97^{th} **KAAS Seminar**

Existence and uniqueness results for biphasic mixture models to tumors

Meraj Alam, Ph.D.
Assistant Professor, Department of Mathematics
Mahindra University Hyderabad-500043, Telangana, India

25th Aug 2021

Outline

1. What we model?
   - Major Objectives
   - Biphasic mixture Theory/Mathematical Models
2. Nonlinear Biphasic mixture model for an in-vivo tumor: existence and uniqueness results
   - Steady-State Governing Equations
   - Assumptions
   - Governing Equations
   - Linear weak formulation
3. Nonlinear Biphasic mixture model for an in-vitro tumor: existence and uniqueness results
   - Case-(a): Hydraulic resistivity as a function of displacement
   - Comments on the inequalities
   - Observations & Future outlook
4. References

What we model?

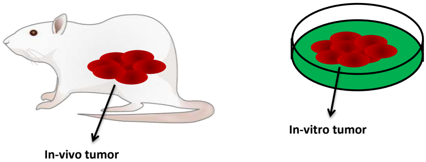


Figure: Cartoon of an in-vivo and in-vitro tumor

- We focuses on the mathematical modeling of the coupled phenomena of fluid flow and solid phase deformation (poroelastohydrodynamics) inside soft biomaterials, such as a tumor.
- Typical approaches: (a) Long time scale - growth model (b) Short time scale - no growth - transport scale

continue...

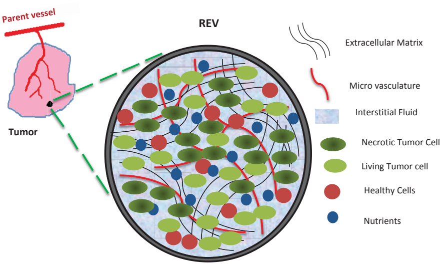


Figure: Anatomy of tumor within a representative elementary volume (REV)

- Deformable solid phase: cell population, fibrous matrix (ECM) and vascular space.
- Fluid phase: blood flow through blood vessels and interstitial fluid.
- Homogenized model: biphasic mixture approach assuming tumor as a homogeneous deformable porous medium

Major Objectives

- Developing biphasic mixture mathematical model (governed by linear/nonlinear PDEs) describing poroelastohydrodynamics in an in-vitro (in-vivo) tumor.
- Studying well-posedness in weak sense to the corresponding governing submodels.
- Developing 1d spherical symmetry solutions in simplified cases of a tumor and numerical simulations in 2d & 3d.

Biphasic mixture Theory

Mass conservation equations for fluid and solid phases:

$$\frac{\partial(\tilde{\rho}_f \varphi_f)}{\partial t} + \nabla \cdot [(\tilde{\rho}_f \varphi_f)\mathbf{V}_f] = \tilde{\rho}_f S_f(x,t) \text{ in } \Omega_T = \Omega \times (0,T) \quad (1)$$

$$\frac{\partial(\tilde{\rho}_s \varphi_s)}{\partial t} + \nabla \cdot [(\tilde{\rho}_s \varphi_s)\mathbf{V}_s] = \tilde{\rho}_s S_s(x,t), \text{ in } \Omega_T = \Omega \times (0,T) \quad (2)$$

Momentum balance equation for fluid and solid phases:

$$\rho_f \left(\frac{\partial \mathbf{V}_f}{\partial t} + (\mathbf{V}_f \cdot \nabla)\mathbf{V}_f \right) = \nabla \cdot \mathbf{T}_f + \mathbf{\Pi}_f + \mathbf{b}_f, \text{ in } \Omega_T \quad (3)$$

$$\rho_s \left(\frac{\partial \mathbf{V}_s}{\partial t} + (\mathbf{V}_s \cdot \nabla)\mathbf{V}_s \right) = \nabla \cdot \mathbf{T}_s + \mathbf{\Pi}_s + \mathbf{b}_s, \text{ in } \Omega_T \quad (4)$$

Fluid stress:

$$\mathbf{T}_f = -[\varphi_f P - \lambda_f \nabla \cdot \mathbf{V}_f]\mathbf{I} + \mu_f(\nabla \mathbf{V}_f + (\nabla \mathbf{V}_f)^{tr}), \quad (5)$$

Solid stress:

$$\mathbf{T}_s = -[(\varphi_s P) - \chi_s(\varphi_s)(\nabla \cdot \mathbf{U}_s)]\mathbf{I} + \mu_s(\varphi_s)(\nabla \mathbf{U}_s + (\nabla \mathbf{U}_s)^{tr}). \quad (6)$$

Barry et al. [1991], Ambrosi and Preziosi [2002], Dey and Sekhar [2016]

Nonlinear Biphasic mixture model for an in-vivo tumor: existence and uniqueness results

Assumptions

(A1). We assume neither the tumor nor the normal tissue are growing and all elastic parameters (Ξ_s^i, χ_s^i and μ_s^i etc.) are independent of volume fractions (Byrne and Preziosi [2003],Dey et al. [2018]).

(A2). Nutrient perfusion and transport occur on much shorter timescales than the timescale for tumor and healthy cell growth$\Rightarrow$ $\frac{\partial \varphi_s^i}{\partial t} = 0$; $\frac{\partial \varphi_s^i}{\partial x} = 0$; and $\tilde{S}_s^i = 0$ (Dey et al. [2018]).

(A3). The motion of the cells and the interstitial fluid flow are so slow that the inertial terms can be neglected $\Rightarrow |(\nabla \cdot \mathbf{V}_j^i)\mathbf{V}_j^i| << 1$ (Wang and Parker [1995], Byrne and Preziosi [2003]).

(A4). The steady-state assumption allows us to ignore the time derivative of the solid and fluid phase velocities in both regions.

(A5). The only interaction forces that come into play in the tumor region are due to the frictional forces that the fluid encounters at the boundaries of the pore (Rajagopal [2007], Dey and Raja Sekhar [2016]).

Steady-State Governing equations

Statement of the Problem: find $(\mathbf{V}_f^o, P^o, \mathbf{U}_s^o)$ and $(\mathbf{V}_f^{in}, P^{in}, \mathbf{U}_s^{in})$ which satisfy the following nonlinear elliptic system of PDEs

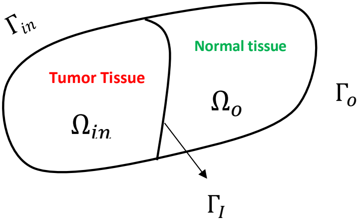
(a) In the normal tissue region, Ω_o :

$$(M_{1a}) \begin{cases} -\nabla \cdot [2\mu_f \mathbb{D}^f(\mathbf{V}_f^o) + (\lambda_f \nabla \cdot \mathbf{V}_f^o - \varphi_f^o P^o)\mathbf{I}] + K_o \mathbf{V}_f^o = \mathbf{b}_f^o, \\ -\nabla \cdot [2\mu_s^o \mathbb{D}^s(\mathbf{U}_s^o) + (\chi_s^o \nabla \cdot \mathbf{U}_s^o - \varphi_s^o P^o)\mathbf{I}] - K_o \mathbf{V}_f^o = \mathbf{b}_s^o, \\ \nabla \cdot (\varphi_f^o \mathbf{V}_f^o) = S_f^o. \end{cases}$$

