ANALYSIS OF A CLASS OF INFINITE DIMENSIONAL SYSTEMS BASED ON MODEL DECOMPOSITION

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Abstract: This paper is concerned with modeling and control of a class of bilinear systems. They are described by infinite number of ODEs. After introduction of model applications, the methodology of analysis of such models, based on system decomposition, is presented. The model description is transformed into a vector integro-differential equation, which makes it possible to analyze its behavior and address a particular optimization problem arising in the given model application. The optimization problem is stated and necessary conditions of optimal control are derived. Subsequently, the gradient method for finding optimal control is shown, illustrated by an example. Finally, some remarks on the model applicability are presented.

Keywords: Systems methodology, Infinite dimensional systems, optimal control.

1. INTRODUCTION

Despite long history of research and rich literature devoted to problems of modeling and control of infinite dimensional systems, almost all efficient methods developed to deal with them present approaches suitable for PDE models. Optimization tasks, on the other hand, are often limited to LQ problems. More general solutions, involving abstract differential equations (Curtain and Zwart, 1995), lead, in turn, to theoretical results, which applicability is arguable.

Models based on infinite number of state equations may be applied to a variety of systems. They may describe e.g. RC ladders, which are approximation of long transmission lines, models of drug resistance evolution caused by gene amplification (Kimmel and Axelrod, 1990, Polanski *et al*., 1997), or some queuing systems (Kleinrock, 1976). Usually, additional assumptions are made, resulting in tridiagonal system matrices. Analysis of such models is often limited to their finite-dimensional approximation. However, in that case, some dynamical properties may be neglected. Other approaches consist in diffusion approximation.

Yet another approach, used in modeling of queuing systems, is based on analysis of linearized models and mean probabilities instead of state variables.

It should be stressed that, as shown in our previous papers, (e.g. Swierniak *et al.*, 1998), work on infinite dimensional models in the form of ODEs may lead to compact results, convenient in further analysis, which would be impossible or very difficult to obtain when using other methods. Moreover, the models dealt with in this paper are nonlinear one and base on state space description.

The main applications of the work seem to be in the fields of biomathematics and controlled queuing systems. The first domain includes, among others, modeling of evolution of cancer cells and design of optimal chemotherapy protocols. The latter may cover applications in computer or telecommunication systems. The examples from both areas are presented in the following sections.

The main contribution of this paper is in presenting a coherent methodology that makes it possible to effectively analyze the introduced class of dynamical systems. Though it bases on our previous works (e.g.

Smieja et al. 2002), the model hitherto presented is much more general than those studied in the past. Moreover, the biomedical model that serves as an example here, has been corrected here (in comparison to (Smieja *et al.*, 2003)) to more closely follow the behavior of a biological system.

2. A MODEL OF CONTROLLED QUEUING SYSTEM.

Let us suppose that in the analyzed queuing system intensity of service can be controlled. It can be achieved, for example by directing incoming requests to different stations that have different performance (with cost of use or leasing them increasing with growing efficiency). It is justifiable to assume that the difference in the efficiency will be visible only for small length of the queue. If $P_i(t)$ denotes the probability that the length of the queue at the time instant t is equal to i, the resulting set of equations describing such system can be presented in the following way:

$$\begin{cases} \dot{P}_0(t) = -\lambda_0 P_0(t) + [1+u(t)]\mu_1 P_1(t) \\ \dot{P}_1(t) = \lambda_0 P_0(t) - (\lambda_1 + [1+u(t)]\mu_1) P_1(t) + \\ \qquad + [1+u(t)]\mu_2 P_2(t) \\ \dots \\ \dot{P}_i(t) = \lambda_{i-1} P_{i-1}(t) - (\lambda_i + [1+u(t)]\mu_i) P_i(t) \\ \qquad + \mu_{i+1} P_{i+1}(t) \\ \qquad\qquad\qquad\qquad for\ 1 \le i < l \\ \\ \dot{P}_i(t) = \lambda P_{i-1}(t) - (\lambda+\mu) P_i(t) + \mu P_{i+1}(t) \\ \qquad\qquad\qquad\qquad for\ l \le i \\ \dots \end{cases} \tag{1}$$

where λ, λ_i, μ and μ_i are model parameters, $0 \le u(t) \le u_{\max}$ represents control effect on the service intensity.

