Laboratoire Jacques-Louis Lions, Sorbonne Université, Inria, Team Mamba

On the incompressible limit of tumor growth models with nutrients and convective effects

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Based on joint works with Benoit Perthame, Markus Schmidtchen, Xinran Ruan

Virtual Summer school on Kinetic and fluid equations for collective dynamics

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Introduction

How to model living tissue? A mechanical point of view

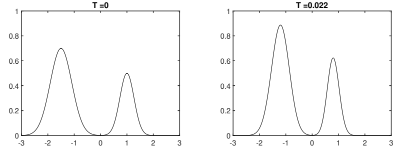
- Tissue: **multi-phase fluid**
  - extra cellular matrix
  - proliferating cells
  - dead cells
  - quiescent cells
  - interstitial fluid
  - ...
- Notion of **pressure**:
  - drives the cells **movement**
  - controls the proliferation: **contact inhibition**

Figure 1: Graphical representation of cell division

Macroscopic models of tumor growth

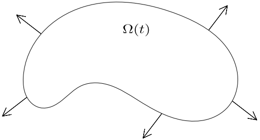
Compressible models

$$\partial_t n = \nabla \cdot (n \nabla p) - \nabla \cdot (n \nabla \Phi) + nG$$



Free boundary problems

$$\begin{cases} -\Delta p = G(p), \text{ in } \Omega(t) = \{p > 0\} \\ V = -\nabla p \cdot \nu, \text{ on } \partial\Omega(t) \end{cases}$$



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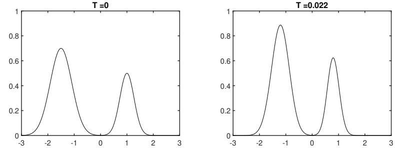

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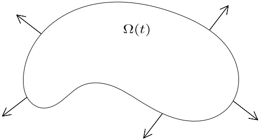

How can we link *compressible* and *geometrical* models?

Incompressible limit

Mechanical tumor growth model with drift and nutrient

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

- $n(x,t)$ cell population density, $x \in \mathbb{R}^d, t \in [0,T]$
- $p(x,t)$ internal pressure
- $\vec{v} = -\nabla p$, Darcy's law

Mechanical tumor growth model with drift and nutrient

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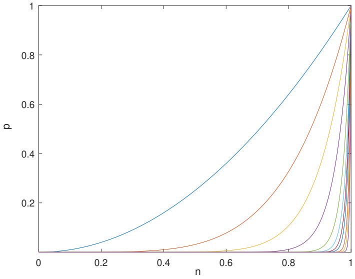
- pressure law of state:

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

Incompressible limit

$$p = n^{\gamma}$$



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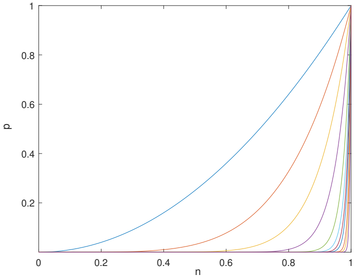

Passing to the **limit $\gamma \to \infty$**

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

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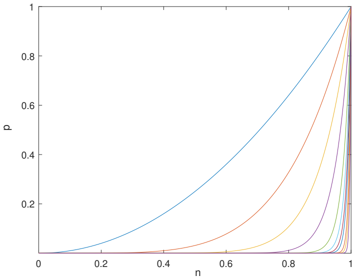

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We define $\Omega(t) := \{x;\ p_\infty(x,t) > 0\} \subset \{x; n_\infty(x,t) = 1\}$

Complementarity relation

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

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The **Hele-Shaw problem** reads

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Moreover

$$V = -\partial_\nu p_\infty + \partial_\nu \Phi, \text{ on } \partial\Omega(t)$$

How to prove it rigorously?

Incompressible limit of model with drift and nutrient

Theorem: limit $\gamma \to \infty$

$p_\gamma \to p_\infty, \ \ n_\gamma \to n_\infty, \ \ c_\gamma \to c_\infty$ in $L^q_{x,t}$ for all $1 \leq q < \infty$

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

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$$\begin{cases} \partial_t n_\infty & = \nabla \cdot (n_\infty \nabla p_\infty) - \nabla \cdot (n_\infty \nabla \Phi) + n_\infty G(p_\infty, c_\infty) \\ \partial_t c_\infty & = \Delta c_\infty - n_\infty H(c_\infty) + K(p_\infty, c_\infty) \end{cases}$$