(b) In the tumor tissue region, Ω_{in} :

$$(M_{1b}) \begin{cases} -\nabla \cdot (-\varphi_f^{in} P^{in} \mathbf{I}) + K_{in} \mathbf{V}_f^{in} = 0, \\ -\nabla \cdot [2\mu_s^{in} \mathbb{D}^s(\mathbf{U}_s^{in}) + (\chi_s^{in} \nabla \cdot \mathbf{U}_s^{in} - \varphi_s^{in} P^{in})\mathbf{I}] - K_{in} \mathbf{V}_f^{in} = \mathbf{b}_s^{in}, \\ \nabla \cdot (\varphi_f^{in} \mathbf{V}_f^{in}) = S_f^{in}. \end{cases}$$

Interface conditions



Interface conditions on Γ_I : [Hou et al., 1989, Young et al., 2019]

$$\mathbf{V}_f^o \cdot \mathbf{n}_1 + \mathbf{V}_f^{in} \cdot \mathbf{n}_2 = 0 \tag{7}$$

$$-\beta(\mathbf{T}_f^o \cdot \mathbf{n}_1) \cdot \mathbf{t} = \mathbf{V}_f^o \cdot \mathbf{t} \tag{8}$$

$$-(\mathbf{T}_f^o \cdot \mathbf{n}_1) \cdot \mathbf{n}_1 = \varphi_f^{in} P^{in} \tag{9}$$

$$\mathbf{U}_s^o = \mathbf{U}_s^{in} \tag{10}$$

$$\mathbf{T}_s^o \cdot \mathbf{n}_1 + \mathbf{T}_s^{in} \cdot \mathbf{n}_2 = 0, \tag{11}$$

Boundary conditions on Γ_o and Γ_{in} :

$$\mathbf{T}_f^o \cdot \mathbf{n}_1 = \mathbf{T}_\infty, \quad \mathbf{U}_s^o = 0 \ \text{ on } \ \Gamma_o, \quad \mathbf{V}_f^{in} \cdot \mathbf{n}_2 = 0, \quad \mathbf{U}_s^{in} = 0 \ \text{ on } \ \Gamma_{in}. \tag{12}$$

Non-dimensional governing equations

(a) In the normal tissue region, Ω_o :

$$(M_{1a}) \begin{cases} -\nabla \cdot [2Da\mathbb{D}^f(\mathbf{V}_1) + (\lambda Da \nabla \cdot \mathbf{V}_1 - \varphi_f^o P_1)\mathbf{I}] + K_o(\varsigma)\mathbf{V}_1 = \mathbf{b}_f^o, \\ -\nabla \cdot [2\varrho_1^o \mathbb{D}^s(\mathbf{U}_1) + (\varrho_2^o \nabla \cdot \mathbf{U}_1 - \varphi_s^o P_1)\mathbf{I}] - K_o(\varsigma)\mathbf{V}_1 = \mathbf{b}_s^o, \\ \nabla \cdot (\varphi_f^o \mathbf{V}_1) + a_0(P_1 - 1) = 0; \end{cases}$$

(b) In the tumor tissue region, Ω_{in} :

$$(M_{1b}) \begin{cases} -(\varphi_f^{in})^2 \nabla \cdot [(K_{in}(\varsigma))^{-1} \nabla P_2] + b_0(P_2 - 1) = 0, \\ -\nabla \cdot [2\varrho_1^{in} \mathbb{D}^s(\mathbf{U}_2) + (\varrho_2^{in} \nabla \cdot \mathbf{U}_2 - \varphi_s^{in} P_2)\mathbf{I}] + \varphi_f^{in} \nabla P_2 = \mathbf{b}_s^{in}. \end{cases}$$

continue...

Interface conditions on Γ_I: (Hou et al. [1989], Young et al. [2019])

$$\mathbf{V}_1 \cdot \mathbf{n}_1 = \varphi_f^{in}(K_{in}(\varsigma))^{-1}\nabla P_2 \cdot \mathbf{n}_2; \qquad \mathbf{U}_1 = \mathbf{U}_2, \tag{13}$$

$$\frac{1}{\beta^*}\sqrt{K_I(\mathbf{x})}\mathbf{V}_1 \cdot \mathbf{t} = -([2Da\mathbb{D}^f(\mathbf{V}_1) + (\lambda Da\nabla \cdot \mathbf{V}_1 - \varphi_f^o P_1)\mathbf{I}] \cdot \mathbf{n}_1) \cdot \mathbf{t}, \tag{14}$$

$$-([2Da\mathbb{D}^f(\mathbf{V}_1) + (\lambda Da\nabla \cdot \mathbf{V}_1 - \varphi_f^o P_1)\mathbf{I}] \cdot \mathbf{n}_1) \cdot \mathbf{n}_1 = \varphi_f^{in} P_2, \tag{15}$$

$$[2\varrho_1^o\mathbb{D}^s(\mathbf{U}_1) + (\varrho_2^o\nabla \cdot \mathbf{U}_1 - \varphi_s^o P_1)\mathbf{I}] \cdot \mathbf{n}_1 + [2\varrho_1^{in}\mathbb{D}^s(\mathbf{U}_2) + (\varrho_2^{in}\nabla \cdot \mathbf{U}_2 - \varphi_s^{in} P_2)\mathbf{I}] \cdot \mathbf{n}_2 = 0. \tag{16}$$

Boundary conditions:

$$[2Da\mathbb{D}^f(\mathbf{V}_1) + (\lambda Da\nabla \cdot \mathbf{V}_1 - \varphi_f^o P_1)\mathbf{I}] \cdot \mathbf{n}_1 = \mathbf{T}_\infty; \qquad \mathbf{U}_1 = 0 \text{ on } \Gamma_o, \tag{17}$$

$$\varphi_f^{in}(K_{in}(\varsigma))^{-1}\nabla P_2 \cdot \mathbf{n}_2 = 0; \qquad \mathbf{U}_2 = 0 \text{ on } \Gamma_{in}. \tag{18}$$

continue...

Here $\mathbb{D}^s$ and $\mathbb{D}^f$ represent the deformation and rate of deformation tensors which are defined as follows:

$$\mathbb{D}^s(\mathbf{U}_1) = \frac{1}{2}(\nabla \mathbf{U}_1 + (\nabla \mathbf{U}_1)^{t_r}), \quad \text{and} \quad \mathbb{D}^f(\mathbf{V}_1) = \frac{1}{2}(\nabla \mathbf{V}_1 + (\nabla \mathbf{V}_1)^{t_r}),$$

with $(\nabla \mathbf{V}_1)^{t_r}$ transpose of the matrix $(\nabla \mathbf{V}_1)$.

