Laboratoire Jacques-Louis Lions, Inria, Team Mamba

On the incompressible limit of a tumor growth model incorporating convective effects

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Introduction

How to model living tissue? A mechanical point of view

- Tissue: **multi-phase fluid**
  - extra cellular matrix
  - proliferating cells
  - dead cells
  - quiescent cells
  - interstitial fluid
  - ...
- Notion of **pressure**:
  - drives the cells **movement**
  - controls the proliferation: **contact inhibition**

Figure 1: Graphical representation of cell division

Macroscopic models

- **Systems of PDEs**
  - **Parabolic - Hyperbolic** (compressible models)
  - **Cahn - Hillard models** (4^{th} order)

$$\begin{cases} \partial_t n = \nabla \cdot (b(n) \nabla p) \\ p = W'(n) - \delta \Delta n \end{cases}$$

- **Free boundary problems**
  - **Geometrical** or **incompressible** models (Hele Shaw model)
  - Dynamics of $\Omega(t)$

$$\begin{cases} -\Delta p = G(p), \text{ in } \Omega(t) \\ V = -\nabla p \cdot \nu, \text{ on } \partial\Omega(t) \end{cases}$$

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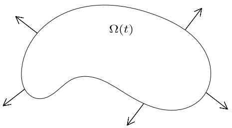

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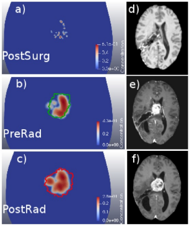

Agosti et al. 2017

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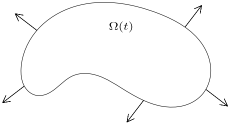

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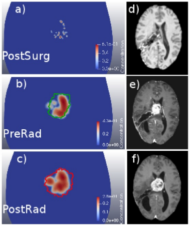

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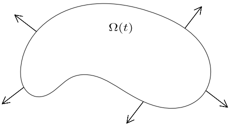

How can we link *compressible* and *geometrical* models?

Incompressible limit

Mechanical tumor growth model with drift

$$\partial_t n = \underbrace{\nabla \cdot (n \nabla p)}_{\text{pressure effect}} + \underbrace{nG(p)}_{\text{growth term}}$$

- $n(x,t)$ cell population density
- $p(x,t)$ internal pressure
- $\vec{v} = -\nabla p,$ Darcy's law

Mechanical tumor growth model with drift

$$\partial_t n = \underbrace{\nabla \cdot (n \nabla p)}_{\text{pressure effect}} - \underbrace{\nabla \cdot (n \nabla \Phi)}_{\text{drift effect}} + \underbrace{nG(p)}_{\text{growth term}}$$

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- $\vec{v} = -\nabla p + \nabla \Phi$,
- $\Phi(x,t)$ concentration of a chemical or a nutrient

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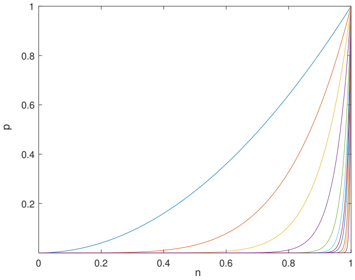
- $\vec{v} = -\nabla p + \nabla \Phi$,
- $\Phi(x, t)$ concentration of a chemical or a nutrient
- pressure law of state:

$$p = n^{\gamma}, \gamma > 1$$

Incompressible limit

$$p = n^\gamma$$



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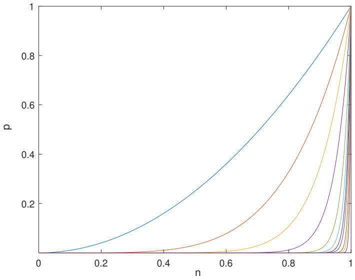

Passing to the **limit $\gamma \to \infty$**

$$\begin{cases} p_\infty = 0, & \text{if } n_\infty < 1 \\ p_\infty \in [0, \infty) & \text{if } n_\infty = 1 \end{cases} \qquad \Rightarrow \qquad p_\infty(1 - n_\infty) = 0$$

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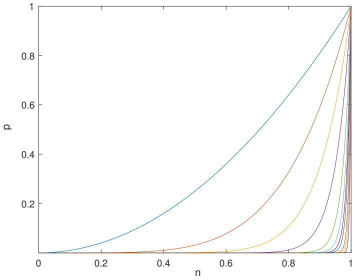

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We define $\Omega(t) := \{x;\ p_\infty(x,t) > 0\} \leftarrow$ **region occupied by the tumor**

Complementarity relation

Multiplying

$$\partial_t n = \nabla \cdot (n \nabla p) - \nabla \cdot (n \nabla \Phi) + nG(p, c), \qquad p = n^\gamma$$

by $\gamma n^{\gamma-1}$

$$\partial_t p = \gamma p(\Delta p - \Delta \Phi + G(p)) + |\nabla p|^2 - \nabla p \cdot \nabla \Phi$$

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Passing, **formally**, to the limit $\gamma \to \infty$:

