Existence theorem for hybrid competition model

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Abstract. An hybrid mathematical system based on competition model and kinetic equations is proposed for the analysis of the more general dynamical system which describes the tumor-immune system competition. A parameter describing the distribution of cells is studied as a solution of an integro-differential system. The existence of solution is discussed.

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1 Introduction

In recent years various mathematical models for studying the competition between tumor cells and the immune system have been proposed by generalizing the dynamical system typical of the competition between biological populations ([9]÷[15],[22, 23]). Methods of non-equilibrium statical mechanics and mathematical kinetic theory have been developed [7]÷[8].

The competition between tumor and immune cells can be modeled at different scales: *supermacroscopic scale* [1] and *microscopic scale* [6, 2, 10].

Mathematical structures were developed by following the Fokker-Plank methods for active particles. Some Boltzmann type equations, with the microscopic state defined by a non-mechanical variable called *activity* as been proposed for the analysis of population dynamics [15, 16, 2].

Qualitative analysis, existence of equilibrium and asymptotic behavior were studied [18, 19, 17], together with various developments on the hiding-learning dynamics [20, 13, 21].

Recently [14] the authors have proposed an hybrid model, based on a two scale separation: a microscopic level, described by ordinary differential equations (a typical

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competition system) but with a random coefficient which is a solution of a partial differential system (kinetic equations) typical, at a macroscopic level, of gas-dynamics interaction. This coefficient depends on the hiding-learning dynamic process between tumor and immune cells.

In this paper, after recalling the hybrid competition model proposed in [14], we introduce a transition density function which occurs in the binary interactions between the tumor and immune cells, and give the existence theorem for the solutions of the integral-differential systems.

2 Hybrid competition model

Let us consider a physical system of two interacting populations each one constituted by a large number of particles with sizes:

$$n_i = n_i(t)\,, \qquad (n_i(t) : [0,T] \;\rightarrow\; \mathbb{R}_+) \tag{2.1}$$

for $i = 1, 2$.

Each population is characterized by a microscopic state, called activity, denoted by the variable u. The physical meaning of the microscopic state may differ for each population. We assume that the competition model depends on the activity through a function of the overall distribution:

$$\mu = \mu[f_i(t,u)] \quad , \qquad (\mu[f_i(t,u)] : \mathbb{R}_+ \rightarrow \mathbb{R}_+). \tag{2.2}$$

The description of the overall distribution over the microscopic state within each populations is given by the probability density function:

$$f_i = f_i(t,u)\,, \qquad (f_i(t,u) : [0,T] \times D_u \;\rightarrow\; \mathbb{R}_+\,, \quad D_u \subseteq \mathbb{R}) \tag{2.3}$$

for $i = 1, 2$, such that $f_i(t,u)\,du$ denotes the probability that the activity u of particles of the i-th population, at the time t, is in the interval $[u, u + du]$:

$$d\mu = f_i(t,u)du \quad , \tag{2.4}$$

and

$$\int_{D_u} f_i(t,u)\,du = 1 \quad , \quad \forall\, t \geq 0\,, \quad i = 1, 2\,. \tag{2.5}$$

The hybrid evolution equations can be formally written as follows [14];

$$\begin{cases} \dfrac{dn_i}{dt} &=& G_i(n_1, n_2; \mu[f])\ , \\ \dfrac{\partial f_i}{\partial t} &=& \mathcal{A}_i[f], \end{cases} \tag{2.6}$$

where G_i, for $i = 1, 2$, is a function of $n = \{n_1, n_2\}$ and μ, acts over $f = \{f_1, f_2\}$; while $\mathcal{A}_i$, for $i = 1, 2$, is a nonlinear operator acting on f, and $\mu[f]$ is a functional $(0 \leq \mu \leq 1)$ which describes the interaction of the second population with the first one. Then, (2.6) denotes a hybrid system, i.e. a deterministic system coupled with a microscopic system statistically described by a kinetic theory approach so that equations $(2.6)_2$ can be explicitly written as

$$
\begin{aligned}
\frac{\partial f_i}{\partial t}(t,u) = & \sum_{j=1}^{2} \int_{D_u \times D_u} \eta_{ij}\ \varphi_{ij}(u_*, u^*, u) f_i(t, u_*) f_j(t, u^*)\, du_*\, du^* \\
& - f_i(t,u) \sum_{j=1}^{2} \int_{D_u} \eta_{ij} f_j(t, u^*)\, du^* \,.
\end{aligned}
\tag{2.7}
$$

Specifically, we consider binary interactions between a test particle with state u_* belonging to the i^{th} population, and the field particle with state u^* belonging to the j^{th} population. Thus η_{ij}, with $i, j = 1, 2$ is the encounter rate and $\varphi_{ij}(u_*, u^*, u)$ is the transition density function which denotes the probability density that a candidate particle with activity u_* belonging to the i^{th} population, falls into the state $u \in D_u$, of the test particle, after an interaction with a field entity, belonging to the j^{th} population, with state u^*.

