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Conditions Regulating Tumor Cell Behaviour in Biological Systems with Memory of States

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Abstract: For biological systems with memory of states there were found conditions which regulate tumor cell behaviour. These conditions depend on parameters of the multi-parametric space. Based on the Masing–Bouc-Wen's framework, the state memory in the biological system was simulated by means of supplemental state variables (internal variables). The additional state variables were introduced into the generalized non-linear multi-scale diffusion cancer invasion model and the chaotic cancer attractors were found. To quantify chaotic cancer attractors, the technique based on the wandering trajectories analysis was applied.

Keywords: biological system with memory of states, tumor growth, carcinogenesis, chaotic attractors, response delay

1. Introduction

This work is the continuation of the studies presented in our earlier publications [1, 2] in which the conditions controlling cancer invasion were defined depending on parameters of the multi-parametric space as well as the influence of the initial state of a biological system on carcinogenesis.

The biological systems with memory of states do not react instantly to external perturbations. Such systems have a response delay. In this study, the memory of states was simulated by means of additional state variables (internal variables) using Masing–Bouc-Wen's framework [3–4]. Applications to different types of hysteresis loops confirmed that models with internal variables are appropriate to simulate hysteresis from very different fields.

2. Mathematical Model and Simulation Results

In the model studied in this work, the tumor development is governed by the inhomogeneous dissipative set of differential equations:

$$\dot{n} = 0, \tag{1}$$

$$\dot{f} = \alpha\eta(m-f) + h_f z_f, \tag{2}$$

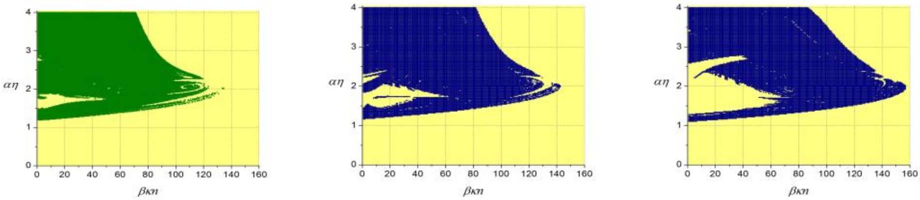
$$\dot{z}_f = \left[A_f - \left(\gamma_f + \beta_f sgn(\dot{f}) sgn(z_f)\right)|z_f|^{n_f}\right]\dot{f}, \tag{3}$$

$$\dot{m} = \beta\kappa n + f(\gamma - c) - m + h_m z_m, \tag{4}$$

$$\dot{z}_m = \left[A_m - \left(\gamma_m + \beta_m sgn(\dot{m}) sgn(z_m)\right)|z_m|^{n_m}\right]\dot{m}, \tag{5}$$

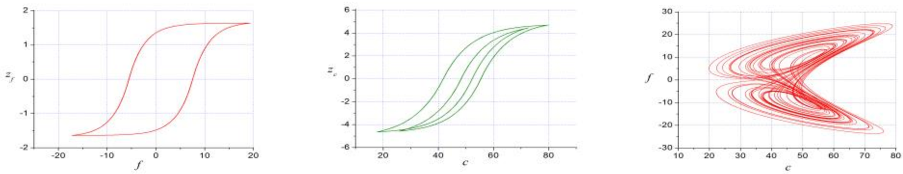
$$\dot{c} = \nu fm - \omega n - \delta\phi c + h_c z_c, \tag{6}$$

$$\dot{z}_c = \left[A_c - \left(\gamma_c + \beta_c sgn(\dot{c}) sgn(z_c)\right) |z_c|^{n_c} \right] \dot{c}. \tag{7}$$



(a) (b) (c)

Fig. 1. Conditions leading to cancer invasion in the biological systems with memory of states (1)-(7) in control parameter plane ($\beta\kappa n$, $\alpha\eta$)–'tumor cell volume vs glucose level': (a) $h_f=h_m=h_c=0$; (b) $h_f=0.5$, $h_m=0.4$, $h_c=0.3$; (c) $h_f=h_m=h_c=0.9$



(a) (b) (c)

Fig. 2. Responses delay of the biological systems with memory of states (1)-(7) with $h_f=0.5$, $h_m=0.4$, $h_c=0.3$: (a), (b) hysteretic loops at $\beta\kappa n=3.0$, $\alpha\eta=1.75$ (a chemical clock); (c) a chaotic attractor in MM, MDE and oxygen concentrations phase space projected to phase plane (c, f) at $\beta\kappa n=3.0$, $\alpha\eta=4.0$

The meaning of variables is as follows: n – tumor cell density; f – matrix–metalloproteinases (MM) concentration; m – matrix-degradative enzymes (MDE) concentration; c – oxygen concentration; z_f, z_m, z_c present the hysteretic part of the system considered. On the other hand, the fitting parameters are defined as follows: α – tumor cell volume; β – glucose level; γ – number of tumor cells; δ – diffusion saturation level; η and κ are coefficients describing a growth and decay of MM and MDE concentration, respectively; υ , ω, φ govern growth and decay of the oxygen concentration. The parameters (A_f, β_f, n_f), (A_m, β_m, n_m), (A_c, β_c, n_c) $\in R^+$ and γ_f, γ_m, $\gamma_c \in R$ govern the shape of the hysteresis loops. The parameters h_f, h_m, h_c characterise a hysteresis contribution to the system considered.

3. Concluding Remarks

Analysis of the results obtained demonstrates a significant influence of the state memory on the evolution of conditions leading to cancer invasion in biological systems depending on components of the multi-parametric space ‘number of tumor cells – tumor cell volume – glucose level – diffusion saturation level’.

References

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