The aim is to minimize probability of a very long queue, simultaneously taking into account the cumulative cost of the control, i.e.

$$\min \leftarrow J = \sum_{i \ge l} P_i(T) + r \int_0^T u(t)dt \tag{2}$$

3. BIOMATHEMATICAL MODELS

In this section certain model of cell population with evolving drug resistance caused by gene amplification or other mechanisms is presented. The model, based on results of (Harnevo and Agur, 1993, Axelrod *et al.*, 1994), is general enough to accommodate different interpretations and its properties has been thoroughly discussed in our previous works (see e.g. Smieja at al., 2000, Smieja and Swierniak, 2003).

We consider a population of neoplastic cells stratified into subpopulations of cells of different types, labeled by numbers i = 0,1,2, … . If the biological process considered is gene amplification, then cells of different types are identified with different numbers of copies of the drug resistance gene and differing levels of resistance. Cells of type 0, with no copies of the gene, are sensitive to the cytostatic agent. Due to the mutational event the sensitive cell can acquire a copy of gene that makes it resistant to the agent. Likewise, the division of resistant cells can result in the change of the number of gene copies but the probability of mutational event in a sensitive cell is of several orders smaller than the probability of the change in number of gene copies in a resistant cell. Since we do not limit the number of gene copies per cell, the number of different cell types is denumerably infinite. Depending on the assumptions about model parameters and chemotherapy properties, its dynamics can be differently presented. Two examples are given below, in which $N_i(t)$ denotes the expected number of cells of type i at time t.

3.1. A model taking into account partial sensitivity of the resistant subpopulation

In this case, it is assumed that the resistant subpopulation consists of two parts – one, which is partially sensitive to the drug, and another one, completely drug-resistant. Then the following set of equations is obtained:

$$\begin{cases} \dot{N}_0(t) = [1-2u_0(t)]\lambda_0 N_0(t) - \alpha N_0(t) + d_1 N_1(t) \\ \\ \dot{N}_1(t) = [1-2\mu_1 u(t)]\lambda_1 N_1(t) - (b_1+d_1) N_1(t) + \\ \qquad + d_2 N_2(t) + \alpha N_0(t) \\ \qquad \dots \\ \dot{N}_{l-1}(t) = [1-2\mu_{l-1}u(t)]\lambda_{l-1} N_{l-1}(t) - (b_{l-1}+d_{l-1}) N_{l-1}(t) + \\ \qquad + d_l N_l(t) + b_{l-2} N_{l-2}(t) \\ \qquad \dots \\ \dot{N}_i(t) = \lambda N_i(t) - (b+d) N_i(t) + d N_{i+1}(t) + \\ \qquad + b N_{i-1}(t), \\ \qquad i \ge l \\ \qquad \dots \end{cases} \tag{3}$$

where $0 \le \mu_i \le 1$ μ_i are "efficiency factors", determining the effectiveness of the drug in relation to particular type of cell. Due to general assumptions about the model, presented at the beginning of this section, these factors satisfy the following relations:

$$0 \le \mu_i \le \mu_{i-1} \le 1,\ i = 1,2,...,l-1. \tag{4}$$

3.2. Phase-specific chemotherapy

The cell cycle is composed of a sequence of phases, traversed by each cell from its birth to division. These phases are: G_1, or the growth phase; S, or the DNA synthesis phase; G_2, or the preparation for division phase; and M, or the division phase. After division, the two daughter cells usually re-enter G_1. It may however happen, that one or both daughters deviate from this path and become dormant or

resting, or in other words, they enter the quiescent G_0 phase. From there after a variable and usually rather long time cells may reenter the cell cycle in G_1 (Baserga, 1985).

The subpopulation sensitive to the cytostatic agent will consist of three types of cells: type $i = 0$, being in the phase G_1 $i = 1$, being in the phase S and $i = 2$ being in the phase G_2M. The cells of type $i \geq 3$ are assumed to be completely drug resistant and therefore no cell cycle phases are explicitly distinguished in them. If $N_i(t)$ denotes the average number of cells of type i at the time t, then the system is described by the following set of equations:

$$\begin{cases} \dot{N}_0(t) = -\lambda_0 N_0(t) + \left(2\lambda_2\left[1-u(t)\right] - \gamma\right)N_2(t) \\ \qquad + dN_3(t) \\ \dot{N}_1(t) = -(1-v)\lambda_1 N_1(t) + \lambda_0 N_0(t) \\ \dot{N}_2(t) = -\lambda_2 N_2(t) + (1-v)\lambda_1 N_1(t) \\ \dot{N}_3(t) = \lambda_3 N_3(t) - (b+d)N_3(t) + \gamma N_2(t) \\ \qquad + dN_4(t) \\ \qquad \cdots \\ \dot{N}_i(t) = \lambda N_i(t) - (b+d)N_i(t) + dN_{i+1}(t) + bN_{i-1}(t), \\ i \geq 3 \\ \qquad \cdots \end{cases} \tag{5}$$