The probability density $\varphi_{ij}(u_*, u^*, u)$ fulfils the condition

$$
\forall i\ , j, \quad \forall u_*\ , u^*\ : \int_{D_u} \varphi_{ij}(u_*, u^*, u) du = 1 \quad , \quad \varphi_{ij}(u_*, u^*, u) > 0. \tag{2.8}
$$

In particular, we are interested in the distance between distributions, therefore we define the functional μ as [16]:

$$
\mu[f](t) = 1 - \int_{D_u} (f_1 - f_2)^2(t,u)\, du \,, \tag{2.9}
$$

where the minimum distance is obtained when the second population is able to reproduce the distribution of the first one: $f_1 = f_2$. In this case it is $\mu = 1$, otherwise $\mu < 1$ with $\mu \downarrow 0$, with increasing distance between f_1 and f_2. Thus we have

$$
0 \leq \mu[f](t) \leq 1 \Longrightarrow 0 \leq \int_{D_u} (f_1 - f_2)^2(t,u)\, du \leq 1\ , \forall t \in [0, T]\ . \tag{2.10}
$$

Notice that μ is the coupling term which links the macroscopic model $(2.6)_1$ to the microscopic model $(2.6)_2$.

3 Transition density function based on Dirac function

In this section the existence theorem for the solution of (2.7) is given for a special class of transition density function, which fulfil (2.8), and the corresponding density distribution (2.4),(2.9), is computed. Starting from the nonrestrictive hypothesis,

$$
\eta_{11} = \eta_{12} = 1\,, \qquad \eta_{21} = \eta_{22} = \varepsilon, \qquad 0 \leq \varepsilon, \tag{3.1}
$$

we can prove

Theorem 3.1. *By assuming that the interaction terms are:*

$$\left\{\begin{array}{lcl}\varphi_{11} & = & a_{11}\delta(u_*-u)+(1-a_{11})\delta(u^*-u)\\ \varphi_{12} & = & a_{12}\delta(u_*-u)+(1-a_{12})\delta(u^*-u)\\ \varphi_{21} & = & a_{21}\delta(u_*-u)+(1-a_{21})\delta(u^*-u)\\ \varphi_{22} & = & a_{22}\delta(u_*-u)+(1-a_{22})\delta(u^*-u)\ ,\end{array}\right. \tag{3.2}$$

with $\delta(u_*-u)$ *Dirac delta and*

$$a_{11}\in[0,1]\ ,\ a_{12}\in[0,1]\ ,\ a_{21}\in[0,1]\ ,\ a_{22}\in[0,1]\ ,$$

then there exists a solution of (2.7) *in the form:*
(3.3)

$$f_1(t,u) = \left\{\begin{array}{ll}\dfrac{1}{a-b}\left\{a\left[f_1(0,u)-f_2(0,u)\right]e^{(a-b)t}-\left[bf_1(0,u)-af_2(0,u)\right]\right\} & ,\quad a\neq b\\ a\left[f_1(0,u)-f_2(0,u)\right]t+f_1(0,u) & ,\quad a=b\ ,\end{array}\right.$$

$$f_2(t,u) = \left\{\begin{array}{ll}\dfrac{1}{a-b}\left\{b\left[f_1(0,u)-f_2(0,u)\right]e^{(a-b)t}-\left[bf_1(0,u)-af_2(0,u)\right]\right\} & ,\quad a\neq b\\ b\left[f_1(0,u)-f_2(0,u)\right]t+f_2(0,u) & ,\quad a=b.\end{array}\right.$$

Proof. Substituting (3.2) into (2.7) yields:

$$\left\{\begin{array}{lcl}\dfrac{\partial f_1}{\partial t}(t,u) & = & (a_{12}-1)f_1(t,u)+(1-a_{12})f_2(t,u),\\ \dfrac{\partial f_2}{\partial t}(t,u) & = & \varepsilon\left[(1-a_{21})f_1(t,u)+(a_{21}-1)f_2(t,u)\right]\ ,\end{array}\right.$$

and, by defining $a=(a_{12}-1)$, $b=\varepsilon(1-a_{21})$, we have

$$\left\{\begin{array}{lcl}\dfrac{\partial f_1}{\partial t}(t,u) & = & a[f_1(t,u)-f_2(t,u)]\ ,\\ \dfrac{\partial f_2}{\partial t}(t,u) & = & b\left[f_1(t,u)-f_2(t,u)\right]\ ,\end{array}\right. \tag{3.4}$$

