{\mathscr{D}_T \setminus \overline{D_T^{\text{thr}}}} := 0$.

Threshold solution

oxygen tension

- $H^{1,c}_{\partial x}(D^{\text{thr}}_T) := \{v \in L^2(D^{\text{thr}}_T) : \partial_x v \in L^2(D^{\text{thr}}_T)$ and $v(t,\ell(t)) = 0 \; \forall t \in (0,T)\}$.
- $c - 1 \in H^{1,c}_{\partial x}(D^{\text{thr}}_T)$ satisfies,

$$-\int_{D^{\text{thr}}_T} c\,\partial_t v \,\mathrm{d}x\,\mathrm{d}t + \lambda \int_{D^{\text{thr}}_T} \partial_x c\,\partial_x v \,\mathrm{d}x\,\mathrm{d}t - \int_{\Omega(0)} c_0(x) v(0,x)\,\mathrm{d}x - Q\int_{D^{\text{thr}}_T} \alpha c v \,\mathrm{d}x\,\mathrm{d}t = 0, \quad (1)$$

$\forall v \in H^{1,c}_{\partial x}(D^{\text{thr}}_T)$ such that $\partial_t v \in L^2(D^{\text{thr}}_T)$. Extend c to $\mathscr{D}_T$ by setting $c|_{\mathscr{D}_T \setminus \overline{D^{\text{thr}}_T}} := 1$.

Threshold value - comments

- To obtain a lower bound strictly greater than zero for α.
- Facilitates bounded variation estimates on α.
- To obtain supremum norm bounds on u and $\partial_x u$.

Threshold value - comments

- To obtain a lower bound strictly greater than zero for α.
- Facilitates bounded variation estimates on α.
- To obtain supremum norm bounds on u and $\partial_x u$.

An unavoidable disadvantage

- Residual volume fraction - creates spurious growth outside the tumour domain.
- Essential from numerical vantage point.
- Modified source term $(\alpha - \alpha_{\text{thr}})^+ f(\alpha, c)$ eliminates spurious growth.
- As $\alpha_{\text{thr}} \to 0$, $(\alpha - \alpha_{\text{thr}})^+ f(\alpha, c)$ approaches $\alpha f(\alpha, c)$.

Discrete scheme

- Space: $0 = x_0 < \cdots < x_J = \ell_m$, Time: $0 = t_0 < \cdots t_n = T$
- Uniform discretisation: $\delta = t_{n+1} - t_n$, $h = x_{j+1} - x_j$.

scheme

- volume fraction: α_h^n - upwind finite volume scheme.
- Set $\ell_h^n = \min\{x_j : \alpha_j^n < \alpha_{\text{thr}} \text{ on } (x_j, \ell_m)\}$ and $\Omega_h^n := (0, \ell_h^n)$.
- Conforming Lagrange $\mathbb{P}^1$-FEM to obtain $u^n_{h|\Omega_h^n}$, and set $u_h^n = 0$ outside Ω_h^n.
- Time-implicit mass lumped $\mathbb{P}^1$-FEM to obtain $c^n_{h|\Omega_h^n}$, and set $c_h^n = 1$ outside Ω_h^n.

Definition (Time-reconstruct)

For a family of functions $(f_h^n)_{\{0 \leq n < N\}}$ on a set X, define the time-reconstruct $f_{h,\delta} : (0,T) \times X \to \mathbb{R}$ as $f_{h,\delta} := f_h^n$ on $[t_n, t_{n+1})$ for $0 \leq n < N$.

Discrete solution

Definition (Time-reconstruct)

For a family of functions $(f_h^n)_{\{0\leq n<N\}}$ on a set X, define the time-reconstruct $f_{h,\delta} : (0,T) \times X \to \mathbb{R}$ as $f_{h,\delta} := f_h^n$ on $[t_n, t_{n+1})$ for $0 \leq n < N$.