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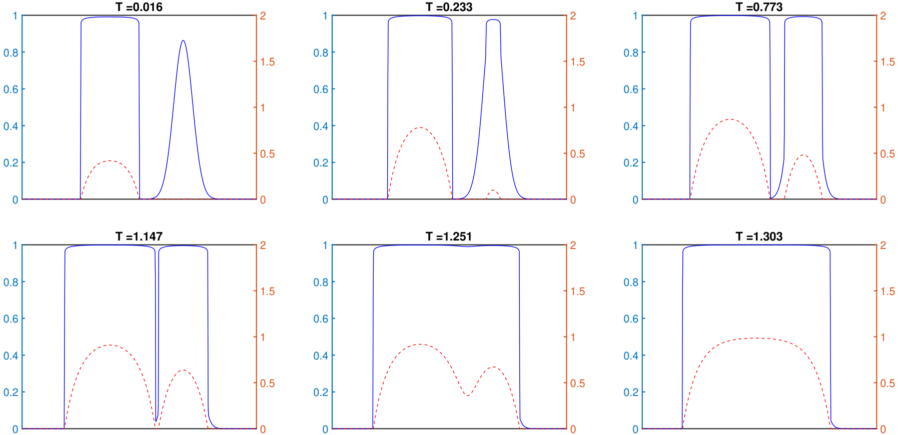
Theorem: complementarity relation

$$p_\infty(\Delta p_\infty - \Delta \Phi + G(p_\infty, c_\infty)) = 0 \quad \text{in} \quad \mathcal{D}'(\mathbb{R}^d \times (0, \infty))$$

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

Solutions behavior in 1D



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

Strategy

$\nabla p_{\gamma_k} \to \nabla p_\infty$ strongly in $L^2_{x,t}$: two new methods

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[1] N.D. and Benoit Perthame, *J. Math. Pures Appl.*, 2021 (nutrient)
[2] N.D. and Markus Schmidtchen, *Preprint*, 2021 (drift)

Focusing solution

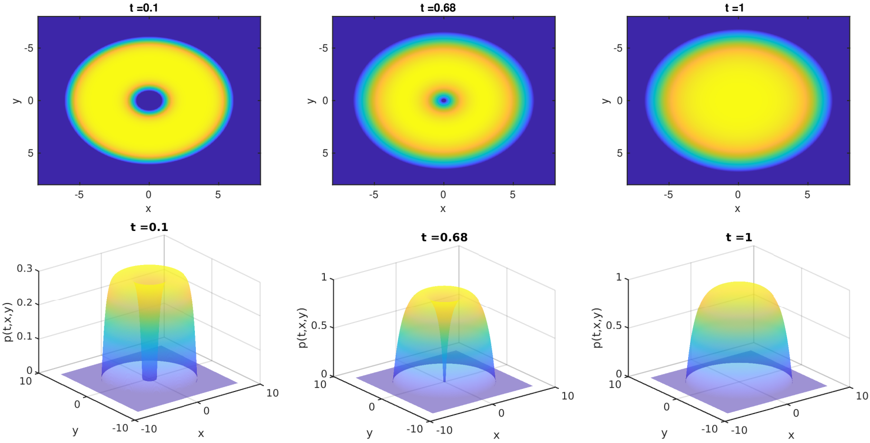

Figure 3: Focusing solution: pressure

[3] N.D. and Xinran Ruan, Preprint, 2021

Gradient blow-up at the focusing time

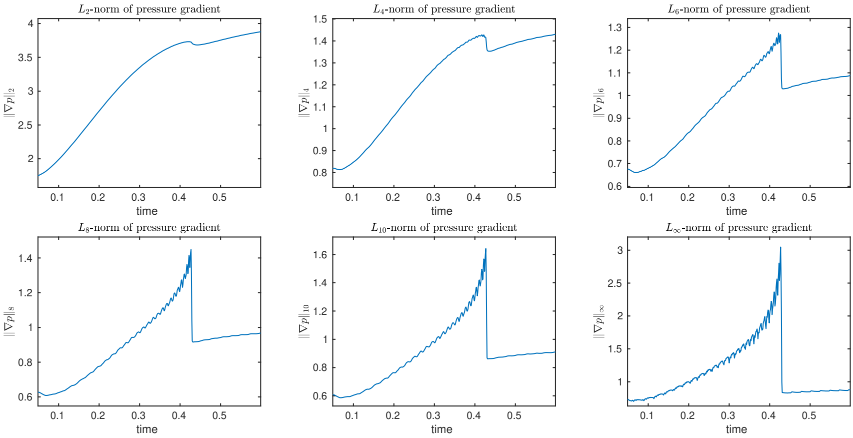

Figure 4: L^p-norms of the pressure gradient

Conclusions and perspectives

Main result

$$p_\infty(\Delta p_\infty - \Delta\Phi + G(p_\infty, c_\infty)) = 0 \quad \text{in} \quad \mathcal{D}'(\mathbb{R}^d \times (0,\infty)).$$

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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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Thank you!

Difficulties

$$\partial_t n = \nabla \cdot (n \nabla p) + nG(p)$$

Aronson-Bénilan estimate:

$$\Delta p + G(p) \geq -\frac{1}{\gamma t}$$

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With nutrients:

$$G(p, c) < 0, \qquad \text{for } c < \bar{c}$$

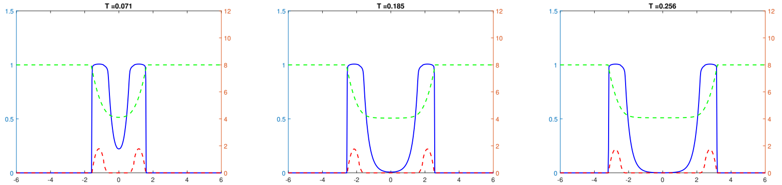

Figure 2: Density (blue line), pressure (red dashed line), nutrient (green dashed line), $\bar{c} < 0.6$, $\gamma = 80$