Due to the interpretation of the control variables u and v

$$0 \leq u(t),\, v(t) \leq 1 \tag{6}$$

The goal is to find the optimal control, which minimises the performance index:

$$J = \sum_{i=0}^{2} N_i(T) + r_1 \sum_{i=3}^{\infty} N_i(T) + r\int_0^T \left[u(\tau) + v(\tau)\right]d\tau \tag{7}$$

where r_1, $r \geq 0$ are weighing factors.

The idea on which such optimisation is based is to minimise the resistant cancer subpopulation at the end of therapy with simultaneous minimisation of negative cumulative effect of the drug represented by the integral component.

4. ANALYSIS OF A GENERAL MODEL

Although more examples could be given, all of them form a class of infinite dimensional, bilinear systems that can be described by following state equation:

$$\dot{x} = \left(\mathbf{A} + \sum_{i=0}^{m} u_i \mathbf{B}_i\right)x, \tag{8}$$

where

$$\mathbf{A} = \begin{bmatrix} \widetilde{\mathbf{A}}_1 & | & \mathbf{0}_1 \\ - & - & - \\ \mathbf{0}_2 & | & \widetilde{\mathbf{A}}_2 \\ & | & \end{bmatrix}, \mathbf{B} = \begin{bmatrix} \widetilde{\mathbf{B}}_i & | & \mathbf{0}_1 \\ - & - & - \\ & \mathbf{0}_3 & \end{bmatrix},$$

$$\widetilde{\mathbf{A}}_1 = \begin{bmatrix} a_{00} & a_{01} & \dots & a_{0,l-1} & 0 \\ a_{10} & a_{11} & \dots & a_{1,l-1} & 0 \\ \vdots & \vdots & \dots & \vdots & 0 \\ a_{l-1,0} & a_{l-1,1} & \dots & a_{l-1,l-1} & a_{l-1,l} \end{bmatrix},$$

$$\widetilde{\mathbf{A}}_2 = \begin{bmatrix} c_1 & a_2 & a_3 & 0 & 0 & \dots \\ 0 & a_1 & a_2 & a_3 & 0 & 0 & \dots \\ 0 & 0 & a_1 & a_2 & a_3 & 0 & \dots \\ \vdots & \vdots & \ddots & \ddots & \ddots & \ddots & \ddots \end{bmatrix},$$

$$\widetilde{\mathbf{B}}_i = \begin{bmatrix} b^i_{0,0} & b^i_{0,1} & \dots & b^i_{0,l-1} \\ b^i_{1,0} & b^i_{1,1} & \dots & b^i_{1,l-1} \\ \vdots & \vdots & \dots & \vdots \\ b^i_{l-1,0} & b^i_{l-1,1} & \dots & b^i_{l-1,l-1} \end{bmatrix} \tag{9}$$

$u(t)$ – m-dimensional control vector $u = [u_0\, u_1\, u_2 \dots u_{m-1}]^T$, $\mathbf{0}_1$, $\mathbf{0}_2$, $\mathbf{0}_3$– zero matrices of dimensions $l \times \infty$, $\infty \times l-1$ and $\infty \times \infty$, respectively, $l > m$.

It is important to note that model parameters satisfy the following relations: $a_3 > a_1 > 0$, and $a_2 < 0$. However, full problem analysis can be done in other possible cases (e.g. when no additional conditions are to be satisfied by parameters a_1, a_3), using exactly the same line of reasoning.

The performance index to be minimised is given by

$$J = \sum_{i=0}^{l-1} x_i(T) + r_1 \sum_{i=l}^{\infty} x_i(T) + r\sum_{k=0}^{m}\int_0^T u_k(\tau)d\tau \tag{10}$$

To make analysis of such models possible it is convenient to present it in the form of a block diagram shown in Fig.1, effectively decomposing the model into two parts The first one, of finite dimension, does not require parameters to meet any particular assumptions. The second subsystem is infinite dimensional, with tridiagonal system matrix, and does not include terms containing control variables and non-zero initial conditions.

