Optimal Chemotherapeutic Strategy for HIV Infections-State Constrained Case

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Abstract

This study investigates two mathematical models of infectious diseases in terms of a set of ordinary differential equations (ODEs) which describe the interactions between the human immune systems and viruses. In this work, we propose modifications of the HIV model (model 1) proposed by [1] and of the SEIR model (model 2) proposed by [5] imposing state constraints in the dynamics. The aim is to obtain new optimal treatment and control strategies where the state constraints play a crucial role. We treat our problems numerically and compare the results with existing literature. We compare two models to illustrate the significant effect of imposing state constraints in the dynamics of the models.

Introduction

Infectious diseases have become increasingly alarming global health concerns nowadays. In the 20th century, new infectious diseases have emerged (e.g. NiV in 1998) and some existing diseases have re-emerged (e.g. Malaria, Dengue) and these diseases are spreading into new regions due to the global climate change [3]. However, one of the most epidemic and life-threatening infectious diseases is the Acquired Immune Deficiency Syndrome (AIDS) and its etiological agent the Human Immunodeficiency Virus (HIV) for which after more than 30 years of it's first detection in the early 1980s, the global health of the whole populations in the world is still under a great threat due to a mysterious and difficult unknown mechanism of HIV infections in the human body. A proper treatment or complete cure from AIDS is yet far away from the reality and even an anti-HIV vaccine is still a dream to the biologists and physicists [2], [4].

Chemotherapy has been the only way of treatment for HIV positive patients. It aims at killing or halting the virus pathogen thus helping the body to fight against infections. Several antiretroviral drugs for the chemotherapy treatments have been approved by the US Food and Drug Administration (FDA) since 1987s aiming at reducing the viral population and improving the immune response. All these drugs cannot cure the diseases completely; rather they can improve the lives of HIV positive patients for a certain period depending on the optimal chemotherapeutic drug dosages strategies. This brings new hope to the treatment of the HIV infection in absence of the HIV vaccine.

In this work we explore new strategies for such treatments using optimal control techniques. We propose the modifications of two infectious diseases models: one is a HIV model and other is an SEIR (Susceptible, Exposed, Infectious and Recovered) model. The modifications are due to imposing the state constraints in the dynamics of the models. We compare the results by illustrating the effects of imposing state constraint in the model and show the better performance in the case of state constrained model (model 2).

Mathematical Model 1 (HIV model)

- The HIV model as proposed by [1] is a set of ordinary differential equations given by

$$\dot{T}_A(t) = \frac{s}{1+V(t)} - \mu_{T_A} T_A(t) - rT_A(1 - \frac{T_A(t)+T_L(t)+T_I(t)}{T_{\max}}) - \mu_i T_A(t)V(t)$$

$$\dot{T}_L(t) = \mu_i T_A(t)V(t) - \mu_{T_L} T_L(t) - \mu_c T_L(t)$$

$$\dot{T}_I(t) = \mu_c T_L(t) - \mu_{T_I} T_I(t)$$

$$\dot{V}(t) = (1-u(t))N\mu_{T_I} T_I(t) - \mu_i T_A(t)V(t) - \mu_V V(t)$$

$T_A(t) \geq \tilde{T}$ ← State constraint

- With the initial conditions:

