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A multiscale model of cell mobility: From a kinetic to a hydrodynamic description

J. Nieto, L. Urrutia *

University of Granada, Departamento de Matemática Aplicada, 18071 Granada, Spain

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ABSTRACT

This paper concerns a model for tumor cell migration through the surrounding extracellular matrix by considering mass balance phenomena involving the chemical interactions produced on the cell surface. The well-posedness of this model is proven. An asymptotic analysis via a suitable hydrodynamic limit completes the description of the macroscopic behavior.

1. Introduction

There is a huge literature describing mathematical models for cell migration through the extracellular matrix (ECM), specially tumor cells, since they usually try to reach a blood vessel to obtain nutrients or simply invade other parts of the body in a metastatic process. There are a lot of biological mechanisms involved in cell movement such as signaling, diffusion, chemotaxis, haptotaxis, reorientation due to the surrounding tissue fibers, cell–cell interactions, etc., and also some mechanical considerations as balance laws, mechanical forces, pressure, etc. (see for example [2,5,7–12]).

In general, there is an analogy with the models for mechanical particles, where biological considerations are included in several ways. For example, reorientations of the particles due to biological interactions can be modeled by a Boltzmann-type equation where the usual collision kernel plays the role of a reorientation kernel. Of course, macroscopic descriptions (Navier–Stokes or Keller–Segel models) are very common, and the connections between kinetic and hydrodynamic models by means of limiting procedures have been largely treated in the literature (see for example [1–5,7,8]).

* Corresponding author.
E-mail addresses: jjmnieto@ugr.es (J. Nieto), lurrutia@ugr.es (L. Urrutia).

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Following the analogy with mechanical models, it is remarkable the framework of Kinetic Theory of Active Particles (KTAP) introduced by Bellomo et al. (see for example [3] and the references therein), where *active particles* play the double role of mechanical entities and living beings. This theory allows to construct models for cell movement that take into account the heterogeneity of cells, the biological interactions, birth/death phenomena, and also different scales of description. In this spirit, a recent paper by Kelkel and Surulescu [9], presents a multiscale model describing the evolution of a tumor cell population density where the movement of the cells is mainly due to receptor dynamics on the cell surface. The model links several processes such as haptotaxis, binding of the cell surface to the ECM fibers, chemotaxis due to a substance originated from the degradation of tissue fibers, and the law of mass action of the receptor on the cell surface.

In this work, we start from the multiscale model presented in [9], and include some mechanical and biological considerations that improve it. Actually, in the equations for the ECM dynamics we introduce the mass balance due to interactions with the cell population. This mass exchange, together with the creation and degradation of substances, constitute a key part in the state of the ECM, and so modifies the dynamics of the population. Moreover, we perform a hydrodynamic limit which provides macroscopic information on the behavior of the cell population and preserves the influence of the two main biological processes, haptotaxis and chemotaxis.

For the sake of selfconsistency, we briefly describe in the next subsection the elements involved in cell motion as well as our improvements. In Section 2, we prove existence and uniqueness of solution for the obtained model, and in Section 3 we perform the high-field limit. In particular, we will obtain closed relations between the averaged chemical substances involved in cell movement and the respective concentration in the ECM.

1.1. The multiscale model

Concerning the two processes introduced before, haptotaxis and chemotaxis, we find two different chemical compounds in the ECM (see [9] for details), each one related to one type of cell-environment interaction: An oriented protein fiber, responsible of haptotaxis, and a chemical compound coming from degeneration of the aforesaid fibers, responsible for chemotaxis. We denote $Q(t,x,\theta)$ the density of protein fibers at time t and position x, oriented towards $\theta \in \mathbb{S}^{n-1}$ for some $n \geq 1$. The density of protein fibers at time t and position x is denoted by $\bar{Q}(t,x)$:

$$\bar{Q}(t,x) := \int_{\mathbb{S}^{n-1}} Q(t,x,\theta)d\theta.$$

Finally, denote $L(t,x)$ the concentration of the other chemical compound, a proteolytic product coming from degradation of ECM fibers. From now on, we will use the same notation for the compounds and for their densities and concentrations. We will call them the $\bar{Q}$ and L compounds, respectively.

The final model is a system consisting of a kinetic model for the cell population (stemming from KTAP) and two macroscopic reaction and reaction–diffusion equations for the chemical compounds. The cell population will be treated as a system of active particles, meanwhile macroscopic models are used for the chemicals. At this point, the aforesaid improvements to the model in [9] are introduced, including a reaction term which takes into account the balance mass of the compounds due to the chemical reactions produced in the cell surface.

We describe the cell population by means of a standard distribution function $f(t,x,v,y)$ depending on time t, space x, velocity v and *activity* y (which will be described below), verifying the following equation deduced in [9],

$$\frac{\partial f}{\partial t} + v \cdot \nabla_x f + \nabla_y \cdot (G(y,\bar{Q},L)f) = \mathcal{H}(f,Q) + \mathcal{L}(f) + \mathcal{C}(f,L), \tag{1}$$