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A NOTE ON THE MODELING OF IMMUNE-CANCER COMPETITION IN THE HOMOGENEOUS SYSTEMS

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ABSTRACT. This work deals with the model focuses on the study of the early stage of the immune cancer competition. The approach used in this model is based on the kinetic theory of active particles (KTAP), which has been developed to modeling systems constituted by a large number of interacting particles (active particles), whose microscopic state includes not only geometrical and mechanical variables (typically position and velocity) but also biological functions called activities related to the intrinsic biological function of particles. The model consider a scalar activity variable $u \in (0,\infty)$. The overall system is divided into six ($M = 6$) different populations (functional subsystems), the first three subsystems contain epithelial (subsystem 1) and cancer cells (subsystems 2,3), the other functional subsystems contain cells of the immune system. After some reasonable assumptions, we obtain for the cancer cells and immune cells of the last hallmark a Lotka-Volterra system that allows us to describe the dynamics of the biological system in a very simple way.

1. Introduction

Cancer, a broad term for a class of diseases, emerges as a global healthy problem, and is characterized by abnormal cells growth that invades healthy cells in the body. Cancer tumor means a mass of cells with uncontrolled cell division as a result of defective cell cycle control mechanisms. Development of cancer is a complex process. The mathematical models seek to understand the dynamics of tumor development and growth by designing effective anticancer therapeutic strategies (external actions, therapeutical actions or other external agents). Many recent studies have been devoted to this field, for example, the paper by De Angelis and Jabin (Angelis and Jabin 2005) consider different types of therapeutical actions such as the activation of the immune system, angiogenesis inhibition factors, and weakening of tumor cells by chemotherapeutical actions, while paper (Frank *et al.* 2008) considers a Boltzmann transport model for dose calculation in radiotherapy. Cancer can be treated by surgery, chemotherapy, radiotherapy, and immunotherapy. The choice of appropriate type of therapy depends upon location and grade of the tumor and the stage of the disease, as well as the general state of the patient (Frank *et al.* 2008). In this paper we refer to the competition between cancer and immune cells. As a background, can be said, the normal cell can grow and divide for several reasons including the need to form new

tissue or to replace old cells. During cell division an original cell ("mother cell") divides into two new cells ("daughter cells") in a highly controlled and organized manner. The normal growth-control mechanism of the cell is lost when they turn to become cancerous which can be classified as benign tumor when they are localized and malignant tumor when they have metastatic. As documented in the seminal paper by Hanahan and Weinberg (Hanahan and Weinberg 2000) and (Hanahan and Weinberg 2011), the complexity of cancer can be reduced to a small number of underlying principles: cancer cells have defects in the control mechanisms that govern how often they divide and are able to stimulate their own growth. They are able to overcome apoptosis to progress. They have the capacity to evade the immune recognition. The immune system plays an important role in these dynamics, where it has a strategy to learn the presence of carriers of a pathology and attempt to deplete them. It is a complex process where immune cells, starting from the innate immunity, improve their action by learning the so-called acquired immunity and identifies the hallmarks of cancer to escape the immune defence (Cooper 2010). The mathematical kinetic theory of active particles (KTAP) has been recently developed to model the system of large populations of interacting individual (Bellomo and Forni 2006; Bellomo *et al.* 2009, 2010; Brazzoli *et al.* 2010) where each of these individuals are characterized not only by mechanical (typically position and velocity) but also biological functions, called activities. This approach to living systems was initiated by the pioneer paper (Bellomo *et al.* 1996) and developed and applied by various authors (Arlotti *et al.* 2002; Bellouquid and Delitala 2005, 2006; Chauviere and Brazzoli 2006; Cattani and Ciancio 2007; De Angelis and Lods 2008; Brazzoli *et al.* 2010; Bellouquid and De Angelis 2011; Bianca 2011; Bianca and Delitala 2011; Bellomo *et al.* 2013; Bellouquid *et al.* 2013). According to KTAP, the overall system is divided into different populations (functional subsystems) each of them consisting of entities, called active particles, which collectively express the same function (internal state). The evolution of each functional subsystem is described by a distribution function and the time evolution of the subsystem is governed by interactions. Here we deal with a spatially homogeneous mathematical model of immune-cancer competition, in which the position and velocity variables are not significant or they are constant in time. In other words, in this case the microscopic state is given by the main biological function u, which $u \in (0, \infty)$. The description of the framework of the model follows the same line in the model by (Bellouquid *et al.* 2013). The overall system is divided into 6 functional subsystem. The first three subsystems contain epithelial (subsystem 1) and cancer cells (subsystems 2,3), the other functional subsystems contain cells of the immune system. In this paper, the contents are organized in three additional sections, which follow this introduction. In section **2**, we present a spatially homogeneous continuous model as the application of competition between immune system and cancer cells. In section **3** we derive equations for macroscopic averaged quantities, and obtaining a strongly non-linear system of 12 differential equations. In section **4**, we deal with a simplified situation and obtain under some reasonable hypotheses a Lotka-Volterra system for the dynamical behavior of the number density of cancer cells and immune system of the last hallmark. This allows us to study the behavior of these quantities and functions use a conditions that must be satisfied to fit a healthy state.