This system can be solved by changing variables as follows. With

$$\nu(t,u)=f_1(t,u)-f_2(t,u)\ ,$$

we infer $\frac{\partial\nu}{\partial t}(t,u)=(a-b)\,\nu(t,u)$, so that

$$\nu(t,u)=\nu_0(u)\,e^{(a-b)t} \tag{3.5}$$

where $\nu_0(u)=\nu(0,u)$ is an arbitrary function which satisfies, according to (2.3),(4.6), the condition

$$\int_{D_u}\nu_0(u)\ du=0 \qquad ,\ \forall t\in[0,T]\ ,$$

with, $\nu_0(u)=f_1(0,u)-f_2(0,u)$. When $\nu(t,u)$ is computed, it is possible to explicitly derive both distributions $f_1(t,u)$, $f_2(t,u)$.

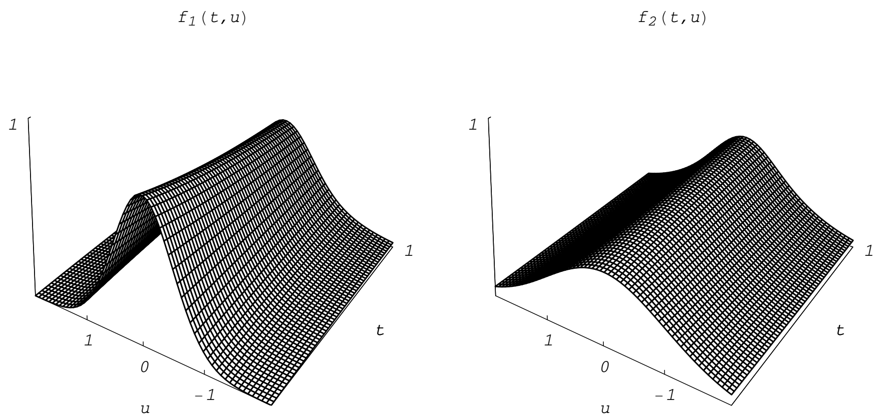

Figure 1: **Solution of** (3.4) **with** $a = -0.9,\ b = 0.4$**.**

From (3.4) we get $\frac{\partial f_1}{\partial t}(t,u) = a\nu_0(u)e^{(a-b)t}$, and then

$$f_1(t,u) = \begin{cases} \dfrac{a}{a-b}\nu_0(u)e^{(a-b)t} + G(u) & , \quad a \neq b \\ a\nu_0(u)t + h(u) & , \quad a = b. \end{cases}$$

Analogously we get

$$f_2(t,u) = \begin{cases} \dfrac{b}{a-b}\nu_0(u)e^{(a-b)t} + H(u) & , \quad a \neq b \\ b\nu_0(u)t + k(u) & , \quad a = b, \end{cases}$$

with $G(u),\ H(u),\ h(u),\ k(u)$ arbitrary functions depending on the initial conditions. It can be easily seen that

$$G(u) = H(u) = \frac{1}{a-b}[af_2(0,u) - bf_1(0,u)] \ ,$$

and

$$h(u) = f_1(0,u) \ , \ k(u) = f_2(0,u) \ ,$$

so that they both satisfy to condition (2.5). From the above, (3.3) follow. □

It should be noticed that the solution is not unique, since it depends on the initial distributions $f_2(0,u),\ f_1(0,u)$. When the initial functions are given, the solution exists and it is unique. A solution of (3.4) with initial conditions

$$f_1(0,u) = 2\frac{e^{-2x^2}}{\sqrt{2\pi}} \quad , \quad f_2(0,u) = \frac{e^{-x^2/2}}{\sqrt{2\pi}}$$

is shown in Fig. 1. Moreover, according to (2.9), we get for μ the expression

$$\mu(t) = 1 - e^{2(a-b)t} \int_{D_u} (f_1 - f_2)^2(0,u)du \ , \tag{3.6}$$

so that, $\mu \uparrow 1$ when $t \to \infty$ and $\mu = 1 - \displaystyle\int_{D_u} (f_1 - f_2)^2(0,u)du$, when $t = 0$.
In particular, if we define $\gamma_0 = \int_{D_u}(f_1 - f_2)^2(0,u)\mathrm{d}u$, we get, according to (2.10), $0 \le \gamma_0 \le 1$, and $\mu(t) = 1 - \gamma_0\ e^{2(a-b)t}$.

Conclusion

In this paper the hybrid system for the competition between tumor cells and immune system has been discussed and in a special case the analytical solution of the system has been explicitly computed. This is the first step towards the solution of the hybrid system with more general transition functions.

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