Hydraulic resistivity

For $\mathbf{x} \in \Omega$, we characterize the hydraulic resistivity in the following way

$$K(\mathbf{x}) = \begin{cases} K_o(\varsigma(\mathbf{x})), & \text{for } \mathbf{x} \in \Omega_o \\ K_{in}(\varsigma(\mathbf{x})), & \text{for } \mathbf{x} \in \Omega_{in} \end{cases} \tag{19}$$

where ς is equals to (a) $\nabla \cdot \mathbf{U}$ and (b) $\mathbf{U}$.

Structure of the hydraulic resistivity

$K(\mathbf{x}) = K(\varsigma(\mathbf{x}))$ where

(i) ς is a known function (Sun et al. [2002])

$$K(\mathbf{x}) = e^{-x}.$$

(ii) ς is **NOT** known

(a) $\boldsymbol{\varsigma} = \nabla \cdot \mathbf{U}_s$ (Klanchar and Tarbell [1987]),

$$K(\nabla \cdot \mathbf{U}_s) = (\gamma_1 + \gamma_2 \nabla \cdot \mathbf{U}_s).$$

(b) $\varsigma = \mathbf{U}_s$ (Sun et al. [2002]),

$$K(\mathbf{U}_s) = (\delta_0 |\mathbf{U}_s| + \delta_1).$$

Mathematical Tools

Let Ω be a bounded, open subset of $\mathbb{R}^d$, d=2,3. $L^2(\Omega)^d$ is the space of all measurable functions $\mathbf{u} = (u_1, u_2, \ldots, u_d)$ defined on Ω for which

$$||\mathbf{u}||_{0,\Omega} = \left(\int_\Omega \sum_{i=1}^{d} |u_i|^2 \, d\Omega \right)^{1/2} < +\infty, \tag{20}$$

For any two functions $\mathbf{u}$ and $\mathbf{v}$ the inner products $(\ ,\ )_\Omega$, is defined as

$$(\mathbf{u}, \mathbf{v})_\Omega = \int_\Omega \mathbf{u} \cdot \mathbf{v} \, d\Omega.$$

Function Spaces

The first order Sobolev space is defined as $H^1(\Omega)^d = \{\mathbf{u} \in L^2(\Omega)^d | \nabla \mathbf{u} \in (L^2(\Omega))^{d\times d}\}$ and the norm of a function $\mathbf{u} \in H^1(\Omega)^d$ is defined as

$$||\mathbf{u}||_{1,\Omega} = \left(||\mathbf{u}||^2_{0,\Omega} + ||\nabla \mathbf{u}||^2_{0,\Omega}\right)^{1/2}, \tag{21}$$

- $H^1_0(\Omega)^d = \{\mathbf{u} \in H^1(\Omega)^d | \ \mathbf{u}|_{\partial\Omega} = 0\}$.
- $H^1_{0,\Gamma}(\Omega)^d = \{\mathbf{u} \in H^1(\Omega)^d : \ \mathbf{u} = 0$ on $\Gamma\}$, where Γ is an open subset of $\partial\Omega$.

Lemma

(Temam [2001]) Let $\mathbb{X}$ be a finite dimensional Hilbert space with scalar product $\langle\cdot,\cdot\rangle$ and norm $||\cdot||$, and let G be a continuous mapping from $\mathbb{X}$ into itself such that

$$\langle G(x), x\rangle > 0 \ \ \textit{for} \ \ ||x|| = r_0 > 0.$$

Then, there exists a $x \in \mathbb{X}$, with $||x|| \leq r_0$ such that

$$\langle G(x), x\rangle = 0.$$

Inequalities

- Cauchy-Schwarz Inequality

$$(\mathbf{u}, \mathbf{v})_\Omega \leq ||\mathbf{u}||_{0,\Omega}||\mathbf{v}||_{0,\Omega}, \ \forall \ \mathbf{u}, \ \mathbf{v} \in L^2(\Omega)^d. \tag{22}$$

- Young's Inequality with ϵ

$$ab \leq \frac{a^2}{2\epsilon} + \frac{\epsilon b^2}{2} \quad (a, b \in \mathbb{R}_+, \ \epsilon > 0). \tag{23}$$

- Korn's Inequality

$$||\mathbf{V}||^2_{1,\Omega} \leq c_k \left(||\mathbf{V}||^2_{0,\Omega} + ||D(\mathbf{V})||^2_{0,\Omega}\right) \quad \forall \ \mathbf{V} \in H^1(\Omega)^d. \tag{24}$$

- Poincare's Inequality

$$||\mathbf{V}||^2_{0,\Omega} \leq c_p||\nabla\mathbf{V}||^2_{0,\Omega}, \ \forall \ \mathbf{V} \in H^1_0(\Omega)^d. \tag{25}$$

- Sobolev or embedding inequality

$$||\mathbf{V}||^2_{L^4(\Omega)} \leq c_s||\mathbf{V}||^2_{1,\Omega}, \ \forall \ \mathbf{V} \in H^1(\Omega)^d. \tag{26}$$

Mathematical Methods

- Derive variational (or weak) formulation using suitable functions spaces (Sobolev Spaces).
- Use Galerkin method, an application of Brouwer fixed point theorem and weak convergence to show the existence of a solution to the linear weak formulation.
- Use iterative method to prove the existence of a solution to the nonlinear weak formulation.
- Prove uniqueness of weak solutions and continuous dependence on the given data using the regular technique.

Alam et al. (2021) Applicable Analysis

Linear weak formulation

Choosing test functions $(\boldsymbol{\eta}, \boldsymbol{\xi}, w, q, \boldsymbol{\xi}) \in H^1(\Omega_o)^d \times H_0^1(\Omega)^d \times L^2(\Omega_o) \times H^1(\Omega_{in}) \times H_0^1(\Omega)^d$, then multiplying to each of the equations of the systems (M_{1a}) and (M_{1b}), respectively. Further, using integration by parts and summing all the equations, we get the following equivalent weak (or variational) formulation.