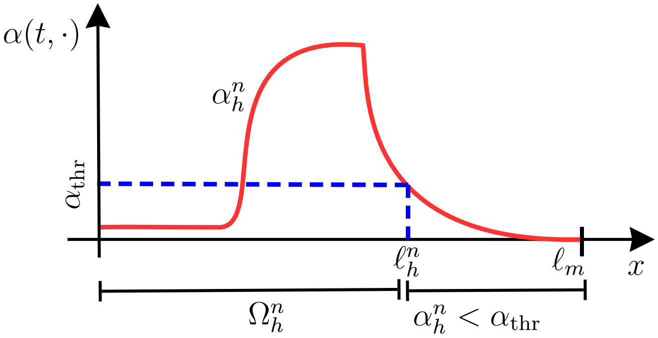
Definition (Discrete solution)

The 4-tuple $(\alpha_{h,\delta}, u_{h,\delta}, c_{h,\delta}, \ell_{h,\delta})$, where $\alpha_{h,\delta}$, $u_{h,\delta}$, $c_{h,\delta}$, and $\ell_{h,\delta}$ are the respective time-reconstructs corresponding to the families $(\alpha_h^n)_n$, $(u_h^n)_n$, $(c_h^n)_n$, and $(\ell_h^n)_n$ is called the discrete solution.

Why a mixed numerical scheme?

Finite volume method

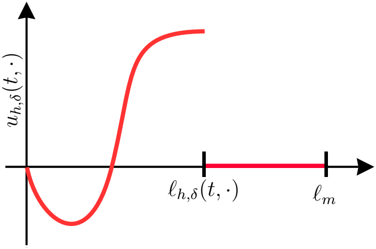
- Respects mass conservation property at the discrete level.
- Upwind flux (+ CFL) yields a stable scheme.
- FVM - significant numerical diffusion.
- Large error in locating ℓ_h^n as the boundary where α_h^n becomes 0.
- Solution: Locate ℓ_h^n as $\min\{x_j : \alpha_h^n < \alpha_{\text{thr}} \text{ on } (x_j, \ell_m]\}$.



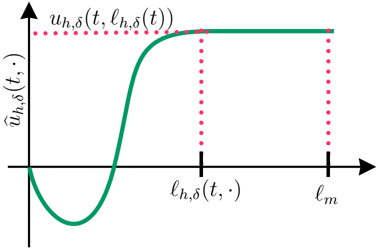
Why a mixed numerical scheme?

Finite element methods

- Velocity equation - elliptic, oxygen tension equation - parabolic.
- Unknown Lagrange $\mathbb{P}^1$-FEM - boundary nodes of (x_j, x_{j+1}), and easy to compute the upwind flux.
- Mass lumping in oxygen tension equation is crucial to obtain L^∞ bounds.
- Time-implicitness yields stability in $L^2(0,T;H^1(0,\ell_m))$.



(a) $u_{h,\delta}(t,\cdot)$.



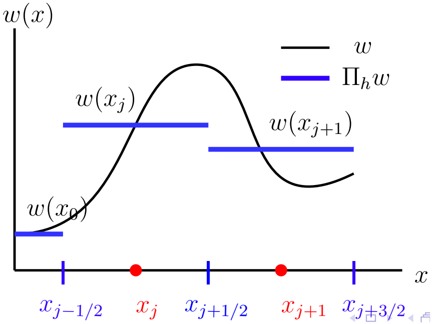
(b) $\widehat{u}_{h,\delta}(t,\cdot)$.

Figure: The left-hand side plot illustrates the discontinuous function $u_{h,\delta}$ and the right-hand side plot illustrates the continuous modification $\widehat{u}_{h,\delta}$.

