On singular limits arising in mechanical models of tumour growth

Tomasz Dębiec
University of Warsaw

UNIVERSITY OF WARSAW

UNIVERSITY OF WARSAW
MIM
FACULTY OF MATHEMATICS, INFORMATICS AND MECHANICS

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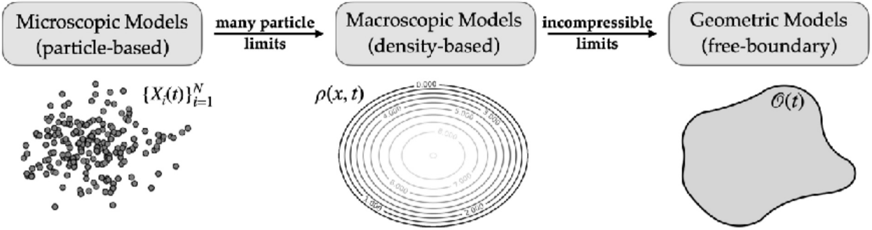
Connecting modelling paradigms



Three scales to address the same phenomenon, hence the questions:

What is the connection between these different modelling choices?

and

How can they be linked?

Macroscopic models of tissue growth

- **Dynamics** of cell density $n(t,x)$ governed by 2 effects:
  - Movement with velocity $v(t,x)$
  - Cell division and cell death (growth rate G)

$$\partial_t n(t,x) + \mathrm{div}(n(t,x)v(t,x)) = n(t,x)G(p(t,x)).$$

(e.g. $G(p) = p_H - p$.)

- **Connection** between **velocity and pressure** via:
  - Darcy's law: $v = -\nabla p$ (local; porous medium)
  - Brinkman's law: $-\nu\Delta v + v = -\nabla p$ (nonlocal; viscoelastic medium)

- **Constitutive law**: assume pressure is an increasing function of the density. Archetypal example:

$$p = \frac{\gamma}{\gamma - 1} n^{\gamma-1}, \quad \gamma > 1.$$

Example: Cauchy problem for the Porous Medium Equation

Consider the problem

$$\begin{cases} \partial_t n_\gamma(t,x) & = \Delta n_\gamma^\gamma(t,x), \quad x \in \mathbb{R}^d, t > 0, \\ n_\gamma(0,x) & = n^0(x), \quad n^0 \in L^1 \cap L^\infty(\mathbb{R}^d). \end{cases}$$

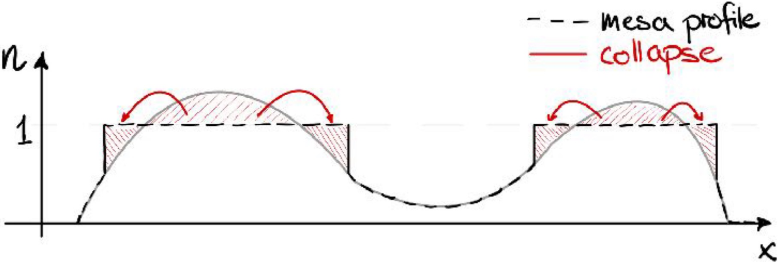
The porous medium equation can be rewritten as a *diffusion equation*:

$$\partial_t n_\gamma(t,x) = \mathrm{div}(n_\gamma \nabla p_\gamma) = \mathrm{div}(D(n_\gamma)\nabla n_\gamma), \quad D(n_\gamma) = \gamma n_\gamma^{\gamma-1}.$$

In the limit $\gamma \to \infty$, the diffusivity coefficient behaves like

$$D(n) \approx \begin{cases} 0, & \text{when } n \in [0,1), \\ +\infty, & \text{when } n \geq 1. \end{cases}$$

Example: Cauchy problem for the Porous Medium Equation



Thus, formally, we expect the solution to the Cauchy problem to converge, as $\gamma \to \infty$, to a *stationary* profile $n_\infty = n_\infty(x)$ with $0 \leq n_\infty \leq 1$.

This can be proved using: the Aronson-Bénilan estimate ($\partial_t n_\infty \geq 0$) and conservation of mass [Caffarelli-Friedman, 1987].

Non-trivial limit evolution: source at the boundary of the domain.

The graph relation

Since $p_\gamma = \frac{\gamma}{\gamma-1} n_\gamma^{\gamma-1}$, we have

$$\left(\frac{\gamma-1}{\gamma} p_\gamma\right)^{\frac{\gamma}{\gamma-1}} = n_\gamma^\gamma = \frac{\gamma}{\gamma-1} n_\gamma p_\gamma.$$

We thus formally deduce $p_\infty = n_\infty p_\infty$, or $p_\infty(1-n_\infty) = 0$.

Equivalently, $p_\infty \in P_\infty(n_\infty)$, where P_∞ is the monotone graph

$$P_\infty(n) = \begin{cases} \{0\}, & \text{when } n < 1, \\ [0,\infty), & \text{when } n = 1, \\ \emptyset, & \text{when } n > 1. \end{cases}$$

Saturation constraint: we have the inclusion $\{p_\infty > 0\} \subset \{n_\infty = 1\}$.

Including cell proliferation

Now consider the equation

$$\partial_t n_\gamma - \mathrm{div}(n_\gamma \nabla p_\gamma) = n_\gamma G(p_\gamma), \quad p_\gamma = \frac{\gamma}{\gamma - 1} n_\gamma^{\gamma-1}.$$

The pressure satisfies

$$\partial_t p_\gamma - |\nabla p_\gamma|^2 = (\gamma - 1) p_\gamma (\Delta p_\gamma + G(p_\gamma)),$$

and in the limit $\gamma \to \infty$ we have [Perthame, Quirós, Vázquez, 2014]:

$$\partial_t n_\infty - \Delta p_\infty = n_\infty G(p_\infty),$$

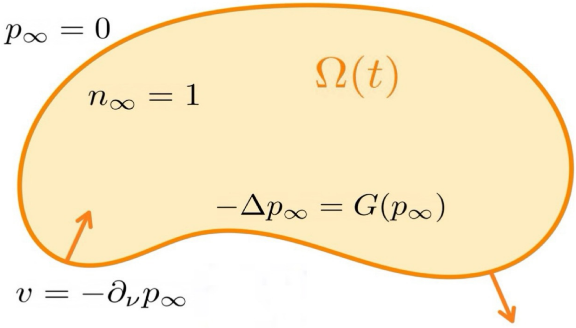
$$p_\infty(1 - n_\infty) = 0 \quad \text{and} \quad p_\infty(\Delta p_\infty + G(p_\infty)) = 0.$$

Note: In this case $\{p_\infty > 0\} = \{n_\infty = 1\}$.

The Hele-Shaw problem

Thus, the limiting pressure solves the following elliptic problem:

$$\begin{cases} -\Delta p_\infty &= G(p_\infty), \quad \text{in } \Omega(t) := \{p_\infty > 0\}, \\ \quad p_\infty &= 0, \qquad\qquad \text{on } \partial\Omega(t). \end{cases}$$



Other problems / My work

- Include **heterogeneity**: systems of equations
- **Rate of convergence** for the incompressible limit $\gamma \to \infty$
- Well-posedness of the model with **Brinkman's law** ($-\nu \Delta v + v = -\nabla p$ instead of $v = -\nabla p$) and its incompressible limit
- The **nonlocal-to-local** limit $\nu \to 0$
- **Continuous phenotype** limit: from N species to a continuously structured equation

More details:
`https://www.mimuw.edu.pl/~tdebiec/publications.html`

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Thank you for your attention!