Linear weak formulation

For a given $\varsigma \in L^2(\Omega)$ (or $L^2(\Omega)^d$), the weak formulation will be: find $(\mathbf{V}_1, \mathbf{U}_1, P_1, P_2, \mathbf{U}_2) \in \mathbf{Y} = H^1(\Omega_o)^d \times H^1_{0,\Gamma_o}(\Omega_o)^d \times L^2(\Omega_o) \times H^1(\Omega_{in}) \times H^1_{0,\Gamma_{in}}(\Omega_{in})^d$ such that

$$
(A_w) \begin{cases}
2Da(\mathbb{D}^f(\mathbf{V}_1), \mathbb{D}^f(\boldsymbol{\eta}))_{\Omega_o} + \lambda Da(\nabla\cdot\mathbf{V}_1, \nabla\cdot\boldsymbol{\eta})_{\Omega_o} - \varphi_f^o(P_1, \nabla\cdot\boldsymbol{\eta})_{\Omega_o} \\
+(K_o(\varsigma)\mathbf{V}_1, \boldsymbol{\eta})_{\Omega_o} + \varphi_f^{in}(P_2, \boldsymbol{\eta}\cdot\mathbf{n}_1)_{\Gamma_I} + \frac{1}{\beta^*}(\sqrt{K_I(\mathbf{x})}\mathbf{V}_1\cdot\mathbf{t}, \boldsymbol{\eta}\cdot\mathbf{t})_{\Gamma_I} \\
+2\varrho_1^o(\mathbb{D}^s(\mathbf{U}_1), \mathbb{D}^s(\boldsymbol{\xi}))_{\Omega_o} + \varrho_2^o(\nabla\cdot\mathbf{U}_1, \nabla\cdot\boldsymbol{\xi})_{\Omega_o} - \varphi_s^o(P_1, \nabla\cdot\boldsymbol{\xi})_{\Omega_o} \\
-(K_o(\varsigma)\mathbf{V}_1, \boldsymbol{\xi})_{\Omega_o} + (\nabla\cdot(\varphi_f^o\mathbf{V}_1), w)_{\Omega_o} + a_0(P_1, w)_{\Omega_o} \\
+(\varphi_f^{in})^2((K_{in}(\varsigma))^{-1}\nabla P_2, \nabla q)_{\Omega_{in}} + b_0(P_2, q)_{\Omega_{in}} - \varphi_f^{in}(\mathbf{V}_1\cdot\mathbf{n}_1, q)_{\Gamma_I} \\
+2\varrho_1^{in}(\mathbb{D}^s(\mathbf{U}_2), \mathbb{D}^s(\boldsymbol{\xi}))_{\Omega_{in}} + \varrho_2^{in}(\nabla\cdot\mathbf{U}_2, \nabla\cdot\boldsymbol{\xi})_{\Omega_{in}} - \varphi_s^{in}(P_2, \nabla\cdot\boldsymbol{\xi})_{\Omega_{in}} \\
+\varphi_f^{in}(\nabla P_2, \boldsymbol{\xi})_{\Omega_{in}} - [(\mathbf{T}_\infty, \boldsymbol{\eta})_{\Gamma_o} + (\mathbf{b}_f^o, \boldsymbol{\eta})_{\Omega_o} \\
+(\mathbf{b}_s^o, \boldsymbol{\xi})_{\Omega_o} + (a_0, w)_{\Omega_o} + (b_0, q)_{\Omega_{in}} + (\mathbf{b}_s^{in}, \boldsymbol{\xi})_{\Omega_{in}}] = 0
\end{cases}
$$

holds for all $(\boldsymbol{\eta}, \boldsymbol{\xi}, w, q, \boldsymbol{\xi}) \in \mathbf{W} = H^1(\Omega_o)^d \times H^1_0(\Omega)^d \times L^2(\Omega_o) \times H^1(\Omega_{in}) \times H^1_0(\Omega)^d$.

Main Result: Linear case

(a). For $i \in \{o, in, I\}$, we assume that there exists two positive constants k_1 and k_2 such that

$$k_1 \leq K_i(x) \leq k_2 \quad \forall \quad x \in \mathbb{R}^d.$$

(b). $\mathbf{b}_i^o \in L^2(\Omega_o)^d$, $\mathbf{b}_s^{in} \in L^2(\Omega_{in})^d$ and $\mathbf{T}_\infty \in L^2(\Gamma_o)^d$.

Theorem

Let the data satisfy the assumptions (**a**) *and* (**b**) *and if the non-dimensional parameters and constants satisfy the following relations*

$$\frac{2\varrho_1^o}{c_k} > \frac{c_p k_2^2}{2k_1}, \qquad \frac{2\varrho_1^{in}}{c_k} > \frac{c_p k_2}{2}, \qquad \varrho_2^o \geq \frac{(\varphi_s^o)^2}{2a_0}, \qquad \varrho_2^{in} \geq \frac{(\varphi_s^{in})^2}{2b_0}, \tag{27}$$

Then, the weak formulation (A_w) *has a unique solution* $(\mathbf{V}_1, \mathbf{U}_1, P_1, P_2, \mathbf{U}_2) \in \mathbf{Y} = H^1(\Omega_o)^d \times H^1_{0,\Gamma_o}(\Omega_o)^d \times L^2(\Omega_o) \times H^1(\Omega_{in}) \times H^1_{0,\Gamma_{in}}(\Omega_{in})^d$ *which depends continuously on the given data.*

continue...

Further, the solution satisfies the following a priori bound.

$$\begin{aligned} &||\mathbf{V}_1||^2_{1,\Omega_o} + ||\nabla \mathbf{U}_1||^2_{0,\Omega_o} + ||\nabla \mathbf{U}_2||^2_{0,\Omega_{in}} + ||P_1||^2_{0,\Omega_o} + ||P_2||^2_{1,\Omega_{in}} \\ &\leq \frac{1}{\alpha_5^2}\Big[(||\mathbf{b}_f^o||_{0,\Omega_o} + \sqrt{c_t}||\mathbf{T}_\infty||_{0,\Gamma_o})^2 + ||\mathbf{b}_s^o||^2_{0,\Omega_o} + ||a_0||^2_{0,\Omega_o} \\ &\qquad + ||b_0||^2_{0,\Omega_{in}} + ||\mathbf{b}_s^{in}||^2_{0,\Omega_{in}}\Big], \end{aligned} \tag{28}$$

where

$$\alpha_5 = \min\left\{\alpha_3, \left(\frac{2\varrho_1^o}{c_k} - \frac{c_p k_2^2}{2k_1}\right), \frac{a_0}{2}, \alpha_4, \left(\frac{2\varrho_1^{in}}{c_k} - \frac{c_p k_2}{2}\right)\right\}, \tag{29}$$

and

$$\alpha_3 = \frac{1}{c_k}\min\left\{2Da, \frac{k_1}{2}\right\}, \quad \alpha_4 = \min\left\{\frac{(\varphi_f^{in})^2}{2k_2}, \frac{b_0}{2}\right\}. \tag{30}$$

Nonlinear case (a)

case-(a) $K = K(\nabla \cdot \mathbf{U})$.

Theorem

We assume that $\mathbf{b}_i^o \in L^2(\Omega_o)^d$, $\mathbf{b}_s^{in} \in L^2(\Omega_{in})^d$ *and* $\mathbf{T}_\infty \in L^2(\Gamma_o)^d$. *Further, assume that the hydraulic resistivities* K_i *are continuous from* $L^2(\Omega_i)$ *to* $L^2(\Omega_i)$ $(i \in \{o, in\})$ *and additionally* K_o *has the following affine structure*[a]

$$K_o(\nabla \cdot \mathbf{U}_1) = \gamma_1 + \gamma_2 \nabla \cdot \mathbf{U}_1, \tag{31}$$

where γ_i *are admissible constant such that* K_o *remains bounded. Then, the problem* $(A(\nabla \cdot \mathbf{U}))$ *has at least one solution* $(\mathbf{V}_1, \mathbf{U}_1, P_1, P_2, \mathbf{U}_2) \in \mathbf{Y} = H^1(\Omega_o)^d \times H^1_{0,\Gamma_o}(\Omega_o)^d \times L^2(\Omega_o) \times H^1(\Omega_{in}) \times H^1_{0,\Gamma_{in}}(\Omega_{in})^d$.