2. Spatially Homogeneous Continuous Case

The model presented in this work is a spatially homogeneous continuous model for immune-cancer competition, which follows the lines of thought pursuing in (Bellouquid *et al.* 2013; Mohammed 2015).

As in Bellouquid *et al.* 2013, the first step of the modeling approach is the identification of the functional subsystems. Here our aim is to build up a model with six functional subsystems, defined as follows:

- $i = 1$ *Normal epithelial cells*. It is supposed that the organism is a source of epithelial cells, so their quantity can be regarded as constant in time;
- $i = 2$ *Cancer cells of the first hallmark*, that have the ability to thrive in a chronically inflamed micro-environment and to evade the immune recognition;
- $i = 3$ *Cancer cells of the last hallmark*, that have acquired the ability to suppress the immune reaction;
- $i = 4$ *Cells of the innate immune system*, which have the capacity of contrasting the development of cancer cells of the first hallmark $i = 2$;
- $i = 5$ *Cells of the adaptive immune system*, which have the ability of contrasting the development of cancer cells $i = 2$;
- $i = 6$ *Cells of the adaptive immune system*, which have the ability of contrasting the development of cancer cells $i = 2$, and $i = 3$.

The model assumes the biological variable (activity) $u \in (0, \infty)$.

The interactions between cells involve three types of particles: test, field and candidate, where candidate particles with activity u_* can acquire, in probability, the state of the test particles with activity u, after an interaction with field particles with activity u^*, while test particles lose their state after interactions.

The overall state of the i-th functional subsystems is described by the one-cell generalized distribution function: $f_i = f_i(t,u) : [t_0, T] \times D_u \to \mathbb{R}^+, \quad \text{for} \quad i \in \{1,2,\dots,6\}$, $D_u = [u^{(0)}, +\infty)$, where $u^{(0)} > 0$ and $f_i(t,u) = 0$, for $u < u^{(0)}$.

The time evolution of the distribution functions f_i is described in the general system as

$$\frac{\partial f_i}{\partial t}(t,u) = C_i[\mathbf{f}](t,u) + P_i[\mathbf{f}](t,u) + M_i[\mathbf{f}](t,u) - D_i[\mathbf{f}](t,u) - L_i[\mathbf{f}](t,u) \quad i \in \{1,2,\dots,6\}, \tag{1}$$

where $C_i[\mathbf{f}], P_i[\mathbf{f}], M_i[\mathbf{f}], D_i[\mathbf{f}], L_i[\mathbf{f}]$ represent the conservative interactions, proliferative interactions, destructive interactions, natural relaxation of the immune system, respectively.