Few notations

Mass lumping operator

- Set $\widetilde{\chi}_j = (x_j - h/2, x_j + h/2)$, $\mathcal{S}_{h,ML}$ – piecewise constant functions on $\widetilde{\chi}_j$.
- Mass lumping operator: $\Pi_h : \mathscr{C}^0([0,L]) \to \mathcal{S}_{h,ML}$ such that $\Pi_h w = \sum_{j=0}^{J} w(x_j) \mathbf{1}_{\widetilde{\chi}_j}$.
- Set $\Pi_{h,\delta} c_{h,\delta}$ by $\Pi_{h,\delta} c_{h,\delta}(t,\cdot) := \Pi_h(c_{h,\delta}(t,\cdot))$.



Few notations

Time-dependent spaces

$$L^2_c(0,T;H^1(0,\ell_m)) := \{f \in L^2(0,T;H^1(0,\ell_m)) : f(t,\ell(t)) = 0 \text{ for a.e. } t \in [0,T]\},$$

$$L^2_u(0,T;H^1(0,\ell_m)) := \{f \in L^2(0,T;H^1(0,\ell_m)) : f(t,0) = 0 \text{ for a.e. } t \in [0,T]\}.$$

Theorem (compactness)

Let the properties stated below be true.

- *The initial volume fraction* α_0 *belongs to* $BV(0,\ell_m)$ *and* $0 < m_{01} \le \alpha_0 \le m_{02} < 1$, *where* m_{01} *and* m_{02} *are constants.*
- *The discretisation parameters* h *and* δ *satisfy the following conditions:*

$$\rho \mathscr{C}_{CFL} \le \frac{\delta}{h} \le \mathscr{C}_{CFL} := \frac{\sqrt{a_*}\mu}{2\ell_m} \frac{|1-a^*|^2}{|a^*-\alpha^*|} \text{ and}$$

$$\delta < \min\left(\frac{1-\rho}{s_2}, \frac{2(1-\rho)}{1+s_2}\right),$$

where ρ, a_* *and* a^* *are constants chosen such that* $\rho < 1$, $0 < a_* < m_{01}$, *and* $0 < m_{02} < a^*$.

Main Theorem I - Conclusions

Theorem (compactness)

Then, there exists a finite time $T_* = T_*(\rho, a_*, a^*)$, *a subsequence of the family of functions* $\{(\alpha_{h,\delta}, \widehat{u}_{h,\delta}, c_{h,\delta}, \ell_{h,\delta})\}_{h,\delta}$ *and a 4-tuple of functions* $(\alpha, \widehat{u}, c, \ell)$ *such that*

- $\alpha \in BV(\mathscr{D}_{T_*})$
- $c \in L^2_c(0, T_*; H^1(0, \ell_m))$
- $\widehat{u} \in L^2_u(0, T_*; H^1(0, \ell_m))$
- $\ell \in BV(0, T_*)$

with $\mathscr{D}_{T_*} = (0, T_*) \times (0, \ell_m)$ *and as* $h, \delta \to 0$,

- $\alpha_{h,\delta} \to \alpha$ *almost everywhere and in* L^∞ *weak** *on* $\mathscr{D}_{T_*}$,
- $\Pi_{h,\delta} c_{h,\delta} \to c$ *strongly in* $L^2(\mathscr{D}_{T_*})$ *and* $\partial_x c_{h,\delta} \rightharpoonup \partial_x c$ *weakly in* $L^2(\mathscr{D}_{T_*})$,
- $\widehat{u}_{h,\delta} \rightharpoonup \widehat{u}$ *and* $\partial_x \widehat{u}_{h,\delta} \rightharpoonup \partial_x \widehat{u}$ *weakly in* $L^2(\mathscr{D}_{T_*})$, *and*
- $\ell_{h,\delta} \to \ell$ *almost everywhere in* $(0, T_*)$.

Main Theorem II

Theorem (convergence)

Let $(\alpha, \widehat{u}, c, \ell)$ *be the limit provided by the compactness theorem. Define* $\Omega(t) := (0, \ell(t))$ *and the threshold domain*

$$D^{\mathrm{thr}}_{T_*} := \{(t,x) : x < \ell(t), t \in (0, T_*)\}$$

and let $u := \widehat{u}$ *on* $D^{\mathrm{thr}}_{T_*}$ *and* $u := 0$ *on* $\mathscr{D}_{T_*} \backslash D^{\mathrm{thr}}_{T_*}$. *Then,* (α, u, c, Ω) *is a threshold solution with* $T = T_*$.

