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LQ control design for the containment of the HIV/AIDS diffusion

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ABSTRACT

An optimal control design approach is applied to a novel HIV/AIDS model to reduce the infection diffusion. Two classes of susceptible subjects, the wise one and the incautious ones, and three classes of infectious subjects, the ones not aware of their condition and the subjects in the pre-aids or in the aids status, are considered. The control input, represented by information campaigns and the medication action, is designed by means of a linear quadratic approach on the linearized model. Moreover, a preliminary state observer for the unmeasurable number of the unconscious infectious subjects is introduced. Numerical results show the effectiveness of the solution, and its robustness with respect to the approximations introduced by the linearization.

1. Introduction

In the last three decades, much progress has been made in the attempts to eradicate the Human Immunodeficiency Virus (HIV) responsible of the Acquired Immune Deficiency Syndrome (AIDS), Chang and Astolfi (2009) Naresh, Tripathi, and Sharma (2009) and Wodarz and Nowak (1999). The virus infects cells of the immune system, destroying or impairing their function: the immune system becomes weaker, and the person is more susceptible to infections. It can be transmitted by body fluids such as blood, semen, pre-seminal fluid, rectal fluid, vaginal fluid, and breast milk; therefore, it is mainly transmitted by a subject during unprotected sex, sharing needles or syringes and, less commonly, by oral sex, blood transfusion or from mother to child during pregnancy or breastfeeding. The AIDS is the most advanced stage of the HIV infection and can be reached in 10–15 years from the infection. Up to now, no vaccine exists and the control actions are the prevention and the medication after a positive diagnosis. Despite the well-known modalities of its transmission, it is still one of the most diffused disease; the recent data of the World Health Organization (last update 2016) report that there are more than 36 million of people with a positive diagnosis of HIV. There is still a serious delay for the infectious subjects to become aware of their status: it is estimated that in Europe more than 122 000 subjects are HIV positive without knowing.

The World Health Organization (WHO) suggests three levels of intervention:

i. the first level is designed for healthy people to reduce the possibility of new infections; it corresponds to increase the effort to induce the subjects to adopt cautious behaviors;

ii. the second level of prevention aims at a fast identification of new infections and risky conditions, thus reducing the percentage of subjects that are not aware of their illness (and therefore to reduce new infections);

iii. the third level is the medication to the aware infectious subjects.

Mathematical modeling of the HIV/AIDS diffusion may be grouped in two main approaches: one focuses on the dynamic at subjects' interactions level (Di Giamberardino, Compagnucci, De Giorgi, & Iacoviello, 2017a, b; Pinto & Rocha, 2012; Wodarz & Nowak, 1999). Generally, four main classes are introduced: the Susceptible subjects (S) that are the healthy people that may contract the virus; the Infectious one (I) that are not aware of their condition; the pre-AIDS patients (P); the AIDS patients (A). In this framework, the control action is mainly focused on the prevention; for example, in Rutherford, Ramadanovic, Michelow, Marshall, Small, Deering, and Vasarhelyi (2016) the attention is devoted to risky subjects, drug users and sex workers, showing, by means of simulations, the effects of prevention. In particular, the Authors studied the consequences of the reduction of syringe sharing and of the reduced time to diagnosis, stressing the relations among these factors and the HIV prevalence.

The second approach focuses on the CD4 T-cells, the essential components of the immune system. An HIV patient is classified as an AIDS one if he has less than 200 CD4 T-cells in mm^3 of blood (Nowak & May, 2000); he could try to reach the long-term non-progression (LTNP) status that allows him to contrast the HIV and other infections. It is shown that two equilibrium points are present: the LTNP and the AIDS condition; the medication strategy aims at driving the patient into the

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LTNP region of attraction (Chang & Astolfi, 2009; Wodarz & Nowak, 1999).

The natural framework to study the control of the epidemic models is the optimal control theory in which conflicting issues can be addressed (Anderson & Moore, 1989); in epidemic spread, the control represents the general prevention effort (in particular the vaccine action, if possible), the medication, the quarantine, allowing to face with limitations of resources.

Optimal control has been applied referring to the classical SIR model (susceptible–infectious–removed subjects) (Bakare, Nwagwo, & Danso-Addo, 2014; Di Giamberardino & Iacoviello, 2017; Jun, 2006), to the influenza (Gupar & Quanyan, 2013; Iacoviello & Stasio, 2013; Lin, Muthuraman, & Lawley, 2010), to the Dengue disease (Supriatma, Anggriani, & Husniah, 2016), to schedule vaccination strategies (Ogren & Martin, 2000; Yuan, Alderson, Stromberg, & Carlson, 2015), to study complex networks and identify spread process (Kryftis, Mastorakis, & Mavromoustakis, 2017).

In this paper, following the first approach that considers the dynamics of the interactions between subjects, the model in Di Giamberardino et al. (2017a, b) presenting a new HIV/AIDS description is assumed. The susceptible individuals, S, are divided into two categories, the one that adopts wise behaviors and the one that does not take into account the dangerousness of this disease. This distinction appears particularly useful if one takes into account the trivial fact that if all the people assumed wise behavior no spread would occur. Therefore, five categories are present: along with the subjects with HIV/AIDS (i.e. classes I, P, A), two classes of susceptible subjects are considered. The control actions introduced are:

i. an effective information campaign, inducing all the people to wise behaviors;
ii. a test campaign to reduce the time in which an infectious subject is not aware of his status and could infect an unwary one;
iii. the medication applied on the patients with positive diagnosis of HIV/AIDS.