[a] Similar approximate structure is used by Klanchar and Tarbell [1987] in case of arterial tissue. We remark here that relaxing the structure (31) and showing the existence of a solution is an open problem.

Lemma

The sequence $\{\nabla \cdot \mathbf{U}^n|_{\Omega_{in}}\}_{n \geq 0}$ *converges strongly to* $\nabla \cdot \mathbf{U}|_{\Omega_{in}}$ *in* $L^2(\Omega_{in})$.

Nonlinear terms-iterative method

$$
\begin{aligned}
&\underbrace{((K_o(\nabla\cdot\mathbf{U}_1^n)-K_o(\nabla\cdot\mathbf{U}_1))\mathbf{V}_1^{n+1},\boldsymbol{\eta})_{\Omega_o}}+\underbrace{(K_o(\nabla\cdot\mathbf{U}_1)(\mathbf{V}_1^{n+1}-\mathbf{V}_1),\boldsymbol{\eta})_{\Omega_o}}\\
&\quad+(K_o(\nabla\cdot\mathbf{U}_1)\mathbf{V}_1,\boldsymbol{\eta})_{\Omega_o}-\underbrace{((K_o(\nabla\cdot\mathbf{U}_1^n)-K_o(\nabla\cdot\mathbf{U}_1))\mathbf{V}_1^{n+1},\boldsymbol{\xi})_{\Omega_o}}\\
&\quad-\underbrace{(K_o(\nabla\cdot\mathbf{U}_1)(\mathbf{V}_1^{n+1}-\mathbf{V}_1),\boldsymbol{\xi})_{\Omega_o}}-(K_o(\nabla\cdot\mathbf{U}_1)\mathbf{V}_1,\boldsymbol{\xi})_{\Omega_o}\\
&\quad+\underbrace{(\phi_f^{in})^2(((K_{in}(\nabla\cdot\mathbf{U}_2^n))^{-1}-(K_{in}(\nabla\cdot\mathbf{U}_2))^{-1})\nabla P_2^{n+1},\nabla q)_{\Omega_{in}}}\\
&\quad+\underbrace{(\phi_f^{in})^2((K_{in}(\nabla\cdot\mathbf{U}_2))^{-1}(\nabla P_2^{n+1}-\nabla P_2),\nabla q)_{\Omega_{in}}}\\
&\quad+(\phi_f^{in})^2((K_{in}(\nabla\cdot\mathbf{U}_2))^{-1}\nabla P_2,\nabla q)_{\Omega_{in}}.
\end{aligned}
$$

Uniqueness

Theorem

Assume that $(\mathbf{V}_{1,I}, \mathbf{U}_I, P_{1,I}, P_{2,I})$ *and* $(\mathbf{V}_{1,II}, \mathbf{U}_{II}, P_{1,II}, P_{2,II})$ *are two solutions of the nonlinear weak formulation* $A(\nabla \cdot \mathbf{U})$, *and the hydraulic resistivities* K_o *and* K_{in} *are Lipschitz continuous with Lipschitz constant* k_L. *Further, assume that there exists two non-negative constants* C_1 *and* C_2 *such that*

$$||\nabla P_{2,i}||_{L^4(\Omega_{in})^d} \leq C_1 \text{ and} \tag{32}$$

$$||\nabla(\mathbf{U}_I - \mathbf{U}_{II})||_{L^4(\Omega_{in})^d} \leq C_2 ||\nabla(P_{2,I} - P_{2,II})||_{0,\Omega_{in}}, \tag{33}$$

where $i \in \{I, II\}$ *and the non-dimensional parameters and constants satisfy the following relations*

$$\alpha_3 > \frac{k_L c_s \alpha_6}{2\alpha_5}, \; \frac{2\varrho_1^o}{c_k} > \left(\frac{c_p k_2^2}{2k_1} + \frac{k_L c_s \alpha_6}{\alpha_5}\right), \; \varrho_2^o \geq \left(\frac{(\varphi_s^o)^2}{2a_0} + \frac{k_L c_s \alpha_6}{2\alpha_5}\right),$$
$$\alpha_4 > \frac{(\varphi_f^{in})^2 k_L C_1 C_2}{k_1^2}, \; \frac{2\varrho_1^{in}}{c_k} > \frac{c_p k_2}{2}, \; \varrho_2^{in} \geq \frac{(\varphi_s^{in})^2}{2b_0}, \tag{34}$$

Then, we have $\mathbf{V}_{1,I} = \mathbf{V}_{1,II}$, *and* $P_{1,I} = P_{1,II}$ *a.e. in* Ω_o, $\mathbf{U}_I = \mathbf{U}_{II}$ *a.e. in* Ω, $P_{2,I} = P_{2,II}$ *a.e. in* Ω_{in}.

Uniqueness

Here,

$$\alpha_6 = \left[(||\mathbf{b}_f^o||_{0,\Omega_o} + \sqrt{c_t}||\mathbf{T}_\infty||_{0,\Gamma_o})^2 + ||\mathbf{b}_s^o||^2_{0,\Omega_o} + ||a_0||^2_{0,\Omega_o} + ||b_0||^2_{0,\Omega_{in}} + ||\mathbf{b}_s^{in}||^2_{0,\Omega_{in}} \right]^{1/2} \tag{35}$$

Corresponding Non-Linear Problem: case-(b)

$$\text{case-(b)}: \ K = K(\mathbf{U}).$$

Theorem

We assume that $\mathbf{b}_i^o \in L^2(\Omega_o)^d$, $\mathbf{b}_s^{in} \in L^2(\Omega_{in})^d$ *and* $\mathbf{T}_\infty \in L^2(\Gamma_o)^d$. *Further, assume that the hydraulic resistivities* K_i *are continuous from* $L^2(\Omega_i)$ *to* $L^2(\Omega_i)$ $(i \in \{o, in\})$. *Then, the problem* $(A(\mathbf{U}))$ *has at least one solution* $(\mathbf{V}_1, \mathbf{U}_1, P_1, P_2, \mathbf{U}_2) \in \mathbf{Y} = H^1(\Omega_o)^d \times H^1_{0,\Gamma_o}(\Omega_o)^d \times L^2(\Omega_o) \times H^1(\Omega_{in}) \times H^1_{0,\Gamma_{in}}(\Omega_{in})^d$.