Idea for proof of Main Theorem I

- Proof is through inductive arguments on time-step, n.
- Fix two constants $a^* \in (\max(\alpha^*, m_{02}), 1)$ and $a_* \in (0, \min(\alpha_{\text{thr}}, m_{01}))$.
- The time of existence T_* on a^* and a_*, and is explicitly provided by Theorem (well-posedness).

Theorem (well-posedness)

For all $n \in \mathbb{N}$ such that $t_n \leq T_*$, $\alpha_{h,\delta}(t_n, \cdot)$, $u_{h,\delta}(t_n, \cdot)$, and $c_{h,\delta}(t_n, \cdot)$ are well defined, and it holds:

- $a_* < \alpha_{h,\delta}(t_n, \cdot)_{|\Omega_h^n} < a^*$,
- $0 \leq c_{h,\delta}(t_n, \cdot)_{|(0,\ell_m)} \leq 1$.

- Necessary compactness results proved using supremum norm bounds from the Theorem (well-posedness).

Proof of well-posedness Theorem

Step 1: Energy estimate of $\tilde{u}_h^n$

There exists a unique solution $\widetilde{u}_h^n$ to discrete weak form of velocity equation in Ω_h^n and it satisfies the following estimates:

$$\left\| \sqrt{\alpha_{h,\delta}(t_n,\cdot)}\partial_x \widetilde{u}_h^n \right\|_{0,\Omega_h^n} \leq \frac{\sqrt{\ell_m}|a^* - \alpha^*|}{\mu|1-a^*|^2} \text{ and}$$

$$\left\| \frac{\sqrt{\alpha_{h,\delta}(t_n,\cdot)}\widetilde{u}_h^n}{\sqrt{1-\alpha_{h,\delta}(t_n,\cdot)}} \right\|_{0,\Omega_h^n} \leq \sqrt{\frac{\ell_m}{k\mu}\frac{|a^* - \alpha^*|}{|1-a^*|^2}}.$$

- Keeping the coefficients yields optimal estimates, which improves the existence time T_*.
- Estimate on $\partial_x \widetilde{u}_h^n$ yields

$$||u_{h,\delta}(t_n,\cdot)||_{L^\infty(0,\ell_m)} \leq \frac{\ell_m}{\sqrt{a_*}\mu}\frac{|a^* - \alpha^*|}{|1-a^*|^2}. \qquad (3)$$

.

Proof of well-posedness Theorem

Step 3: BV and L^∞ bound on $\partial_x u_{h,\delta}(t_n,\cdot)$

It holds:

$$||\mu\alpha_{h,\delta}(t_n,\cdot)\partial_x u_{h,\delta}(t_n,\cdot) - \mathscr{H}(\alpha_{h,\delta}(t_n,\cdot))||_{BV(0,\ell_m)} \leq \ell_m \sqrt{\frac{k}{\mu}} \frac{|a^* - \alpha^*|}{|1-a^*|^{5/2}},$$

$$||(\mu\alpha_{h,\delta}(t_n,\cdot)\partial_x u_{h,\delta}(t_n,\cdot))^-||_{L^\infty(0,\ell_m)} \leq \ell_m \sqrt{\frac{k}{\mu}} \frac{|a^* - \alpha^*|}{|1-a^*|^{5/2}},$$ and

$$||\mu\alpha_{h,\delta}(t_n,\cdot)\partial_x u_{h,\delta}(t_n,\cdot)||_{L^\infty(0,\ell_m)} \leq \ell_m \sqrt{\frac{k}{\mu}} \frac{|a^* - \alpha^*|}{|1-a^*|^{5/2}} + \frac{a^*(a^*-\alpha^*)}{(1-a^*)^2}.$$