The mathematical structure related with 1 is written as follows:

$$C_i[\mathbf{f}](t,u) = \sum_{k=1}^{6}\int_{D_u\times D_u}\eta_{ik}[\mathbf{f}]\,\mathscr{B}_{ik}[\mathbf{f}]\,f_i(t,u_*)\,f_k(t,u^*)\,du_*\,du^* - f_i(t,u)\sum_{k=1}^{6}\int_{D_u}\eta_{ik}[\mathbf{f}]\,f_k(t,u^*)\,du^* \quad (2)$$

$$P_i[\mathbf{f}](t,u) = \sum_{k=1}^{6}\int_{D_u\times D_u}\eta_{ik}[\mathbf{f}]\,\mathscr{P}_{ik}[\mathbf{f}]\,f_i(t,u_*)\,f_k(t,u^*)\,du_*\,du^* \quad (3)$$

$$M_i[\mathbf{f}](t,u) = \sum_{h,k=1}^{6}\int_{D_u\times D_u}\eta_{hk}[\mathbf{f}]\,\mathscr{M}_{hk(h\neq i)}[\mathbf{f}]\,f_h(t,u_*)\,f_k(t,u^*)\,du_*\,du^* \quad (4)$$

$$D_i[\mathbf{f}](t,u) = f_i(t,u)\sum_{k=1}^{n}\int_{D_u}\eta_{ik}[\mathbf{f}]\,\mathscr{D}_{ik}[\mathbf{f}]f_k(t,u^*)du^* \quad (5)$$

$$L_i[\mathbf{f}](t,u) = \lambda_i[\mathbf{f}][f_i(t,u)-f_i(t_0,u_0)], \quad (6)$$

The quantities related to the interaction terms above are defined as follows:

- The encounter rate between the h-th and the k-th functional subsystems, is denoted by η_{hk} and is defined as follows:

1- For $(h=1,2,3)$ and $(k=1)$: $\eta_{h1}[\mathbf{f}]=\eta_0 h$.
2- For $(h,k)=(4,2),(5,2),(6,2),(6,3)$: $\eta_{hk}[\mathbf{f}]=\eta_0\sigma, \quad \sigma>0$.

The transition density function, denoted $\mathscr{B}_{ik}$, is the probability density that a candidate particle of the i -th functional subsystem with microscopic state u_* falls into the state u of the test particle of the same functional subsystem after the interaction with the field particle, with state u^*, of the k-th functional subsystem. It must satisfy the relation:

$$\int_{D_u}\mathscr{B}_{ik}[\mathbf{f}](u_*\to u|u_*,u^*)\,du=1, \quad \forall u_*,u^*\in D_u.$$

Here we assumed that the transition probability function does not depend on the activity u^*, of the k-th functional subsystem, and is assumed as follows:

1- For $(h=1)$ and $(k=1,2,3)$, the translation probability function for the pair $(1,1),(1,2),(1,3)$, is given as follows:

$$\mathscr{B}_{1k}(u_*,u)=\delta(u_*-u) \qquad \text{for} \qquad k=1,2,3 \quad (7)$$

2- For $h=2,3$ and $k=1$, the transition probability function for the pair $(2,1),(3,1)$, is given as follows:

$$\mathscr{B}_{i1}=\alpha_1[1-(u_*+a)]\,\delta(u-(u_*+a))+[1-\alpha_1(1-(u_*+a)]\,\delta(u-u_*), \quad (8)$$

where $a>0$ and α_1 characterizes the probability of transition in the cancer cell populations.

3- For $(i,k)=(4,2)$, we assume:

$$\mathscr{B}_{42}(u_*,u)=\delta(u_*-u) \quad (9)$$

4- For $(i,k)=(5,2),(7,3)$, we assume

$$\mathscr{B}_{ik}=\alpha_2[1-(u_*+a)]\,\delta(u-(u_*+a))+[1-\alpha_2(1-(u_*+a))]\,\delta(u-u_*), \tag{10}$$

where $a>0$ and α_2 characterizes the probability of transition in the immune system cell populations.