Nonlinear terms-iterative method

$$
\begin{aligned}
&\underbrace{((K_o(\mathbf{U}_1^n) - K_o(\mathbf{U}_1))\mathbf{V}_1^{n+1}, \boldsymbol{\eta})_{\Omega_o}} + \underbrace{(K_o(\mathbf{U}_1)(\mathbf{V}_1^{n+1} - \mathbf{V}_1), \boldsymbol{\eta})_{\Omega_o}} \\
&\quad + (K_o(\mathbf{U}_1)\mathbf{V}_1, \boldsymbol{\eta})_{\Omega_o} - \underbrace{((K_o(\mathbf{U}_1^n) - K_o(\mathbf{U}_1))\mathbf{V}_1^{n+1}, \boldsymbol{\xi})_{\Omega_o}} \\
&\quad - \underbrace{(K_o(\mathbf{U}_1)(\mathbf{V}_1^{n+1} - \mathbf{V}_1), \boldsymbol{\xi})_{\Omega_o}} - (K_o(\mathbf{U}_1)\mathbf{V}_1, \boldsymbol{\xi})_{\Omega_o} \\
&\quad + \underbrace{(\phi_f^{in})^2(((K_{in}(\mathbf{U}_2^n))^{-1} - (K_{in}(\mathbf{U}_2))^{-1})\nabla P_2^{n+1}, \nabla q)_{\Omega_{in}}} \\
&\quad + \underbrace{(\phi_f^{in})^2((K_{in}(\mathbf{U}_2))^{-1}(\nabla P_2^{n+1} - \nabla P_2), \nabla q)_{\Omega_{in}}} + (\phi_f^{in})^2((K_{in}(\mathbf{U}_2))^{-1}\nabla P_2, \nabla q)_{\Omega_{in}}.
\end{aligned}
$$

Theorem

Assume that $(\mathbf{V}_{1,I}, \mathbf{U}_I, P_{1,I}, P_{2,I})$ *and* $(\mathbf{V}_{1,II}, \mathbf{U}_{II}, P_{1,II}, P_{2,II})$ *are two solutions of the nonlinear weak formulation* $(A(\mathbf{U}))$*, and the hydraulic resistivities* K_o *and* K_{in} *are Lipschitz continuous. Further, assume that there exists a non-negative constant* C_1 *such that*[a]

$$||\nabla P_{2,i}||_{L^4(\Omega_{in})^d} \leq C_1, \tag{36}$$

where $i \in \{I, II\}$ *and the non-dimensional parameters and constants satisfy the following relations*

$$\alpha_3 > \frac{k_L c_s \alpha_6 c_p^{1/2}}{2\alpha_5}, \; \frac{2\varrho_1^o}{c_k} > \left(\frac{c_p k_2^2}{2k_1} + \frac{k_L c_s \alpha_6 c_p^{1/2}}{\alpha_5}\right), \; \varrho_2^o \geq \frac{(\varphi_s^o)^2}{2a_0},$$
$$\alpha_4 > \frac{(\phi_f^{in})^2 k_L C_1 c_s^{1/2}}{2k_1^2}, \; \frac{2\varrho_1^{in}}{c_k} > \left(\frac{c_p k_2}{2} + \frac{(\varphi_f^{in})^2 k_L C_1 c_s^{1/2}}{2k_1^2}\right), \; \varrho_2^{in} \geq \frac{(\varphi_s^{in})^2}{2b_0}, \tag{37}$$

Then, we have $\mathbf{V}_{1,I} = \mathbf{V}_{1,II}$*,* $P_{1,I} = P_{1,II}$ *a.e. in* Ω_o*,* $\mathbf{U}_I = \mathbf{U}_{II}$ *a.e. in* Ω*,* $P_{2,I} = P_{2,II}$ *a.e. in* Ω_{in}*.*

[a] This is the smallness condition on the fluid phase velocity in the tumor region.

Nonlinear Biphasic mixture model for an in-vivo tumor: existence and uniqueness results

Non-dimensional governing equations

In Ω, we have

$$-\nabla\cdot(2D(\mathbf{V}_f)+\lambda(\nabla\cdot\mathbf{V}_f)\mathbf{I}-\phi_f P\mathbf{I})+\frac{1}{Da}\mathbf{K}(\varsigma)\mathbf{V}_f=\mathbf{b}_f, \tag{38}$$

$$-\nabla\cdot(\alpha_1 D(\mathbf{U}_s)+\alpha_2(\nabla\cdot\mathbf{U}_s)\mathbf{I}-\phi_s P\mathbf{I})-\frac{1}{Da}\mathbf{K}(\varsigma)\mathbf{V}_f=\mathbf{b}_s, \tag{39}$$

$$\nabla\cdot(\phi_f\mathbf{V}_f)=-a_0(P-1). \tag{40}$$

$$(2D(\mathbf{V}_f)+\lambda(\nabla\cdot\mathbf{V}_f)\mathbf{I}-\phi_f P\mathbf{I})\cdot\mathbf{n}=\mathbf{T}_\infty \text{ and } \mathbf{U}_s=0 \text{ on } \partial\Omega. \tag{41}$$

Nonlinear Weak formulation

Here, we assume $\varsigma = \mathbf{U}_s$ i.e. $\mathbf{K} = \mathbf{K}(\mathbf{U}_s)$ and denote $\mathbf{X} = H^1(\Omega)^d$, $\mathbf{X}_0 = H_0^1(\Omega)^d$, $M = L^2(\Omega)$. In this case, the weak formulation (Q_w) becomes: find $(\mathbf{V}_f, \mathbf{U}_s, P) \in \mathbf{X} \times \mathbf{X}_0 \times M$ such that

$$(Q(\mathbf{U}_s)) \begin{cases} 2(D(\mathbf{V}_f) : D(\mathbf{W}))_\Omega + \lambda(\nabla \cdot \mathbf{V}_f, \nabla \cdot \mathbf{W})_\Omega - \phi_f(P, \nabla \cdot \mathbf{W})_\Omega \\ + \frac{1}{Da}(\mathbf{K}(\mathbf{U}_s)\mathbf{V}_f, \mathbf{W})_\Omega + 2\alpha_1(D(\mathbf{U}_s) : D(\mathbf{Z}))_\Omega + \alpha_2(\nabla \cdot \mathbf{U}_s, \nabla \cdot \mathbf{Z})_\Omega \\ -\phi_s(P, \nabla \cdot \mathbf{Z})_\Omega - \frac{1}{Da}(\mathbf{K}(\mathbf{U}_s)\mathbf{V}_f, \mathbf{Z})_\Omega + \phi_f(\nabla \cdot \mathbf{V}_f, q)_\Omega + a_0(P, q)_\Omega \\ = (\mathbf{b}_f, \mathbf{W})_\Omega + (\mathbf{T}_\infty, \mathbf{W})_{\partial\Omega} + (\mathbf{b}_s, \mathbf{Z})_\Omega + (a_0, q)_\Omega \end{cases}$$

holds for all $(\mathbf{W}, \mathbf{Z}, q) \in \mathbf{X} \times \mathbf{X}_0 \times M$.