Complementarity relation

$$p_\infty(\Delta p_\infty - \Delta \Phi + G(p_\infty)) = 0$$

Limit model

The **Hele-Shaw problem** reads

$$\begin{cases} -\Delta p_\infty = G(p_\infty) - \Delta\Phi, & \text{in } \Omega(t) = \{x;\ p_\infty(x,t) > 0\} \\ p_\infty = 0, & \text{on } \partial\Omega(t) \end{cases}$$

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Moreover,

$$\partial_t p_\infty = |\nabla p_\infty|^2 - \nabla p_\infty \cdot \nabla\Phi,\ \text{on } \partial\Omega(t)$$

so the normal **boundary velocity** is

$$V = -\partial_\nu p_\infty + \partial_\nu \Phi$$

Free boundary problem

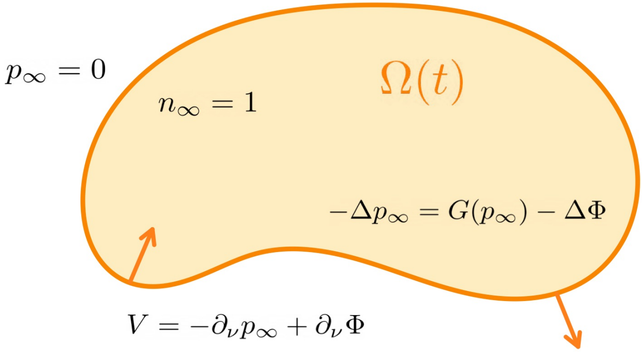

Figure 2: Graphical representation of the limit model when $\gamma \to \infty$

How to prove it rigorously?

Incompressible limit of model with drift (D.- Schmidtchen 2021)

Theorem: limit $\gamma \to \infty$

$p_\gamma \to p_\infty, \;\; n_\gamma \to n_\infty \le 1$ in $L^1_{x,t}$

$\nabla p_\gamma \rightharpoonup \nabla p_\infty$ weakly in $L^2_{x,t}$

$$\partial_t n_\infty = \nabla \cdot (n_\infty \nabla p_\infty) - \nabla \cdot (n_\infty \nabla \Phi) + n_\infty G(p_\infty)$$

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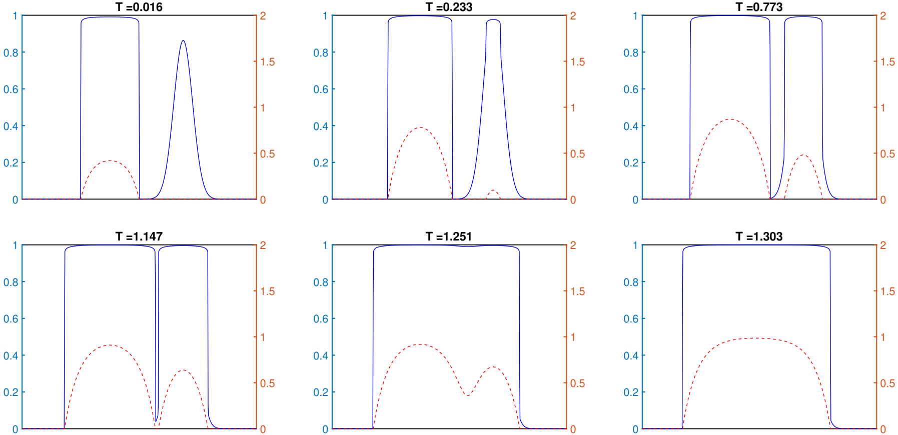
Complementarity relation $\Longleftrightarrow$ L^2-strong compactness of ∇p_γ

Solutions behavior in 1D



Density (blue line), pressure (red dashed line), $\gamma = 90$

Strategy

Uniform a priori estimates:

- $n_\gamma, p_\gamma \in BV(\mathbb{R}^d \times (0,\infty))$
- $\nabla p_\gamma \in L^2(\mathbb{R}^d \times (0,\infty))$

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- an L^4-**optimal** bound of ∇p_γ

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$$|\nabla p_\gamma| \in L^4(\mathbb{R}^d \times (0,\infty))$$

- an L^3-version of the **Aronson-Bénilan estimate**

$$|\Delta p_\gamma + G(p_\gamma)|_- \in L^3(\mathbb{R}^d \times (0,\infty))$$

Important: on the free boundary Δp_γ is a measure: crucial to control Δp_γ itself and not merely $p_\gamma \Delta p_\gamma$

Conclusions and perspectives

Main result

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Perspectives:

$$\begin{cases} \partial_t n_1 = \nabla \cdot (n_1 \nabla p) + n_1 F_1(p) + n_2 G_1(p), \\ \partial_t n_2 = \nabla \cdot (n_2 \nabla p) + n_1 F_2(p) + n_2 G_2(p), \\ p = (n_1 + n_2)^\gamma, \quad \gamma > 1 \end{cases}$$

- Incompressible limit? (recent preprint by J.G. Liu and X. Xu)

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- Incompressible limit?
- Existence?

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Thank you!