- $\mathscr{P}_{hk}$ models the proliferative rate, where generation of a daughter cell occurs in the same subsystem of the mother cell. We model these events as follows:

1- For $(h,k)=(2,1),(3,1)$, and $k=1$: $\mathscr{P}_{h1}=h\beta u_*\delta(u_*-u),\quad \beta>0$
2- For $(h,k)=(5,2),(6,2),(6,3)$: $\mathscr{P}_{hk}=\beta'\delta(u_*-u),\quad \beta'>0$

- $\mathscr{M}_{hk}$ models the mutations rate,

where generation of a daughter cell occurs in a subsystem different from that of the mother cell. We model these events as follows:

1- For $i=2,3$ and $k=1$: $\mathscr{M}_{(i-1)1}=\varepsilon u_*\delta(u-u^{(0)}),\quad \varepsilon>0$
2- For $i=5,6$ and $k=2,3$: $\mathscr{M}_{(i-1)(i-3)}=\varepsilon' u_*\delta(u-u^{(0)}),\quad \varepsilon'>0$

- $\mathscr{D}_{ik}$ models the destruction rate. Interactions can induce net destructive events in the sense that the immune system has the ability to kill a cancer cell. We assume that the ability of the immune cells is proportional to their activity u^*. Therefore, we have:

1- For $(i,k)=(2,5),(2,6),(3,6)$: $\mathscr{D}_{ik}[\mathbf{f}](u,u^*)=\gamma u^*,\quad \gamma>0$

- The Relaxation Term is denoted by $L_i[\mathbf{f}](t,u)$ and refers to the natural loss of activity and death (apoptosis, necrosis, mitotic catastrophe) of the cells of the immune system. Then, we will assume that the immune cells in the absence of tumor cells tend to return to their healthy initial state. Therefore we will choose $\lambda_i=0$ for $i=2,3$, and $\lambda_i=\lambda$ for $i=5,6$, with $\lambda>0$.

Equations at the Cellular Scale. By substituting the above assumptions in evolution equations (1), we obtain $\frac{\partial f_1}{\partial t}(t,u)=0$, $\frac{\partial f_4}{\partial t}(t,u)$=0 and the following system of integro-differential equations given as:

$$\begin{cases}
\frac{\partial f_2}{\partial t}(t,u)=2\alpha_1 n_1(1-u)\left[f_2(t,u-u^{(0)})-(1-(u+u^{(0)}))f_2(t,u)\right]\\
\qquad\qquad +4\beta n_1 u f_2(t,u)+\varepsilon n_1 A_1\delta(u-u^{(0)})-f_2(t,u)(\sigma\gamma A_5+\sigma\gamma A_6)\\
\frac{\partial f_3}{\partial t}(t,u)=3\alpha_1 n_1(1-u)\left[f_3(t,u-u^{(0)})-(1-(u+u^{(0)}))f_3(t,u)\right]\\
\qquad\qquad +9\beta n_1 u f_3(t,u)+2\varepsilon n_1 A_2\delta(u-u^{(0)})-f_3(t,u)(\sigma\gamma A_6)\\
\frac{\partial f_5}{\partial t}(t,u)=\sigma\alpha_2 n_2(1-u)\left[f_5(t,u-u^{(0)})-(1-(u+u^{(0)}))f_5(t,u)\right]\\
\qquad\qquad +\sigma n_2\beta' f_5(t,u)+\sigma\varepsilon' n_2 A_4\delta(u-u^{(0)})-\lambda[f_5(t,u)-f_5(t_0,u_0)]\\
\frac{\partial f_6}{\partial t}(t,u)=\sigma\alpha_2 n_3(1-u)\left[f_6(t,u-u^{(0)})-(1-(u+u^{(0)}))f_6(t,u)\right]\\
\qquad\qquad +(\sigma n_2+\sigma n_3)\beta' f_6(t,u)+\sigma\varepsilon' n_3 A_5\delta(u-u^{(0)})-\lambda[f_6(t,u)-f_6(t_0,u_0)]
\end{cases} \tag{11}$$

The quantities n_i and A_i appearing in system (11) denote averaged quantities, which will be introduced in the following section. The obtained system is a complicated system of four integro-differential equations in the unknown functions f_2, f_3, f_5, f_6.

3. Macroscopic model

In what follows, we shall derive macroscopic equations for averaged quantities, from the underlying microscopic description. We expect that the macroscopic model formulated here can shed some light on several interesting phenomena related to various aspects of the immune-cancer competition.

If the distribution functions f_i are known, then macroscopic variables can be computed, under suitable integrability properties, as moments weighted by the above distribution function (Bellouquid and Delitala 2006; Bellomo 2008).