It has been shown in our previous works devoted to biomedical modeling (Smieja and Swierniak, 2003, Swierniak *et al*. 1999), that for initial condition $x_i(0) = \delta_{ik}$ (Kronecker delta), i.e. $x_k(0) = 1$, $x_i(0) = 0$ for $i \neq k$, following relations hold true:

$$x_l^k(s) = \frac{1}{a_3}\left(\frac{s - a_2 - \sqrt{(s-a_2)^2 - 4a_1a_3}}{2a_1}\right)^{k-l+1} \tag{11}$$

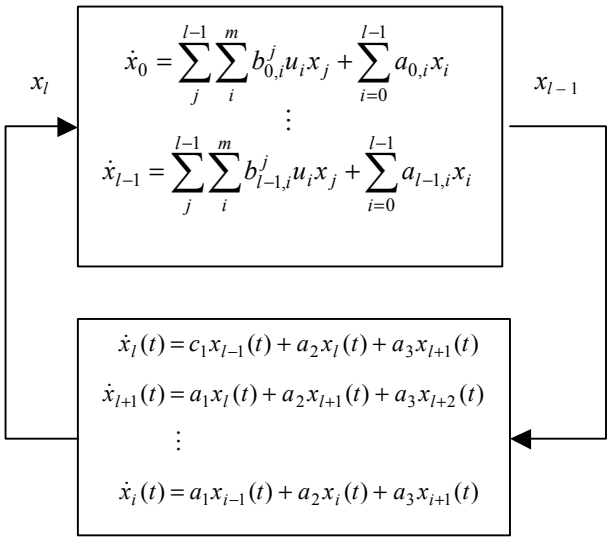

Figure 1. Decomposition of the general system model

$$x_\Sigma^k(s) = \frac{1}{s-(a_1+a_2+a_3)} \cdot \left[1-\left(\frac{s-a_2-\sqrt{(s-a_2)^2-4a_1a_3}}{2a_1}\right)^{k-l}\right] \quad (12)$$

where $x_l^k(s)$, $x_\Sigma^k(s)$ - Laplace transforms of $x_l^k(t)$ and $\sum_{i\geq 1} x_i^k(t) = x_\Sigma^k(t)$, respectively (superscript k is introduced to underscore the index of the state variable with non-zero initial condition). Now, let us assume that $k = l$. Then, after calculating inverse Laplace transform the following formulae are obtained:

$$x_l^l(t) = \frac{1}{a_3}\left(\sqrt{\frac{a_3}{a_1}}\right)\frac{I_1\left(2\sqrt{a_1a_3}\,t\right)}{t}\exp(a_2t) \quad (13)$$

$$x_\Sigma^l(t) = \sum_{i\geq l} N_i(t) = \exp\left[(a_1+a_2+a_3)t\right] \cdot \left[1-\left(\sqrt{\frac{a_3}{a_1}}\right)\int_0^t \frac{I_1\left(2\sqrt{a_1a_3}\,\tau\right)}{\tau}\exp\left[-(a_1+a_3)\tau\right]d\tau\right] \quad (14)$$

where $I_k(t)$ – modified Bessel function of the k-th order.

Taking into account the meaning of the impulse response and transfer function it can be easily proved that the following relation holds true:

$$K_1(s) = \frac{x_l(s)}{x_{l-1}(s)} = \frac{s-a_2-\sqrt{(s-a_2)^2-4a_1a_3}}{2a_1} \quad (15)$$

This makes it possible to analyze stability of the closed-loop system (Smieja et al. 2002).

Let us now assume the initial conditions $x_i(0) = 0$ for $i \geq l$-1. The assumption does not constrain applicability of the model, since it is justified in most cases. Moreover, unless there is non-zero initial condition on infinite number of state variables it is always possible to decompose the model in such way that the condition is satisfied.

Then, the last equation in the first subsystem, influenced directly by control, as presented on Fig. 1, can be transformed into an integro-differential form:

$$\dot{x}_{l-1}(t) = \sum_{j=0}^{l-1}\sum_{i=0}^{m} b_{l-1,i}^j u_i(t) x_j(t) + \sum_{i=0}^{l-1} a_{l-1,i} x_i(t) + a_{l-1,l}\int_0^t k_1(t-\tau)x_{l-1}(\tau)d\tau \quad (16)$$

where $k_1(t)$ is the inverse Laplace transform of $K_1(s)$, given by (13) multiplied by a_3.