Proof of well-posedness Theorem

Step 3: L^∞ bound on $\alpha_{h,\delta}(t_n,\cdot)$

There exists $T_* > 0$ such that if $n+1 \leq N_* := T_*/\delta$, then

$$a_* \leq \min_{j\,:\,x_j\in\Omega_h^{n+1}} \alpha_j^{n+1} \leq \max_{0\leq j\leq J-1} \alpha_j^{n+1} \leq a^*.$$

Step 4: L^∞ bound on $c_{h,\delta}(t_n,\cdot)$

The discrete weak form corresponding to the oxygen tension equation has a unique solution $\widetilde{c}_h^{n+1}$ in Ω_h^n, and it holds $0 \leq \widetilde{c}_h^{n+1} \leq 1$.

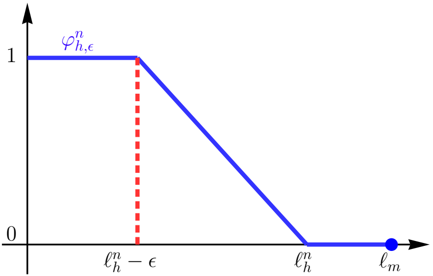
Check-list of compactness estimates

1. a uniform $L^2(0,T_*;H^1(0,\ell_m))$ estimate for the family $\{c_{h,\delta}\}_{h,\delta}$ − weak $L^2(0,T_*;H^1(0,\ell_m))$ convergence.
2. a uniform spatial and temporal BV estimate for the family $\{\alpha_{h,\delta}\}_{h,\delta}$ − strong $L^p(\mathscr{D}_{T_*})$ convergence.
3. a uniform BV estimate for the family $\{\ell_{h,\delta}\}_{h,\delta}$ − strong $L^p(0,T_*)$ convergence.
4. the family $\{\Pi_{h,\delta}c_{h,\delta}\}_{h,\delta}$ is relatively compact in $L^2(\mathscr{D}_{T_*})$ − strong $L^2(\mathscr{D}_{T_*})$ convergence.
5. a uniform $L^2(0,T_*;H^1(0,\ell_m))$ estimate for the family $\{\widehat{u}_{h,\delta}\}_{h,\delta}$ − weak $L^2(0,T_*;H^1(0,\ell_m))$ convergence .

Definition

Auxiliary function Define $\widehat{c}_{h,\delta} := c_{h,\delta} - 1$. For a fixed $\epsilon > 0$, define the auxiliary function $\varphi^n_{h,\epsilon} : [0, \ell_m] \to [0, 1]$ by

$$\varphi^n_{h,\epsilon}(x) = \begin{cases} 1 & 0 \le x \le \ell^n_h - \epsilon, \\ (\ell^n_h - x)/\epsilon & \ell^n_h - \epsilon < x \le \ell^n_h, \\ 0 & \ell^n_h < x \le \ell_m. \end{cases}$$



- The mass lumped function can be split into

$$\Pi_{h,\delta}\widehat{c}_{h,\delta} = \Pi_{h,\delta}(\widehat{c}_{h,\delta}\varphi_{h,\epsilon}) + \Pi_{h,\delta}(\widehat{c}_{h,\delta}(1-\varphi_{h,\epsilon})),$$

where $\varphi_{h,\epsilon} = \varphi^n_{h,\epsilon}$ on $[t_n, t_{n+1})$ for $0 \le n \le N_* - 1$.

- The second term can be bounded by:

$$||\Pi_{h,\delta}(\widehat{c}_{h,\delta}(1-\varphi_{h,\epsilon}))||_{L^2(\mathscr{D}_{T_*})} \le \sqrt{T_*\epsilon}.$$

Theorem

The family of functions $\{\Pi_{h,\delta}(\varphi_{h,\epsilon}\widehat{c}_{h,\delta})\}_{h,\delta}$ *is relatively compact in* $L^2(\mathscr{D}_{T_*})$.

