Nonlinear Phenomena and Chaos in a Tumor Growth Model

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Abstract. In this work the effect of the population of the normal cells in the mechanism for avascular, vascular and metastatic tumor growth is studied. For this reason, a recently new system, proposed by Llanos-Perez *et al*. (2016), which is based on a chemical network model, is used. A dynamical investigation of system's behavior is performed by invoking key concepts of nonlinear dynamics, such as the phase portrait, the Poincaré map, the bifurcation diagram the Kaplan-Yorke dimension and the diagrams of Lyapunov exponents. Various cases of the system are examined by changing the populations of the host cells of the model for a specific value of the population of the immune cells. As a result, many interesting phenomena related to chaos theory arise, including period-doubling route to chaos, crisis phenomena, and antimonotonicity.

Introduction

In the last decade many research teams work on using dynamical system analysis for studying specific phenomena related to distinct stages (avascular, vascular and metastatic) of cancer. The reason of this is because the growth of malignant tumors can be described as an ordinary differential equation (ODE) models including two main populations: effector cells and tumor cells. Especially, dynamical systems with chaotic behavior have been used widely for this purpose. Recently, an interesting model, which is based on a chemical network, in order to introduce a mechanism for avascular, vascular and metastasis tumor growth, is introduced by Llanos-Perez *et al*. [1]. Since then many researchers have used this model. In more details, Betancourt-Mar *et al*. [2] extended this model on existing thermodynamics formalism for the metabolic rate of human cancer cells. Montero *et al*. [3] worked on a biological approach of this problem. Guerra *et al*. [4] generalized the aforementioned work with the inclusion of the epithelial-mesenchymal transition, which is a biologic process that allows a polarized epithelial cell, which normally interacts with basement membrane via its basal surface, to undergo multiple biochemical changes. These changes enable it to assume a mesenchymal cell phenotype that includes enhanced migratory capacity, invasiveness, and increased resistance to apoptosis.

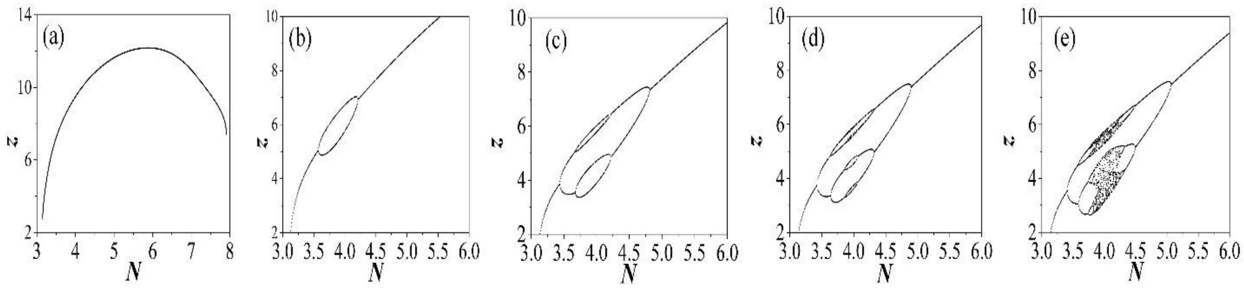

Figure 1: Bifurcation diagrams of the proposed system for increasing values of the population of the normal cells N, for $I = 2$ and (a) $H = 2$, (b) $H = 3.5$, (c) $H = 4.2$, (d) $H = 4.3$, (e) $H = 4.5$.

Results and Discussion

By using a well-known tool from the nonlinear theory, the bifurcation diagram, interesting phenomena related to chaos theory, such as a period-doubling route to chaos, crisis phenomena, and antimonotonicity are revealed, for the first time for the specific model, by considering the population of the normal cells N as a bifurcation parameter. In this case, the population of immune cells I has a specific value, while the population of the host cells H varies. Consequently, the procedure of forming periodic (Figs.1(a) - 1(c)) and chaotic bubbles (Fig1(d)), as the value of H increases, is revealed. Furthermore, the system's phase portraits, Poincaré maps and diagrams of Lyapunov exponents have been used in order to study the special features of the specific model.

References

[1] Llanos-Pérez, J.A., Betancourt-Mar, J.A., Cocho, G., Mansilla, R., Nieto-Villar J.M. (2016) Phase Transitions in Tumor Growth: III Vascular and Metastasis Behavior. *Physica A*, **462**, 560-568.

[2] Betancourt-Mar, J.A., Llanos-Pérez, J.A., Cocho, G., Mansilla, R., Martin, R.R., Montero, S., Nieto-Villar, J.M. (2017) Phase Transitions in Tumor Growth: IV Relationship Between Metabolic Rate and Fractal Dimension of Human Tumor. *Physica A*, **473**, 344-351.

[3] Montero, S., Martin, R., Mansilla, R., Cocho, G., Nieto-Villar, J. M. (2018) Parameters Estimation in Phase-Space Landscape Reconstruction of Cell Fate: A System's Biology Approach. In Systems Biology (pp. 125-170). Humana Press, New York, NY.

[4] Guerra, A., Rodriguez, D.J., Montero, S., Betancourt-Mar, J.A., Martin, R.R, Silva, E., Bizzarri, M., Cocho, G., Mansilla, R., Nieto-Villar, J.M. (2018) Phase Transitions in Tumor Growth VI: Epithelial–Mesenchymal Transition. *Physica A*, **499**, 208-215.