If we denote

$$\tilde{x} = \begin{bmatrix} x_0 \\ \vdots \\ x_{l-1} \end{bmatrix} \quad (17)$$

then the system (8) of infinite number of differential equations can be transformed into the set of l-1 differential and one integro-differential equations

$$\dot{\tilde{x}} = h(u,\tilde{x}) + \int_0^t \tilde{f}(\tilde{x},t,\tau)d\tau, \quad (18)$$

where $h(..), \tilde{f}(...)$ - respective l–dimensional vector functions

$$h_k(u,\tilde{x}) = \sum_{j=0}^{l-1}\sum_{i=0}^{m} b_{k,i}^j u_i(t) x_j(t) + \sum_{i=0}^{l-1} a_{k,i} x_i \quad (19)$$

$$\tilde{f}_k(\tilde{x},t,\tau) = \begin{cases} 0 & for \quad k < l-1 \\ a_{l-1,l}k_1(t-\tau)x_{l-1}(t) & for \quad k = l-1 \end{cases} \quad (20)$$

Furthermore,

$$\sum_{i\geq l} x_i(t) = x_\Sigma^l(t) + x^+(t) \quad (21)$$

where

$$x^+(t) = c_1 \int_0^t x_\Sigma^l(t-\tau) x_{l-1}(\tau) d\tau \qquad (22)$$

and $x_\Sigma^l(t)$ is defined by (14).

It should be emphasized that the transformation of the system description from (8) to (18) does not require any additional conditions. Moreover, the methodology can be further extended to systems, whose first subsystem can take any form – not necessarily linear. The only constraining assumption is the form of the second, infinite-dimensional subsystem, which must be given exactly in the form presented here. However, in more general case, in which the function $h_k(\,)$ is not constrained by the form given by (18), though the transformation of system description is possible, it does not yield a specific solution to the optimization problem unless the class to which this function belongs, is defined.

This description can be used for model simulation. Indeed, in most applications even though the full state is infinite-dimensional, only the first state variables are of interest (e.g. the probability that the length of a queue is relatively low, i.e. below given l). What should be stressed is that the formulae obtained by model decomposition, at least in some cases are much simpler than those found in literature. For example, the relation describing probability in M/M/1 system includes terms containing infinite series of Bessel function (Kleinrock, 1976)

$$P_n(t) = e^{(\lambda+\mu)t}\left[\rho^{\frac{n-j}{2}} I_{n-j}(at) + \right.$$

$$\left. + \rho^{\frac{n-j+1}{2}} I_{n+j+1}(at) + (1-\rho)\rho^n \sum_{i=n+j+2}^{\infty} \rho^{-\frac{j}{2}} I_i(at)\right] \qquad (23)$$

$$a = 2\mu\sqrt{\frac{\lambda}{\mu}},$$

For the sake of modeling, the description presented in this paper is clearly much more convenient.

5. SOLVING THE OPTIMAL CONTROL PROBLEM

The optimization problem is defined by the system (19), performance index (10) and constraints on control

$$0 \le u_k(t) \le 1$$

A number of formulations of necessary conditions for the optimization problem for dynamical systems governed by integro-differential equations can be found in literature. However, they usually either are too general to be efficiently applied in such particular problem or have too strong constraints for example smoothness of the control function. Nevertheless, following the line of reasoning presented in (Bate 1969), it is possible to derive the necessary conditions for optimal control (Smieja and Swierniak, 2003):

$$u^{opt}(t) = \arg\min_u \left[r\sum_{k=0}^{m} u_k(t) + p^T(t) h(u,\tilde{x}) + \right.$$

$$\left. + a_{l-1,l} \int_t^T p_{l-1}(\tau) k_1(t-\tau) N_{l-1}(\tau) d\tau \right] \qquad (24)$$

$$\dot{p}^T(t) = -\left[q^T(t) + p^T(t) h_{\tilde{x}}(u,\tilde{x})) + \int_t^T p^T(\tau) \tilde{f}_{\tilde{x}}(t-\tau) d\tau \right]$$

(25)

$$q(t) = \begin{bmatrix} 0 & \dots & 0 & r_1 c_1 N_\Sigma^l(T-t) \end{bmatrix}^T \qquad (26)$$

$$p_i(T) = 1,\ i = 0,1,...,l-1 \qquad (27)$$

$p(t)$ – adjoint vector.