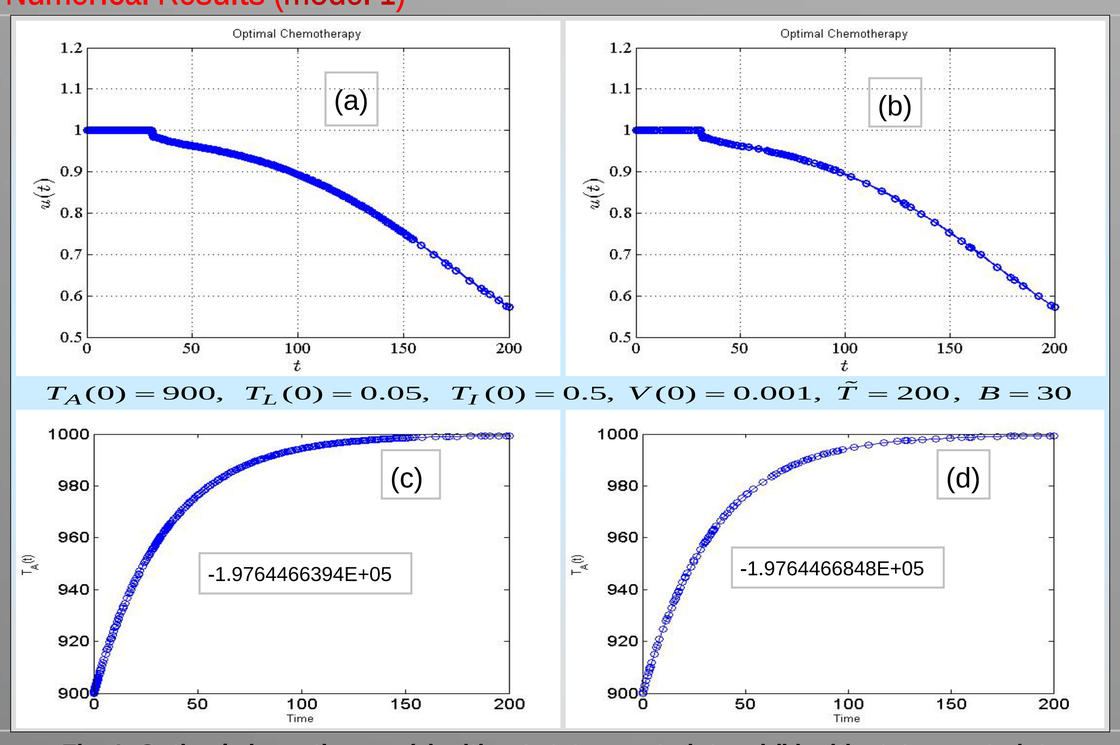
$$T_A(0) = T_{A0},\ T_L(0) = T_{L0},\ T_I(0) = T_{I0},\ V(0) = V_0$$

- The objective functional as in [1] is given by

$$\text{Minimize } J(u) = \int_0^T (-T_A(t_f) + \frac{1}{2}Bu^2(t))dt$$

- where **B** is the 'weight' parameter balancing the cost,
  u is the percentage of the chemotherapy rate restricted by $0 \leq u(t) \leq 1$

Numerical Results (model 1)



$T_A(0) = 900,\ T_L(0) = 0.05,\ T_I(0) = 0.5,\ V(0) = 0.001,\ \tilde{T} = 200,\ B = 30$

Fig. 1. Optimal chemotherapy (a) without state constraint and (b) with state constraint.

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Mathematical Model 2 (SEIR model)

- The SEIR model as proposed by [5] is given by

$$\dot{S}(t) = bN(t) - dS(t) - cS(t)I(t) - u(t)S(t)$$

$$\dot{E}(t) = cS(t)I(t) - (e+d)E(t)$$

$$\dot{I}(t) = eE(t) - (g+a+d)I(t)$$

$$\dot{R}(t) = gI(t) - dR(t) + u(t)S(t)$$

$$\dot{N}(t) = (b-d)N(t) - aI(t)$$

$S(t) \leq \tilde{S}$ ← State constraint

- With the initial conditions:

$$S(0) = S_0,\ E(0) = E_0,\ I(0) = I_0,\ N(0) = N_0$$

- Suppose a limited number of susceptible population as in [5] can be vaccinated by

$$\int_0^T u(t)S(t)dt = X$$

- This can be modelled by

$$\dot{W}(t) = u(t)S(t)$$
$$W(0) = 0$$
$$W(T) = X$$

- The objective functional is chosen as:

$$\text{Minimize } J(u) = \int_0^T B(I(t) + \frac{1}{2}u^2(t)dt$$

- where **B** is the 'weight' parameter balancing the cost,
  u is the percentage of the vaccination rate restricted by $0 \leq u(t) \leq 1$

Numerical Results (model 2)