In this paper, the control actions are chosen in order to minimize a cost index aiming at reducing the number of infectious subjects with as less resources as possible. These goals appear in line with the spread characteristics of the HIV virus: the reduction of the number of infectious subjects implies both the increase of the information and the test campaign. The third level of intervention, the medication on the patients, cannot influence the HIV/AIDS spread; however, it is preserved in the paper for completeness. The dynamical model is nonlinear, whereas for the cost index a quadratic Lagrangian is chosen. A linearization of the model in the neighborhood of an equilibrium point is discussed, aiming at applying the linear quadratic (LQ) regulator theory, Rodrigues, Kuiava, and Ramos (2011), which provides a state feedback control law. Since only the number of the patients with HIV (P) or AIDS (A) is available, an observer is determined to estimate the full state and, in particular, the number of the subjects in the class I, infectious but not aware of their status.

The paper is organized as follows. In Section 2 the adopted nonlinear model is briefly recalled and the optimal control problem is formulated. In Section 3 the control design is proposed; three subsections are introduced: in the first one the linear approximation of the model is discussed; then the regulator is determined in the linear quadratic framework; finally, the state estimator design, along with the full control action, are determined. In Section 4 numerical results are presented and discussed, showing the effectiveness of the proposed control law. Conclusions and future work are outlined in Section 5.

2. Model description and optimal control problem formulation

In this paper, the model of the HIV/AIDS diffusion presented in Di Giamberardino et al. (2017a, b) is adopted and is here briefly recalled. It suitably models the two main particularities of the HIV/AIDS spread that significantly distinguish this disease from the others:

- there is a period, more or less long, in which the symptoms of the infection are not evident;
- the HIV can be transmitted only by some body fluids and sharing needles or syringes.

The first characteristic is responsible of the dangerousness of HIV/AIDS since an infectious individual could be unaware of his status for a long time and could infect unwise susceptible subjects. Therefore, it is useful to stress (and to model) the second characteristic described: the infection can be transmitted when unsafe behaviors are adopted. In fact, everyone is susceptible, but one can distinguish between the category of wise people that adopt safe behaviors, and the one of unwary subjects that could become infectious because they share syringes or needles, or for unprotected sex. These two particularities of the HIV/AIDS spread, introduced in Di Giamberardino et al. (2017a, b), are considered in this paper with the control actions consistent with the three levels of intervention previously recalled are introduced.

The effort to induce the population to participate to test campaign should reduce the risky time in which an infectious subject, not aware of his status, could infect healthy unwise susceptible ones, being able, of course, also to start a medication program.

A schedule of the control action is advisable, since the costs of primary and secondary preventions represent an immediate economic effort, whereas their effects could be appreciated only in the future, as will be discussed later.

Considering all these aspects, the variables introduced in the model are the following:

- $S_1(t)$ represents the number of healthy people that are not aware of dangerous behaviors and then can contract the virus;
- $S_2(t)$ represents the number of healthy people that, suitably informed, gives great attention to the protection;
- $I(t)$ represents the number of infectious subjects who are still not aware of their status;
- $P(t)$ represents the number of patients which have received a diagnosis of HIV;
- $A(t)$ represents the number of the patients which have received a diagnosis of AIDS positiveness.

As far as the control actions is concerned, they are:

- $u_1(t)$, related to the information campaign (thus reducing $S_1(t)$);
- $u_2(t)$, denoting the effort to improve a test campaign to the discovery of the infection as soon as possible (thus reducing the interactions between I and S_1) ;
- $u_3(t)$, representing a therapy, aiming at reducing the transition from P to A.

Therefore, the model used, described in Di Giamberardino et al. (2017a, b), is:

$$\dot{S}_1(t) = Z - dS_1(t) - \frac{\beta S_1(t)I(t)}{N_c(t)} + \gamma S_2(t) - S_1(t)u_1(t) \tag{1}$$

$$\dot{S}_2(t) = -(\gamma + d)\, S_2(t) + S_1(t)u_1(t) \tag{2}$$

$$\dot{I}(t) = \frac{\beta S_1(t)I(t)}{N_c(t)} - (d+\delta)\, I(t) - \psi \frac{I(t)}{N_c(t)}u_2(t) \tag{3}$$

$$\dot{P}(t) = \varepsilon\delta I(t) - (\alpha + d)\, P(t) + \phi\psi \frac{I(t)}{N_c(t)}u_2(t) + P(t)u_3(t) \tag{4}$$

$$\begin{aligned}\dot{A}(t) &= (1-\varepsilon)\,\delta I(t) + \alpha P(t) - (\mu + d)\, A(t) + \\ &(1-\phi)\,\psi \frac{I(t)}{N_c(t)}u_2(t) - P(t)u_3(t)\end{aligned} \tag{5}$$

where:

- $N_c(t) = S_1(t) + S_2(t) + I(t)$ denotes the number of subjects that actually are ($S_1(t)$ and $S_2(t)$) or think ($I(t)$) to be healthy;