Assumptions on the data

(A) The parameters $\phi_f > 0,\ \phi_s > 0,\ \lambda \geq 0,\ \alpha_1 > 0,\ \alpha_2 > 0,\ a_0 > 0,\ Da > 0$ are known real constants, and the functions $\mathbf{b}_j \in L^2(\Omega)^d$ where $j = f,\ s,\ \mathbf{T}_\infty \in L^2(\partial\Omega)^d$ are also known.
$c_k > 0,\ c_p > 0,\ c_t > 0,\ c_s > 0$ are some real constants that appear in Korn's, Poincare's, trace and Sobolev inequalities, respectively[1].

(B) Assume $\mathbf{K} : \mathbb{R}^d \to \mathbb{R}^{d^2}$ is a symmetric uniformly positive definite matrix which is bounded. This ensures that there exist positive constants k_1 and k_2 such that for $\boldsymbol{\xi},\ \mathbf{x} \in \mathbb{R}^d$

$$\text{(i) } k_1 \boldsymbol{\xi} \cdot \boldsymbol{\xi} \leq \mathbf{K}(\mathbf{x})\boldsymbol{\xi} \cdot \boldsymbol{\xi} \quad \text{and} \quad \text{(ii) } |\mathbf{K}(\mathbf{x})| \leq k_2. \tag{42}$$

Existence and uniqueness results

Theorem

Suppose the assumptions **(A)** *and* **(B)** *hold. If the constants and the non-dimensional parameters satisfy the following conditions*

$$\frac{2\alpha_1}{c_k} > \frac{c_p k_2^2}{2k_1 Da}, \quad \alpha_2 \geq \frac{\phi_s^2}{2a_0}, \tag{43}$$

then for a given $\varsigma \in L^2(\Omega)^d$*, the problem* $(Q(\varsigma))$ *has a unique solution* $(\mathbf{V}_f, \mathbf{U}_s, P) \in \mathbf{X} \times \mathbf{X}_0 \times M$*. which continuously depends on the given data.*

Theorem

Assume that the hydraulic resistivity $\mathbf{K}$ *satisfies Lipschitz continuity property and the assumptions* **(A)** *and* **(B)** *hold then the nonlinear problem* $(Q(\mathbf{U}_s))$ *has a solution* $(\mathbf{V}_f, \mathbf{U}_s, P) \in \mathbf{X} \times \mathbf{X}_0 \times M$*. Further, if the constants and non-dimensional parameters satisfy the following conditions*

$$2\alpha Da > \frac{k_L \alpha_4 c_s}{\alpha_3}, \quad \frac{4\alpha_1 Da}{c_k} > \left(\frac{c_p k_2^2}{k_1} + \frac{k_L \alpha_4 c_s (c_p + 2\sqrt{c_p})}{\alpha_3}\right), \quad 2\alpha_2 \geq \frac{\phi_s^2}{a_0} \tag{44}$$

then $(Q(\mathbf{U}_s))$ *has a unique solution that continuously depends on the given data.*

Unbounded case: Existence

Theorem

Assume that the data and parameters satisfy the assumption **(A)** *and the condition* (i) *of assumption* **(B)** *and in addition the hydraulic resistivity* $\mathbf{K}$ *is Lipschitz continuous. If the constants satisfy the following assumption*

$$\frac{2\alpha_1}{c_k} > \frac{c_s k_0 c_p^{1/2} \alpha_4^*}{\alpha_3^* Da}, \tag{45}$$

then the nonlinear weak formulation $(Q(\mathbf{U}_s))$ *has a solution* $(\mathbf{V}_f, \mathbf{U}_s, P) \in \mathbf{X} \times \mathbf{X}_0 \times M$ *such that*

$$||(\mathbf{V}_f, P)||_{\mathbf{X}\times M} \leq \frac{1}{\min\{\alpha^*, a_0\}} \left[(||\mathbf{b}_f||_{0,\Omega} + \sqrt{c_t}||\mathbf{T}_\infty||_{0,\partial\Omega})^2 + a_0^2|\Omega| \right]^{1/2}, \tag{46}$$

where

$$||(\mathbf{V}_f, P)||_{\mathbf{X}\times M} = (||\mathbf{V}_f||_{1,\Omega}^2 + ||P||_{0,\Omega}^2)^{1/2},$$

continue...

$$||\nabla \mathbf{U}_s||_{0,\Omega} \leq \frac{1}{\left(\frac{2\alpha_1}{c_k} - \frac{c_s k_0 c_p^{1/2} \alpha_4^*}{\alpha_3^* Da}\right)} \left[c_p^{1/2}||\mathbf{b}_s||_{0,\Omega} + \frac{\alpha_4^*}{\alpha_3^*}\left(\phi_s + \frac{c_s k_0 |\Omega|}{Da}\right)\right], \tag{47}$$

where $|\Omega|$ denotes the area or volume of the domain Ω, and

$$\alpha_4^* = \left[(||\mathbf{b}_f||_{0,\Omega} + \sqrt{c_t}||\mathbf{T}_\infty||_{0,\partial\Omega})^2 + a_0^2|\Omega|\right]^{1/2}, \quad \alpha_3^* = \min\{\alpha^*, a_0\}. \tag{48}$$

Here, $\alpha^* = \frac{1}{c_k}\min\{2, \frac{k_1}{Da}\}$.

Unbounded case: uniqueness

Remark

We note that uniqueness in this case holds whenever the non-dimensional parameters and constants satisfy the following assumptions

$$\frac{2\alpha^* Da}{c_s} > \left[\frac{k_L \alpha_4^*}{\alpha_3^*} + \sqrt{2}k_0(\sqrt{|\Omega|} + \sqrt{c_p}\alpha_5^*)\right], \quad \alpha_2 \geq \frac{\phi_s^2}{2a_0}, \tag{49}$$

$$\frac{4\alpha_1 Da}{c_k c_s} > \left[\frac{k_L \alpha_4^*}{\alpha_3^*}(c_p + 2\sqrt{c_p}) + \sqrt{2}k_0(\sqrt{|\Omega|} + \sqrt{c_p}\alpha_5^*)\right]. \tag{50}$$

The detailed proof of uniqueness can be shown as in Theorem 4.

Case-(b)

Theorem

Assume that the hydraulic resistivity $\mathbf{K}$ admits the following form

$$\mathbf{K}(\nabla \cdot \mathbf{U}_s) = (\gamma_1 + \gamma_2 \nabla \cdot \mathbf{U}_s)\mathbf{I}, \tag{51}$$

with γ_1 and γ_2 such that $\mathbf{K}$ satisfies the assumption **(B)**, *($\mathbf{I}$ identity matrix of order d) and given data as in assumption* **(A)** *then the nonlinear problem $(Q(\nabla \cdot \mathbf{U}_s))$ has a solution $(\mathbf{V}_f, \mathbf{U}_s, P) \in \mathbf{X} \times \mathbf{X}_0 \times M$. Further, if the constants and the non-dimensional parameters satisfy the following conditions*

$$2\alpha Da > \frac{\gamma_2 c_s \alpha_4}{\alpha_3}, \frac{4\alpha_1 Da}{c_k} > \left(\frac{c_p k_2^2}{k_1} + \frac{\gamma_2 c_s \alpha_4}{\alpha_3} \right), \alpha_2 \geq \left(\frac{\phi_s^2}{2a_0} + \frac{\gamma_2 c_s \alpha_4}{\alpha_3 Da} \right) \tag{52}$$

then $(Q(\nabla \cdot \mathbf{U}_s))$ has a unique solution that continuously depends on the given data.

