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Free boundary problems for tumor growth: A viscosity solutions approach

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ABSTRACT

The mathematical modeling of tumor growth leads to singular “stiff pressure law” limits for porous medium equations with a source term. Such asymptotic problems give rise to free boundaries, which, in the absence of active motion, are generalized Hele-Shaw flows. In this note we use viscosity solutions methods to study limits for porous medium-type equations with active motion. We prove the uniform convergence of the density under fairly general assumptions on the initial data, thus improving existing results. We also obtain some additional information/regularity about the propagating interfaces, which, in view of the discontinuities, can nucleate and, thus, change topological type. The main tool is the construction of local, smooth, radial solutions which serve as barriers for the existence and uniqueness results as well as to quantify the speed of propagation of the free boundary propagation.

1. Introduction

Motivated by models of tumor growth (see for instance the survey papers by Friedman [6], Lowengrub et al. [9]) and extending Perthame, Quiros and Vazquez [11], in a recent paper Perthame, Quiros, Tang and Vauchelet [10] studied the limiting behavior, as $m \to \infty$, of the solution (density) ρ_m of the porous medium diffusion equation (pme for short)

$$\rho_{m,t} - \Delta\rho_m^m - \nu\Delta\rho_m = \rho_m G(p_m) \quad \text{in } \; Q_T := \Omega \times (0,T), \tag{1.1}$$

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where Ω is either a bounded domain in $\mathbb{R}^n$ or $\Omega = \mathbb{R}^n$, with boundary and initial conditions

$$\rho_m = \rho_L \quad \text{in } \partial_p Q_T := \partial\Omega \times [0,T) \quad \text{and} \quad \rho_m = \rho_{0,m} \text{ on } \Omega \times \{0\}, \tag{1.2}$$

satisfying

$$0 \le \rho_L < 1 \quad \text{and} \quad 0 \le \rho_0 \le 1 \text{ if } \Omega \text{ is bounded or } \rho_0 \in L^1(\mathbb{R}^n) \text{ if } \Omega = \mathbb{R}^n. \tag{1.3}$$

Here

$$p_m := \frac{m}{m-1}\rho_m^{m-1} \tag{1.4}$$

is the pressure, $\nu > 0$, and $G : \mathbb{R} \to \mathbb{R}$ is a smooth function, which describes the cell multiplication, satisfying

$$G(p_M) = 0 \quad \text{for some } p_M > 0 \quad \text{and} \quad G' < 0. \tag{1.5}$$

Using the pressure variable, (1.1) can be rewritten as

$$\rho_{m,t} - \operatorname{div}(\rho_m Dp_m - \nu D\rho_m) = \rho_m G(p_m),$$

a form which represents better the mechanical interpretation of the model with $v_m := -Dp_m$ the tissue bulk velocity according to Darcy's law.

Note that, if, as $m \to \infty$, the p_m's and ρ_m's converge respectively to p and ρ, then p will be nonzero only where $\rho = 1$. This indicates, that, in the limit, a phase transition may take place with an evolving free boundary between the tumor region (the support of p) and the pre-tumor zone (the support of $1-\rho$). The convergence, as $m \to \infty$, of the p_m's and ρ_m's has already been investigated using a distributional solution approach in [10].

Here we study the asymptotic behavior of p_m and ρ_m in the limit $m \to \infty$ using viscosity solutions. This yields a different description of the limit problem, allows for more general initial data and yields pointwise information about the free boundary evolution, uniform convergence results as well as some quantified statements about the speed of propagation of the tumor zone.

In order to state the result it is necessary to introduce the limit problem which we derive next formally following [10]. We use the auxiliary variable

$$u_m := -\rho_m^m + \nu(1-\rho_m), \tag{1.6}$$

which is close to $-p_m + \nu(1-\rho_m)$ for large m, and, recalling that (1.1) can also be written as

$$p_{m,t} - (m-1)p_m\Delta p - |Dp_m|^2 - \nu\Delta p_m = (m-1)p_m G(p_m) - \nu\frac{m-2}{m-1}\frac{|Dp_m|^2}{p}, \tag{1.7}$$

we find that u_m satisfies

$$[b_m(u_m)]_t - \nu\Delta u_m = -\nu\rho_m G(p_m) \quad \text{with } b_m'(u_m) = \frac{\nu}{m\rho_m^{m-1} + \nu}. \tag{1.8}$$

Assume next that, as $m \to \infty$, the ρ_m's, p_m's and u_m's converge respectively to ρ, p and u. Then, formally, we find

$$p = u^-, \qquad \nu(1-\rho) = u^+ \quad \text{where } u^+ := \max(u,0) \quad \text{and} \quad u^- := -\min(u,0). \tag{1.9}$$

Letting $m \to \infty$ in (1.7) and noting that $\{p > 0\} = \{\rho = 1\}$ yields that p and ρ solve respectively

$$-\Delta p(\cdot,t) = G(p)(\cdot,t) \quad \text{in } \Omega(t) := \{p(\cdot,t) > 0\}, \tag{1.10}$$

and

$$\rho_t - \nu\Delta\rho = \rho G(0) \quad \text{in } \{\rho < 1\};$$