Analysis of a Dynamical Model for HIV Infection with One or Two Inputs

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ABSTRACT

A dynamical model that describes the interaction of the HIV virus and the immune system is presented. The effect of introducing antiretroviral therapy on the model, consisting of RTI and PI drugs is investigated, along with the result of undesired treatment interruption. Furthermore, the effect of both drugs can be combined into a single parameter that further simplifies the model into a single input system. Drug administration can be adjusted by feedback control, through monthly blood tests that measure the viral load. Furthermore, the system is linearized around the equilibrium, leading to a system of linear differential equations of first order that can be integrated into courses of control systems engineering, linear and nonlinear systems in higher education.

KEYWORDS

AIDS, Control, Control Systems Engineering, Differential Equations, Education, HIV, Immune System, Matlab, Modeling, Nonlinear Systems

1. INTRODUCTION

The infection from the human immunodeficiency virus constitutes a global pandemic. According to the recent report of the Joint United Nations Programme on HIV/AIDS (UNAIDS, 2014), from its first occurrence until today, more than 78 million people have been infected with HIV and 39 million have died from causes related to HIV/AIDS. By the end of 2014, 36.99 million people were living with HIV, of which 3.2 million are children, 2.1 million are young adults and 4.2 million are over 50 years old. Around 70% of HIV positive persons live in regions of sub-Saharan Africa.

The number of people being infected with HIV is decreasing in most countries. In 2015 there was an accounting of 2.1 million new HIV infections, a number that is 38% lower than the 3.4 million infections reported in 2001. There also exists a steady decrease in the number of deaths from AIDS. In 2013 for example there have been reported 1 million deaths from AIDS, which corresponds to a 35% decrease compared with 2005.

Results regarding antiretroviral therapy are positive and reflect the steps forward that have been taken in the last years. The number of persons with no access to therapy in 2006 was as high as 90%, while in 2013 they has been decreased to 63%. In 2015, the number of people with access to therapy was 15.8 million while today they are about 17 million, 2 million higher than the aim that the United Nations had set for 2015.
An important part in the epidemiological analysis of HIV infection constitute the high risk groups. By that, we refer to population groups where the infection occurs with a higher frequency than that of the general population. These groups have a higher infection risk all around the globe. More specifically, men who have sex with men are 19 times more likely to have been infected with HIV. Injecting drug users have 28 times more likelihood than the general population. Around 12.7 million injecting drug users are reported worldwide, of which 13% are HIV positive. Another risk group is the one of workers in the sex industry, with 12 times more likelihood than the general population. In addition, transgender women are 49 times more likely to live with the HIV virus than other adults of the same age.

Specifically, in Greece, according to the most recent HIV/AIDS surveillance report on October of 2015 (H.C.D.C.P., 2015), the Hellenic Center For Disease Control & Prevention (H.C.D.C.P.) has so far reported 15.109 positive HIV infections. Of these, 3.782 have already developed AIDS and around 7.700 are subject to antiretroviral therapy (ART). The number of deaths resulting from the infection amounts to 2.562. According to the H.C.D.C.P. 2014 report (H.C.D.C.P., 2014), the largest portion of HIV cases has been diagnosed in men who had sex with men (46.2%), followed by the categories of heterosexual sexual contact (21.3%) and injecting drug users (10.8%).

More specifically, during the period of 2011-2013, there was a big rise in the number of cases in injecting drug users. This rise that amounted in 2012 to 9.6 new infections per 100000 people is strongly contributed to the economic crisis in Greece, and is a testament to the key part that social (homelessness, imprisonment) and economic factors (austerity) play in the disease transmission in high risk groups (Hatzakis et al. 2015; Tsang et al. 2015). This was followed by a steady decrease during the last two years (2014-2015) with around 6.2 infections per 100000 people. Yet, as the Office for HIV and Sexually Transmitted Diseases emphasizes, although the last data on the decrease infections are positive, they should not be considered comforting. There must be constant actions for the awareness of both the high risk groups and the general population.

Motivated by similar and even more alarming statistics in South Africa, the University of Pretoria, being aware of the fact that the student population generally falls into the high risk groups, mainly due to lack of awareness, decided to organize an action to inform the students about the problem. The department of Electrical, Electronic and Computer Engineering, the department of Telematic Learning and Education Innovation and the Center for the Study of AIDS came together and developed a CD (Craig & Xia, 2005; Craig et al. 2005), with the aim of presenting a model for the HIV infection from a control theory perspective. Their aim was to present the problem through a mathematical model that would introduce the students to the field of control systems engineering, motivating them at the same time to learn more about this sensitive subject.

Based on this innovative idea by the University of Pretoria, we propose an analytical description of the dynamic model for HIV infection, with the purpose of fulfilling two different objectives. First, to present a detailed control engineering problem that can be implemented in a vast variety of undergraduate courses in the field of dynamical systems, thus making the syllabus much more interesting through the perspective of real life applications. This study, as will be shown later, is subject to extensive research (SMART study group, 2006; Mhawej et al. 2010; Mhawej et al. 2009; Rivadeneira & Moog, 2012; Callaway & Perelson, 2002; Ho & Ling, 2010; Department of Pathology, 2012; Perelson & Nelson, 1999; Rivadeneira et al. 2014; Xia, 2007; Kramer, 1999; Barão & Lemos, 2007; Radisavljevic-Gajic, 2009; Jeffrey et al. 2002; Jeffrey et al. 2003; Perelson & Ribeiro, 2013) and can be extended to master and doctoral studies. Secondly, the awareness among students on the subject should be a natural consequence of taking such a subject.

2. A DYNAMIC MODEL FOR HIV INFECTION

The Human Immunodeficiency Virus (HIV) acts by attacking the immune system, causing its progressive failure over time and its collapse after years (when no treatment is administered). The
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