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Stability and existence results for a time-delayed nonlocal model of hematopoietic stem cells dynamics

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ABSTRACT

In this paper, we consider a time-delayed nonlocal model describing the dynamics of hematopoietic stem cells (HSCs), which represent the immature cells in the hematopoiesis process. By the method of characteristics, the nonlocal model is obtained from an age-structured reaction–diffusion system in bounded domain with Dirichlet boundary conditions. Along this paper, we focus on the mathematical analysis of it. Firstly, we give some results on the existence, uniqueness, positivity and boundedness of solutions. Next, we obtain a threshold value $\mathcal{R}_s$ and prove that the trivial steady state is globally asymptotically stable when $\mathcal{R}_s < 1$. When $\mathcal{R}_s > 1$, we prove the existence and uniqueness of positive stationary solution under the respective additional conditions on the monotonicity and non-monotonicity of the integral term. Finally, we prove the uniform weak persistence of the system when $\mathcal{R}_s > 1$. Some numerical simulations are provided to verify the validity of our theoretical results.

1. Introduction

The regulation of blood cells production (red blood cells, white cells and platelets) is a very complex process in which a daily renewal is so highly controlled. The set of all mechanisms that ensure the continuous replacement of the various blood cells is called hematopoiesis. This process involves a small population of immature cells called hematopoietic stem cells (HSCs). The HSCs are undifferentiated cells, located in the bone marrow before the mature blood cells enter the blood stream. They have a unique ability to produce either similar cells (self-renewal), or cells engaged in one of different lineages of blood cells (differentiation). Details about HSC dynamics can be found in [15].

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In our knowledge, the first mathematical model of HSC dynamics was proposed in 1978 by Mackey [18] and it has been improved and analyzed by many other authors [1–4,6,7,19,22,23] and the references therein. In these papers, the two phases of cell's population were considered: mature and immature cells that represent the cells in resting phase and proliferating phase, respectively (see Mackey [18]). In the previous works, the considered models were based on the system of delayed differential equations obtained by reducing an age-structured system using the characteristics method. The age here means the age of cell in each phase where it is located. In this paper, we generalize the model of Mackey by taking also account the spatial heterogeneity of resting cells and the diffusion of proliferating cells. The domain taken is the one dimensional bounded one with Dirichlet boundary conditions. Then, the resulting model is an age-structured reaction–diffusion system. This model can be reduced by using the characteristics method to a time-delayed nonlocal system.

In our knowledge, the spatial model of hematopoiesis in bounded domain is never studied before mathematically, specially, when it contains a nonlocal term. When the domain is unbounded, a spatial hematopoiesis normal or diseases models have been previously studied without taking the delay effect in [10] to model the development of myelogenous leukemia disease, in [8] to describe the dynamics of erythroid and erythroleukemia and with delay in [4,17] to model the blood cell production. In these previous works, the authors investigated spatially the existence of traveling wave fronts, which are special solutions helpful to describe the propagation phenomena. There has been extensive investigations of the time delayed models with spatial diffusion effects for the biological systems, see, Gourley and Wu's survey paper [12] and references therein. In another side, the dynamics of a nonlocal and time delayed population model in a bounded or unbounded domain has not been much investigated (for instance, see [26,27]). Recently in [27], the authors considered such model in bounded domain and they studied the existence and uniqueness of positive steady states and their global stability by using the method of super-sub solutions, combined with the careful analysis of the kernel function in the nonlocal term. In [26], the authors studied the global dynamics of a class of such differential equations with temporal delay and spatial non-locality in an unbounded domain.

As in [27], we focus on understanding the dynamics of the considered model. We obtain a threshold value and construct a Lyapunov function which shows the global asymptotic stability of the trivial steady state when the threshold value is less than one. See [16,24] for recent papers in which Lyapunov functions were constructed for spatially heterogeneous biological models. Then, we investigate the existence and uniqueness of positive steady states of our problem when the threshold value is greater than one. We distinguish two cases such as monotone and non-monotone newly proliferating HSC populations: $p(t,x,0) = \beta(N(t,x))N(t,x)$. For the monotone and non-monotone cases, we use the method of super-sub solutions and the Krasnoselskii fixed point theorem [14], respectively. Thereafter, we establish the uniform persistence of system when the threshold value is greater than one after proving the uniform weakly one.

In the next section, we first propose the HSC system, which takes the form of an age-structured system with diffusion in one dimensional bounded domain. We reduce the structured system to a time-delayed nonlocal hematopoietic stem cell model. In Section 3, the existence, uniqueness, positivity and boundedness of solutions are studied. In Section 4, we define the threshold value that plays a role for the existence and stability of steady state. The Section 5 is devoted to the study of the global asymptotic stability of the trivial steady state. In the Section 6, we investigate the existence of positive steady states, which is related to the existence of a functional-integral equation. The Section 7 is devoted to study the uniform persistence of solutions. Along the paper, some numerical simulations are carry out to illustrate the validity of our theoretical results.

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