Comments on the inequalities

Dimensionless parameter	Description	Range of values	Supporting References
Da	Darcy's number (Dimensionless specific permeability of tumor)	$10^{-4} - 10^{-1}$	Dey and Sekhar [2016], Dey et al. [2018]
α_t	Strength of transvascular solute perfusion inside tumor tissue	$0 < \alpha_t \leq 10$	Netti et al. [1997]
ϱ_t	Dimensionless Young's modulus (YM) corresponding to tumor tissues	$10^2 \leq \varrho_t \leq 10^5$	Dey et al. [2018]
ν_p	Poisson ratio (PR) corresponding to tumor tissues	$0.45 \leq \nu_p \leq 0.49$	Roose et al. [2007], Islam et al. [2020]
ϕ_f	Volume fraction of fluid phase inside tumor tissue	$0.6 \leq \phi_f \leq 0.8$	Dey and Sekhar [2016], Dey et al. [2018]
K	Non-dimensional hydraulic conductivity corresponding to tumor interior	$0.00006 \leq K \leq 1.4$	Dey et al. [2018]

Table: Different dimensionless poro-elasto-hydrodynamics parameters corresponding to tumor tissue with their value range.

Comments on the inequalities

For $d = 3$, choose Ω as a d-dimensional ($d = 3$) sphere of unit radius (in dimension 1mm) $|\Omega| = \frac{4\pi}{3}$, $|\partial\Omega| = 4\pi$.

$\mathbf{b}_i = 0$, $i \in \{f, s\}$, $\mathbf{T}_\infty = 1$,

$c_k(\Omega) > 0,\; c_p(\Omega) > 0,\; c_s(d) > 0,\; c_t(\Omega, d) > 0$ as follows:
$c_k = 2$ $(or\ 3)$ for $H_0^1(\Omega)^d$, (or $H^1(\Omega)^d$), Bernstein and Toupin [1960], Salsa [2016]

$c_p = 1/2$, $c_s = 1/2$, Attouch et al. [2014], $c_t = 2$ Salsa [2016].

For $Da = 10^{-3}$, $\alpha_t = 1$, $\varrho_t = 10^4$, $\nu_p = 0.45$, $k_1 = 0.5$, $k_2 = 1.4$, $\phi_s = 0.4$, $L_r A_r = 1$, $k_L = 2 \times 10^{-3}$, $\gamma_2 = 2 \times 10^{-3}$, and $0 < k_0 \leq 1$, we verify the inequalities (43), (44), (45), and (52).

The constraints (49) and (50) which ensure the uniqueness for arbitrary $\mathbf{K}$ hold when we choose $Da = 10^{-1}$, and $k_0 = 10^{-2}$ with the remaining parameters as chosen above.

Observations & Future outlook

- We observed that the nonlinear structure of hydraulic resistivity plays an important role to establish the existence and uniqueness results. In the case of dilatation dependent hydraulic resistivity, one has to consider an affine structure to develop the existence and uniqueness results.
- Open questions observed during above analysis.
- Closed form solution in 1d and Numerical simulation in higher dimensions (2d & 3d).

References

Davide Ambrosi and Luigi Preziosi. On the closure of mass balance models for tumor growth. *Mathematical Models and Methods in Applied Sciences*, 12(05):737–754, 2002.

Hedy Attouch, Giuseppe Buttazzo, and Gérard Michaille. *Variational analysis in Sobolev and BV spaces: applications to PDEs and optimization*. SIAM, 2014.

SI Barry, KH Parkerf, and GK Aldis. Fluid flow over a thin deformable porous layer. *Zeitschrift für angewandte Mathematik und Physik ZAMP*, 42(5):633–648, 1991.

B Bernstein and R Toupin. Korn inequalities for the sphere and circle. *Archive for Rational Mechanics and Analysis*, 6(1):51–64, 1960.

Helen Byrne and Luigi Preziosi. Modelling solid tumour growth using the theory of mixtures. *Mathematical Medicine and Biology*, 20(4):341–366, 2003.

Bibaswan Dey and GP Raja Sekhar. A theoretical study on the elastic deformation of cellular phase and creation of necrosis due to the convection reaction process inside a spherical tumor. *International Journal of Biomathematics*, 9(06):1650095, 2016.

Bibaswan Dey and GP Raja Sekhar. Hydrodynamics and convection enhanced macromolecular fluid transport in soft biological tissues: Application to solid tumor. *Journal of Theoretical Biology*, 395:62–86, 2016.

Bibaswan Dey, GP Raja Sekhar, and Sourav Kanti Mukhopadhyay. In vivo mimicking model for solid tumor towards hydromechanics of tissue deformation and creation of necrosis. *Journal of biological physics*, pages 1–40, 2018.

JS Hou, MH Holmes, WM Lai, and VC Mow. Boundary conditions at the cartilage-synovial fluid interface for joint lubrication and theoretical verifications. *Journal of Biomechanical Engineering*, 111(1):78–87, 1989.

Md Tauhidul Islam, Songyuan Tang, Chiara Liverani, Ennio Tasciotti, and Raffaella Righetti. Non-invasive imaging of young's modulus and poisson's ratio in cancers in vivo. *Science Report*, 10:7266, 2020.

M Klanchar and JM Tarbell. Modeling water flow through arterial tissue. *Bulletin of Mathematical Biology*, 49(6):651–669, 1987.

Paolo A Netti, Laurence T Baxter, Yves Boucher, Richard Skalak, and Rakesh K Jain. Macro-and microscopic fluid transport in living tissues: Application to solid tumors. *AIChE journal*, 43(3):818–834, 1997.

KR Rajagopal. On a hierarchy of approximate models for flows of incompressible fluids through porous solids. *Mathematical Models and Methods in Applied Sciences*, 17(02):215–252, 2007.

Tiina Roose, S Jonathan Chapman, and Philip K Maini. Mathematical models of avascular tumor growth. *SIAM Review*, 49(2): 179–208, 2007.

Sandro Salsa. *Partial differential equations in action: from modelling to theory*, volume 99. Springer, 2016.

Shuyu Sun, Béatrice Riviere, and Mary F Wheeler. A combined mixed finite element and discontinuous galerkin method for miscible displacement problem in porous media. In *Recent progress in computational and applied PDEs*, pages 323–351. Springer, 2002.

Roger Temam. *Navier-Stokes equations: theory and numerical analysis*, volume 343. American Mathematical Soc., 2001.

Wen Wang and Kim H Parker. The effect of deformable porous surface layers on the motion of a sphere in a narrow cylindrical


Thank you