- Proof follows from the Discrete Aubin - Simon Theorem.

Theorem

The family of functions $\{\Pi_{h,\delta}c_{h,\delta}\}_{h,\delta}$ *is relatively compact in* $L^2(\mathscr{D}_{T_*})$.

- Proof follows from the fact $\epsilon > 0$,

$$\{\Pi_{h,\delta}\widehat{c}_{h,\delta}\}_{h,\delta} \subset \{\Pi_{h,\delta}(\varphi_{h,\epsilon}\widehat{c}_{h,\delta})\}_{h,\delta} + B_{L^2(\mathscr{D}_{T_*})}\left(0; \sqrt{T_*\epsilon}\right).$$

Idea of proof of convergence theorem

1. The domains

$$A_{h,\delta} := \{(t,x) : x < \ell_{h,\delta}(t), t \in (0,T_*)\}$$

converge to

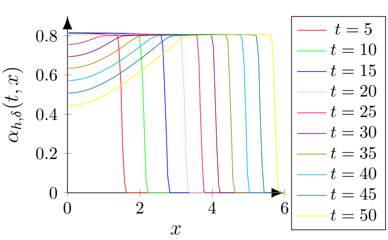
$$D_{T_*}^{\mathrm{thr}} := \{(t,x) : x < \ell(t), t \in (0,T_*)\}.$$

2. The limit function α satisfies the weak form (volume fraction) with $T = T_*$.
3. The restricted limit function $\widehat{u}_{|D_{T_*}^{\mathrm{thr}}}$ satisfies weak form (cell velocity) with $T = T_*$.
4. The limit function $c_{|D_{T_*}^{\mathrm{thr}}}$ satisfies weak form (oxygen tension) with $T = T_*$.

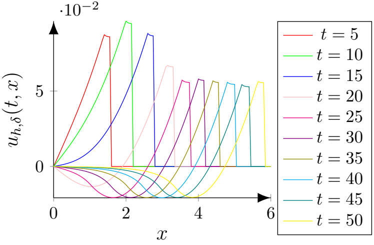
Parameters

- $k = 1$, $\mu = 1$, $Q = 0.5$, $s_1 = 10 = s_4$, $s_2 = 0.5 = s_3$, $\alpha^* = 0.8$[1].
- The bounds of the cell volume fraction are set to be $a_* = 0.4$ and $a^* = 0.82$.
- The extended domain length ℓ_m is set as 10.
- The threshold value is taken as $\alpha_{\text{thr}} = 0.1$.
- $\rho = 0.1$, $\delta = 1\text{E}-3$ and $h = 5\text{E}-2$.
- Set $T_* = 50$.
- Predicted time by compactness theorem: $1\text{E}-7$ to $1\text{E}-1$.

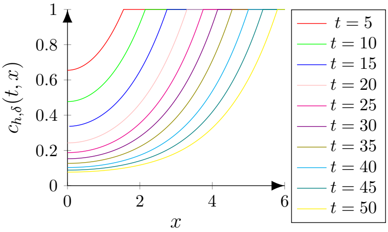
[1] Breward, C.J.W., Byrne, H.M. and Lewis, C.E., 2002. The role of cell-cell interactions in a two-phase model for avascular tumour growth. *J. of Math. Bio.*, 45(2), pp. 125-152.



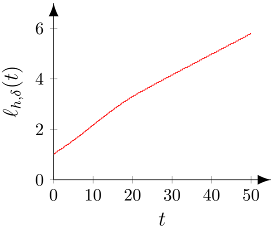
(a) cell volume fraction



(b) cell velocity



(c) oxygen tension



(d) tumour radius

Conclusive remarks

- Sufficiency of compactness and convergence theorems - Existence of solutions beyond T_* is possible.
- Convergence theorem guarantees existences of a domain $D_T^{\alpha_{\text{thr}}}$. However, it is not known whether it is unique.
- Framework can be extended to similar problems and models.
- Higher dimensional study (on going work).

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Thanks