Taking into account constraints on control variable and bilinear form of (19), it can be proved that, in order to satisfy (24), the optimal control must be of bang-bang type, under condition of nonexistence of singular arcs. Then, to find optimal number of switches and switching times, a gradient method can be developed, following the line of reasoning presented in (Smieja *et al*. 2000) that was developed for a scalar control. One must remember, however, that in the case of infinite dimensional model and bang-bang control, finding the optimal number of switches is almost impossible. Therefore our algorithm will find optimal switching times for arbitrarily chosen number of switches. Of course, it should be afterwards modified to analyse the effect of this number on the performance index, nevertheless the conclusions regarding the global minimum are a very delicate matter.

Let us denote the switching times for control variables u_k by $\tau_{j_k}^{u_k}$.

$$\tilde{H} = r\sum_{k=0}^{m} u_k(t) + p^T(t) h(u,\tilde{x}) \qquad (28)$$

The change of the switching time required to minimize value of the performance index J is given by the following relation:

$$\delta\tau_{j_k}^{u_k} = (-1)^j \alpha_j \left.\frac{\partial \tilde{H}}{\partial u_k}\right|_{\tau = \tau_{j_k}^{u_k}} \qquad (29)$$

$j_k = 1,2, \dots, M_k$, κ_j - positive number

Taking this into account the following algorithm can be applied:

1. Assume number of switches for control variables u and v, as well as initial switching times for those controls.
2. Solve the equation describing the system (18) for bang-bang control with assumed switching times.
3. Compute $p(t)$ from the adjoint equation (25) integrating it backward in time.
4. Calculate values of $\delta\tau_{j_k}^{u_k}$ from (29).
5. Compute new switching times.
6. Repeat steps 2-5 until stop condition is satisfied.

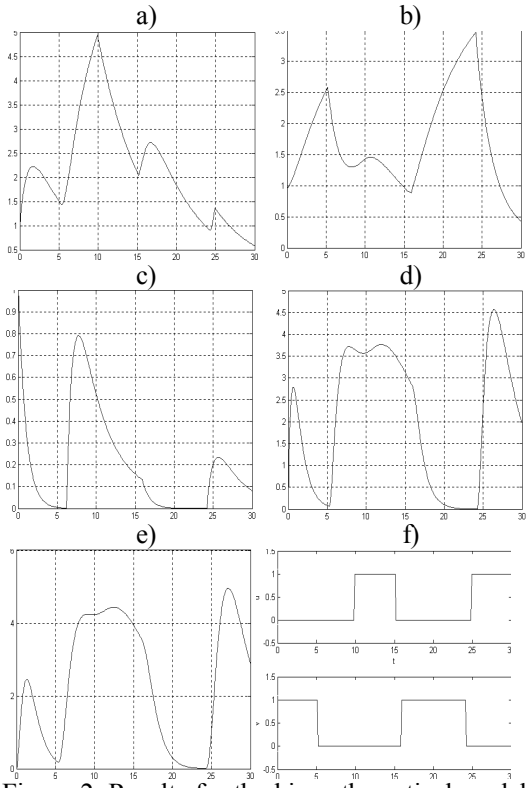

Figure 2. Results for the biomathematical model (5): a) $N_0(t)$, b) $N_1(t)$, c) $N_2(t)$, d) $N_3(t)$, e) $N_\Sigma(t)$, f) $u(t)$ (upper part) and $v(t)$.

The gradient method has been applied to the biomedical model given by (5) and the results are shown in the Fig.2. Their main implication is that the two drugs should be administered in alternate fashion, which confirms the currently used medical procedures

Though the concept of choosing arbitrary number of switches may seem arguable, at best, one must remember that the maximum number of switches is limited by what can realistically be done during chemotherapy and therefore it is possible to test solutions for all admissible number of switches.

6. CONCLUSIONS

This paper is concerned with an infinite dimensional bilinear dynamical model with a variety of applications. Basing on model decomposition, it is possible to analyze analytically some of dynamical properties of the model. The transformation of system description into one integro-differential equation allows both effective simulation and solving an optimal control problem with the performance index defined in l^1 space of summable sequences.

Though it must be acknowledged that the solution to the optimization problem presented here is only in the open-loop control form, the biological application justifies that approach, since it is not possible in this case, at least for the time being, to build a closed loop control system, preferred in standard control applications. Nevertheless, such theoretical approach is currently under investigation in hope that advances in experimental biomedicine will make it applicable in the future.

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