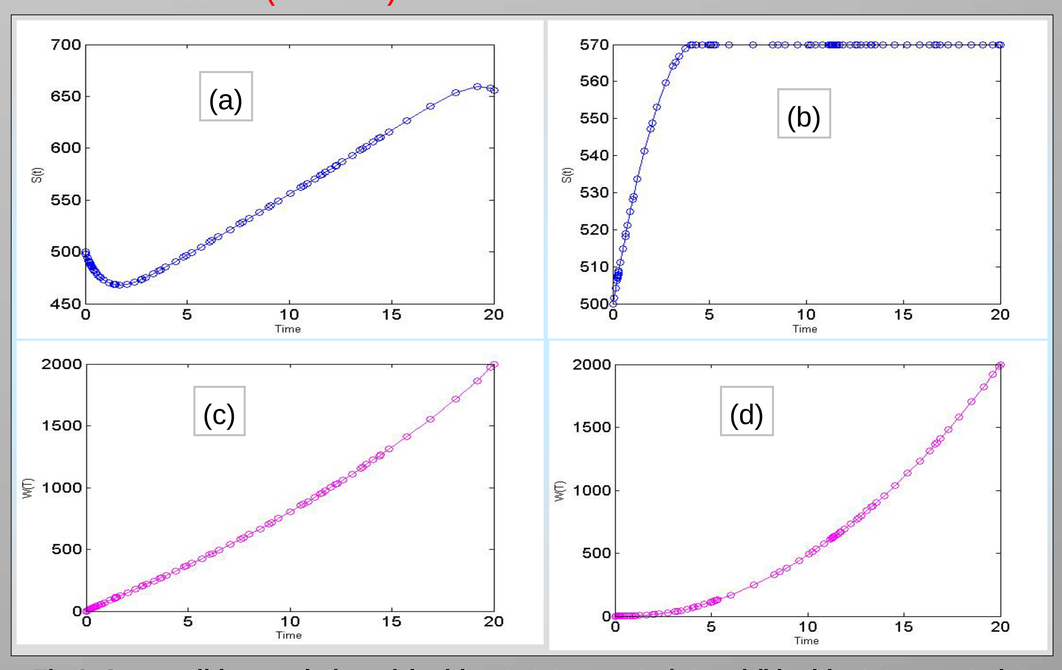

Fig.2. Susceptible populations (a) without state constraint and (b) with state constraint

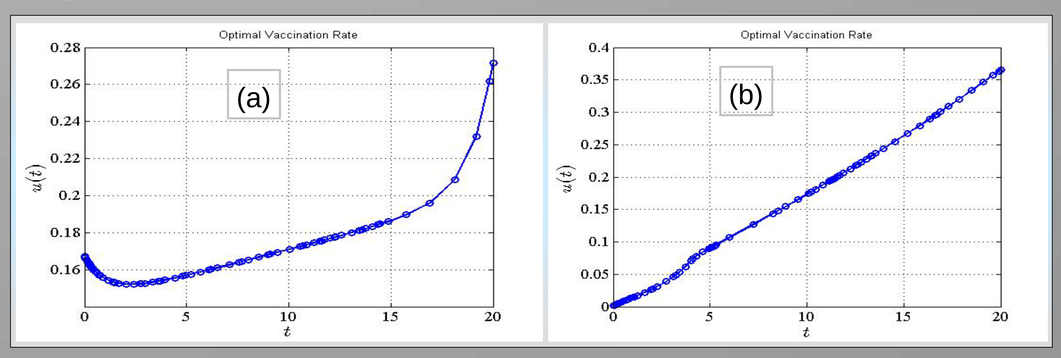

Fig.3. Optimal vaccination schedules with the cost (a) 3.2453093126E-01 without state constraint and (b) 4.2635784845E-01 in presence of state constraint

Conclusion

- In this work we have presented the numerical results for the optimal chemotherapy of HIV infections (model 1) and optimal vaccination schedules (model 2) both for the constrained and without constrained cases. We compare the two cases by illustrating the significant effect of imposing state constraint on the data.
- The results show that the state constrained case (model 2) gives a better performance than without state constrained case for a certain treatment schedule over time. State constraint causes no effective changes on model 1 as one would expect.
- Further investigations are going on.

References

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