For our purpose, we consider the following macroscopic variables of each cellular population:

- *Number density*: The *size* of the i-th population at time t, given by

$$n_i[\mathbf{f}](t) = \int_{D_u} f_i(t,u)\,du \quad \text{for} \quad i \in \{1,2,\dots,6\}, \tag{12}$$

  where $D_u = [u_0, +\infty)$.
- *Activation density*: The *activation* at time t of the i-th population, defined as:

$$A_i[\mathbf{f}](t) = \int_{D_u} u f_i(t,u)\,du \quad \text{for} \quad i \in \{1,2,\dots,6\}, \tag{13}$$

- *Quadratic activation density*:

$$E_i[\mathbf{f}](t) = \int_{D_u} u^2 f_i(t,u)\,du \quad \text{for} \quad i \in \{1,2,\dots,6\}, \tag{14}$$

- *Cubic activation density*:

$$Q_i[\mathbf{f}](t) = \int_{D_u} u^3 f_i(t,u)\,du \quad \text{for} \quad i \in \{1,2,\dots,6\}. \tag{15}$$

Now by differentiating each of the both sides of the equations (12), (13), (14), with respect to t, and using the equations in system (11), we obtain a macroscopic model allowing to examine the number density n_i, the activation density A_i and the energy density E_i of each cellular population.

Indeed, for $i = 2$ we get:

$$\frac{dn_2}{dt} = 2a\alpha_1 n_1 n_2 + 4\beta n_1 A_2 + \varepsilon n_1 A_1 - n_2 \sigma\gamma(A_5 + A_6) \tag{16}$$

$$\frac{dA_2}{dt} = 2a\alpha_1 n_1 A_2 + 4\beta n_1 E_2 + \varepsilon n_1 A_1 u^{(0)} - A_2 \sigma\gamma(A_5 + A_6) \tag{17}$$

$$\frac{dE_2}{dt} = 2a\alpha_1 n_1 E_2 + 4\beta n_1 Q_2 + \varepsilon n_1 A_1 [u^{(0)}]^2 - E_2 \sigma\gamma(A_5 + A_6) \tag{18}$$

For $i = 3$ we get:

$$\frac{dn_3}{dt} = 3a\alpha_1 n_1 n_3 + 9\beta n_1 A_3 + 2\varepsilon n_1 A_2 - n_3\sigma\gamma A_6 \quad (19)$$

$$\frac{dA_3}{dt} = 3a\alpha_1 n_1 A_3 + 9\beta n_1 E_3 + 2\varepsilon n_1 A_2 u^{(0)} - A_3\sigma\gamma A_6 \quad (20)$$

$$\frac{dE_3}{dt} = 3a\alpha n_1 E_3 + 9\beta n_1 Q_3 + 2\varepsilon n_1 A_2 [u^{(0)}]^2 - E_3\sigma\gamma A_6 \quad (21)$$

For $i = 5$ we get:

$$\frac{dn_5}{dt} = \sigma a\alpha_2 n_2 n_5 + \sigma\beta' n_2 n_5 + \sigma\varepsilon' n_2 A_4 - \lambda n_5 \quad (22)$$

$$\frac{dA_5}{dt} = \sigma a\alpha_2 n_2 A_5 + \sigma\beta' n_2 A_5 + \sigma\varepsilon' n_2 A_4 u^{(0)} - \lambda A_5 \quad (23)$$

$$\frac{dE_5}{dt} = \sigma a\alpha_2 n_2 E_5 + \sigma\beta' n_2 E_5 + \sigma\varepsilon' n_2 A_4 (u^{(0)})^2 - \lambda E_5 \quad (24)$$

For $i = 6$ we get:

$$\frac{dn_6}{dt} = \sigma a\alpha_2 n_3 n_6 + \sigma\beta' n_6(n_2 + n_3) + \sigma\varepsilon' n_3 A_5 - \lambda n_6 \quad (25)$$

$$\frac{dA_6}{dt} = \sigma a\alpha_2 n_3 A_6 + \sigma\beta' A_6(n_2 + n_3) + \sigma\varepsilon' n_3 A_5 u^{(0)} - \lambda A_6 \quad (26)$$

$$\frac{dE_6}{dt} = \sigma a\alpha_2 n_3 E_6 + \sigma\beta' E_6(n_2 + n_3) + \sigma\varepsilon' n_3 A_5 (u^{(0)})^2 - \lambda E_6 \quad (27)$$

