BioSystems 96 (2009) 172–177

Contents lists available at ScienceDirect

BioSystems

journal homepage: www.elsevier.com/locate/biosystems

Observation and control in a model of a cell population affected by radiation

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ARTICLE INFO

Article history:
Received 19 October 2008
Received in revised form 20 January 2009
Accepted 22 January 2009

Keywords:
Population dynamics
Observability
Observer system
Cell radiation

ABSTRACT

The effect of radiation on a cell population is described by a two-dimensional nonlinear system of differential equations. If the radiation rate is not too high, the system is known to have an asymptotically stable equilibrium. First, for the monitoring of this effect, the concept of observability is applied. For the case when the total number of cells is observed, without distinction between healthy and affected cells, a so-called observer system is constructed, which, at least near the equilibrium state, makes it possible to recover the dynamics of both the healthy and the affected cells, from the observation of the total number of cells without distinction.

Results of simulations with illustrative data are also presented. If we want to control the system into a required new equilibrium state, and maintain this new equilibrium by a constant control, a technique of theory of optimal control can be applied to construct a feedback control system.

1. Introduction

Organisms can be exposed to radiation under different circumstances. For example, in case of a nuclear disaster, normal cells of the human body can be dangerously affected by radiation. In radiotherapy instead, killing cancerous cells is one of the most important treatments of malignant tumors. Although therapeutic radiation (both in external and internal treatment) targets specific areas where tumors are formed, it can also affect healthy cells in the immediate vicinity. In all cases the knowledge of the dynamics of the effect of radiation to a cell population is of crucial importance.

A primary effect of radiation is causing chromosome damage. As a result, the affected cells can not reproduce and will eventually die. It happens however, that some broken chromosomes recombine and in this way an affected cell, with certain probability, returns to normal, see Sachs et al. (1992); Schöllnberger et al. (1999); Nickoloff and Hoekstra (1998). This is an important information for the dynamical modeling of the effect of radiotherapy.

Over the last decades, mathematical modeling supporting different cancer therapy methods has gained growing attention. For a mathematical and simulation analysis of chemotherapy, see e.g. Pinho et al. (2002). Nani and Freedman (2000) dealt with the qualitative analysis of a dynamic model of immunotherapy. Sachs et al. (2001) surveyed various differential equation models supporting radiotherapy. A recent general overview of mathematical modeling of different cancer therapy methods can be obtained from the special issue Horn and Webb (2004).

In the present paper a single cell population exposed to radiation will be divided into the subpopulations of affected and unaffected cells, respectively. (Such a model, in principle, can be applied separately to the cancerous and to the healthy cells.) Specifically, in our model the terms healthy and irradiated (affected) cells correspond to the radiation of the normal (i.e. not cancerous) cells. However, the same methodology invariably applies to the case of the tumoral cell population. A more complex approach will be based on the model involving both cancerous and healthy cell populations, see Belostotski and Freedman (2005); Freedman (2006). The necessary stability analysis of such model has been recently published in Freedman and Pinho (2009).

Our investigations will be based on the model considered in Freedman and Pinho (2008), where a two-dimensional nonlinear system of ordinary differential equations describes the respective dynamics of the population of the healthy cells and those affected by radiation, and the irradiated cells at a certain rate recombine into healthy cells. In this model the growth of the healthy cells is supposed to be logistic.

Mathematical systems theory offers a methodology for the analysis of qualitative properties of the models of cancer therapy, such as stability of equilibria, controllability and observability. In Belostotski and Freedman (2005), Freedman and Pinho (2008, 2009) important results are published on the stability of cell populations under radiotherapy. We will also use some of these results. Concerning different radiation models, in Belostotski and Freedman

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doi:10.1016/j.biosystems.2009.01.004