Journal of Nonlinear Modeling and Analysis
Volume 3, Number 3, September 2021, 477–493
http://jnma.ca; http://jnma.ijournal.cn
DOI:10.12150/jnma.2021.477

Turing and Hopf Bifurcation in a Diffusive Tumor-immune Model*

Jingnan Wang[1,†] and Shengnan Liu[1]

Abstract In order to understand the effect of the diffusion reaction on the interaction between tumor cells and immune cells, we establish a tumor-immune reaction diffusion model with homogeneous Neumann boundary conditions. Firstly, we investigate the existence condition and the stability condition of the coexistence equilibrium solution. Secondly, we obtain the sufficient and necessary conditions for the occurrence of Turing bifurcation and Hopf bifurcation. Thirdly, we perform some numerical simulations to illustrate the complex spatiotemporal patterns near the bifurcation curves. Finally, we explain spatiotemporal patterns in the diffusion action of tumor cells and immune cells.

Keywords Tumor-immune model, Diffusion, Hopf bifurcation, Turing bifurcation, Stability.

MSC(2010) 34C23, 35K57.

1. Introduction

The immune system of a body can monitor the development of tumor cells, and kill them by immune mechanisms [1]. However, immune responses frequently fail to prevent the growth of tumor cells. The reason is that tumor cells can escape the immune attack of the body in many ways, including low immunogenicity of tumor cells, down-regulation of MHC class I molecules, and the lack co-stimulatory molecules. Recently, a growing body of evidence supports the conclusion that a combination of immunotherapy with conventional chemotherapy and radiotherapy may improve the outcome for treating tumors. Therefore, researchers have been shifting their focus from the method of cancer treatment to the research of tumor immunotherapy mechanisms, which arouse great interest among medical scientists, biomathematicians and statisticians in [7–10, 12–15].

In 1973, Steinman discovered that dendritic cells (DC) are the most powerful antigen-presenting cells. Immature dendritic cells have strong migration ability, which can directly ingest antigens through phagocytosis and endocytosis. Mature dendritic cells present antigens to T cells, and improve the activation of B cells. In 2012, Paluka and Banchereau [12] studied the cancer immunotherapy via dendritic cell. In 2015, Nagata and Furuta et al. constructed a mathematical model representing dynamical behaviors of T cell tumor response under the support of dendritic

†the corresponding author.
Email address: wangjingnan@hrbust.edu.cn (J. Wang)
[1]Department of Applied mathematics, Harbin University of Science and Technology, Harbin, Heilongjiang 150080, China
*The authors were partially supported by National Natural Science Foundation of China (No. 11801122) and the Natural Science Foundation of Heilongjiang Province (No. A2018008).

cells in [9]. They obtained that mutual dependence of dendritic cells and T cells in activation and tumor elimination leads to bistability between tumor immune escape and control states (immunosuppressive states). In 2016, Nakada and Nagata et al. constructed and analyzed a new mathematical model describing tumor killing by T cell response under the support of dendritic cells in [10]. In their models, there exist a handling time representing a waiting time required for T cells to be activated during antigen presentation as follows:

$$\begin{cases} \frac{\mathrm{d}C_H(t)}{\mathrm{d}t} = r\left(1-\frac{C_H(t)}{K}\right)C_H(t) - cC_H(t)N_T(t) \\ \frac{\mathrm{d}N_T(t)}{\mathrm{d}t} = \frac{\tilde{b}N_{DC}(t)}{h_{DC}+N_{DC}(t)}N_T(t) - \delta_T N_T(t) \\ \frac{\mathrm{d}N_{DC}(t)}{\mathrm{d}t} = aN_T(t)C_H(t) - \delta_{DC}N_{DC}(t) \end{cases} \tag{1.1}$$

where C_H,N_{DC} and N_T denote the densities of tumor, dendritic cells, and activated T cells respectively. r denotes replication rate, and K denotes carrying capacity. c denotes proportionality constant of tumor elimination by activated T cells. $\tilde{b}$ represents the T cell conversion rate under the action of dendritic cells and T cells, and a denotes the activation rate of dendritic cell by the mass action of activated T cells and tumors. δ_{DC} and δ_T denote in-activation rates of dendritic and T cells respectively. h_{DC} denotes the waiting time of T cell activation upon antigen presentation.

To investigate the mathematical property of (1.1) in more details, Nakada et al. applied the quasi-steady state approximation to system (1.1) by assuming that δ_{DC} is sufficiently large in [10], by substituting $N_{DC}(t) = \frac{aN_T(t)C_H(t)}{\delta_{DC}}$ into system (1.1), and by denoting $h = \frac{h_{DC}\delta_{DC}}{a}, \delta = \delta_T$, and obtained a reduced system as follows

$$\begin{cases} \frac{\mathrm{d}C_H(t)}{\mathrm{d}t} = r\left(1-\frac{C_H(t)}{K}\right)C_H(t) - cC_H(t)N_T(t) \\ \frac{\mathrm{d}N_T(t)}{\mathrm{d}t} = \frac{\tilde{b}C_H(t){N_T}^2(t)}{h+C_H(t)N_T(t)} - \delta N_T(t) \end{cases} \tag{1.2}$$

In fact, some tumor cells will enter the circulating blood and invade other tissues or organs (such as chronic and acute myelogenous Leukemia [6, 20]), which arouse our interest in studying the dynamics of diffusion reaction on the interaction between tumor cells (myelogenous cells) and immune cells. In [6, 20], we know that Chronic Myelogenous Leukemia (CML) is a cancer that results in the overproduction of immature white blood cells. The main characteristic of Chronic Myelogenous Leukemia is that immature leukocytes uncontrollably proliferate in the bone marrow, and inhibit normal hematopoiesis of the bone marrow. Then, large numbers of immature leukocytes are in the circulating blood through the blood vessels, and spread throughout various tissues (and organs). Therefore, in this paper, we introduce the diffusion term into model (1.2) to describe the spread behaviors of tumor cells (myelogenous cells) and immune cells in the circulating blood. Furthermore, we study the dynamics of the diffusive tumor-immune model.

This paper is organized as follows: In Section 2, we present the existence condition and the stable condition of the coexistence equilibrium solution. In addition, we obtain sufficient and necessary conditions for the occurrence of Turing bifurcation and Hopf bifurcation. In Section 3, numerical simulations are illustrated to support analyses results and show complex spatiotemporal patterns near the bifurcation curves based on the bifurcation diagram of two parameters for the diffusive tumor-immune model. Finally, discussions and conclusions are shown in Section 4.