4. Lotka-Volterra model

Equations (16)–(27) show a strongly nonlinear system of ordinary differential equations. We start our study of this complex nonlinear system, going to study the time evolution of the number density of the cancer cells n_3 and that of the number density of the immune system cells n_6. Thus, we will consider only the equation (19) and (25), and will choose for the other unknown quantities suitable constitutive relations, which allows us to use the idea of two specie Lotka-Volterra model (Anisiu 2014):

$$\frac{dn_3}{dt} = 3a\alpha_1 n_1 n_3 + 9\beta n_1 A_3 + 2\varepsilon n_1 A_2 - n_3\sigma\gamma A_6 \quad (28)$$

$$\frac{dn_6}{dt} = \sigma a\alpha_2 n_3 n_6 + \sigma\beta' n_6(n_2 + n_3) + \sigma\varepsilon' n_3 A_5 - \lambda n_6 \quad (29)$$

In system (28)–(29), we make the following assumptions:

$$n_1 = 1, \quad (30)$$

$$n_2 = h_1 n_3, \quad (31)$$

$$A_2 = h_2 n_3, \quad (32)$$

$$A_3 = h_3 n_3, \quad (33)$$

$$A_5 = k_1 n_6, \quad (34)$$

$$A_6 = k_2 n_6, \quad (35)$$

which lead to the two specie Lotka-Volterra model. Indeed, we get:

$$\frac{dn_3}{dt} = (3a\alpha_1 + 9\beta h_3 + 2\varepsilon h_2)n_3 - \sigma\gamma k_2 n_3 n_6 \tag{36}$$

$$\frac{dn_6}{dt} = -\lambda n_6 + (\sigma a\alpha_2 + \sigma\beta^{'} h_1 + \sigma\beta^{'} + \sigma\varepsilon^{'} k_1)n_3 n_6 \tag{37}$$

In equation (36), we can see exponential growth of the cancer cells population n_3 in the absence of immune system, with intrinsic rate of increase $3a\alpha_1 + 9\beta h_3 + 2\varepsilon h_2$, while, when cancer cells and immune cells are both present, we note a decay in the population of cancer cells at a rate proportional $\sigma\gamma k_2 n_6$. In equation (37), in the absence of cancer cells, the immune cells population n_6 would decay to its initial size with a rate proportional to λ, which refers to the natural loss of activity and death of the cells, due to their damage or age, while, when cancer cells and immune cells are both present, we note a growth in the immune cell population a rate proportional to $(\sigma a\alpha_2 + \sigma\beta^{'} h_1 + \sigma\beta^{'} + \sigma\varepsilon^{'} k_1)n_3$.

Equilibrium. Imposing the vanishing of the temporal derivatives of n_3 and n_6, we obtain the simple algebraic system

$$\tilde{a}n_3 - \tilde{b}n_3 n_6 = 0 \tag{38}$$

$$-\lambda n_6 - \tilde{c}n_3 n_6 = 0 \tag{39}$$

where

$$\tilde{a} = 3a\alpha_1 + 9\beta h_3 + 2\varepsilon h_2, \tag{40}$$

$$\tilde{b} = \sigma\gamma k_2, \tag{41}$$

$$\tilde{c} = \sigma a\alpha_2 + \sigma\beta^{'} h_1 + \sigma\beta^{'} + \sigma\varepsilon^{'} k_1. \tag{42}$$

Hence, there are two steady solutions: $\{n_3 = 0, n_6 = 0\}$ and $\{n_3 = N_3, n_6 = N_6\}$, where

$$N_3 = \frac{\lambda}{\tilde{c}} = \frac{\lambda}{\sigma a\alpha_2 + \sigma\beta^{'} h_1 + \sigma\beta^{'} + \sigma\varepsilon^{'} k_1}, \tag{43}$$

$$N_6 = \frac{\tilde{a}}{\tilde{b}} = \frac{3a\alpha_1 + 9\beta h_3 + 2\varepsilon h_2}{\sigma\gamma k_2}. \tag{44}$$

The first solution effectively represents the extinction of both species. If both populations are at 0, then they will continue to be so indefinitely. The second solution represents a fixed point at which both populations sustain their steady non-zero values. The levels of population at which this equilibrium is achieved depend on the chosen values of the parameters, $\sigma, a, \alpha_1, \alpha_2, \lambda, \beta, \beta^{'}, \varepsilon, \varepsilon^{'}, \gamma$. We observe that if $N_3/N_6 >> 1$ the cancer cells are prevalent over the immune system and the disease can becomes malignant, on the contrary, if $N_3/N_6 << 1$ the cells of the immune system are able to contrast the formation of cancer cells and a healthy state is easily readied.

In a straightforward way, one sees that in the plane (n_3, n_6), the non steady solutions of the system are the family of lines:

$$\lambda \ln n_3 + \tilde{a} \ln n_6 - \tilde{c}n_3 - \tilde{b}n_6 + K = 0. \tag{45}$$

Where K is a constant which depends only on the initial condition.

To plot the behavior of n_3 and n_6 over time, we use for the parameters appearing in equations(36) and (37) the same values that have been used in the doctoral thesis (Dabnoun 2018) and in paper Dabnoun and Mongiovì (2018). The values are $\alpha_1 = 10^{-3}, \alpha_2 = 10^{-3}, \beta = 10^{-4}, \beta^{'} = 10^{-1}, \varepsilon = 10^{-3}, \varepsilon^{'} = 10^{-2}, \sigma = 0.5, \gamma = 1, \lambda = 0.01$, and we will select for the parameters $a, h_1, h_2, h_3, k_1, k_2$, the following values $a = 0.5, h_1 = 0.01, h_2 = 0.01, h_3 = 0.01, k_1 = 0.01, k_2 = 0.01$.

In correspondence of this choice we get $N_3 = 0.109$, $N_6 = 0.17$ and $N_3/N_6 = 0.64$. The critical point (N_3, N_6) is obtained for $K = 0.02$.

In Figure1 we plot functions $n_3(t)$ and $n_6(t)$, choosing as initial conditions $n_3(0) = 0.108$ and $n_6(0) = 0.16$, we use blue for the cancer population and red for the immune system population.

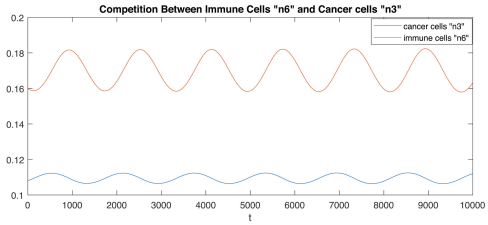

FIGURE 1. *Plot $n_3(t)$ and $n_6(t)$. The red line shows the time evolution of the immune system population, the blue one to the cancer cell population. A solution with initial conditions $(n_3(0), n_6(0)) = (0.108, 0.16)$ at the time $t = 10000$ is shown.*

5. Conclusions

In this work, we presented a spatially homogeneous model with continue activity $u \in (0, \infty)$. The mathematical approach is based on the kinetic theory of active particles developed to describe the competition between immune system and cancer cells. This continuous model is appropriate to examine macroscopic averaged quantities, as the number density n, the activation density A and the quadratic activation density E of each cellular population. It is worth mentioning that in this work we concluded that, the Lotka-Volterra model can be applied to analyze the mathematical model of the biological system "competition between the immune system and cancer cells", where the interaction of the two species give rise to periodic oscillation in their populations, see Figure 1. In the analysis, we employed a pair of ordinary differential equations to model the dynamics between the healthy cells and cancer cells. The model has taken the most basic Lotka-Volterra competition type, that known as interspecific competition.

In the forthcoming papers, the mathematical study of the system (16)–(27) will be further analyzed with the aim to obtain a better knowledge of cancer–immune system competition.

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