Assignment 5 – BT5240 – Systems Biology in Health and Disease

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This report is based on the following research article.

Mhlanga, A. Dynamical analysis and control strategies in modelling Ebola virus disease. Adv Differ Equ 2019, 458 (2019). https://doi.org/10.1186/s13662-019-2392-x

Introduction

Ebola virus disease (EVD) is an infectious disease that originated from the family of *Pteropodidae* (fruit bats) and later spread to a vast sub-population of the mammalian kingdom. EVD has been recognised since early 20th century, but the recent event has taken a toll at North Kivu, Ituri and the Democratic Republic of the Congo (Central Africa). The disease initially spread from wild animals to humans through direct contact with an infected organism via blood, secretions or other bodily fluids, and is now recognised to spread through human-to-human transmission. EVD often causes fatal illness in humans and it was therefore very important to analyse the mechanisms through which the disease spreads and how any preventive measure that was suggested, could alter these mechanisms and eventually, the rate of spread.

Building the model

Mhlanga carefully structures a detailed model that encompasses various parameters that influence the given situation. This model also focuses on the impact of control theory via educational campaigns and how it helped the African community analyse the spread of EVD in greater details. Mhlanga structures the community under analysis into a two-patch model, i.e., two subpopulations within the entire set, and thereby track the transmission dynamics. The objective of this modelling was to find ways to reduce the spread of EVD while economically managing the campaigns. The entire population in both the patch were divided into 4 classes – Susceptible $(S_i(t))$, Infected $(I_i(t))$, Recovered $(R_i(t))$, Deceased $(D_i(t))$. An additional variable that was essential to be tracked was the virus itself – $W_i(t)$.

ODE Formulation

The following constraints were faithfully incorporated into the model -

The variations in the Susceptible class was mainly because of the migration of susceptible and recovered individuals between the two patches. People get infected when they come in contact with the virus either directly or indirectly and the recovery of individuals varies at a constant rate in proportion to the population set. Amidst the chaos, the virus in the environment and on the deceased individuals also decays at specific rates. The model also captures other modes of death. Evidence from various studies shows that none of the recovered individuals was susceptible to the virus again.

Analysis of the model

The transmission of any disease is highly dependent on the number of transmissions possible from a single affected individual amidst a pool of susceptible individuals. This is referred to as the "basic reproductive number" ($\mathcal{R}_0$) and is a threshold parameter for the given model as it decides the equilibria of the system. The reproductive number and the various equilibria states assumed by the system are calculated based on "next-generation method approach" and "centre manifold theory" respectively. These states are -

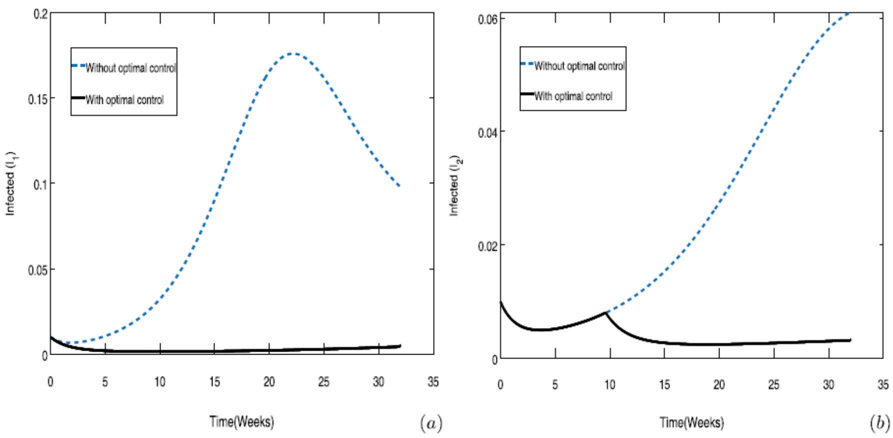
- Disease-free equilibria – no disease persists at the end of the simulation.
- Three endemic equilibria –
  - Two boundary equilibria –
    - The disease continues to persist in patch 1 and dies out in patch 2.
    - The disease continues to persist in patch 2 and dies out in patch 1.
  - Interior endemic equilibrium –
    - The disease continues to persist in both the sub-populations.

Impact of Control theory - Organization of educational campaigns

The main motive of the entire analysis was to break the chain of transmission and thereby limit the spread of EVD. A control system was therefore introduced in the model, to encourage the susceptible to practice protective behaviours, and its effects were observed. The result for the optimality system was based on "Pontryagin maximum principle" and this was calculated by introducing two parameters (u_1, u_2) that were involved in the control efforts. These altered the infected class of people in each patch, by lowering their rate of acquiring the virus via a negative correlation with u_i.

The following **observations** were made corresponding to different scenarios of the rate of migration of the susceptible class between different patches –

- When the migration is higher from the second patch to the first, the campaigns (while held at its maximum efficacy) reduce the population of the infected class throughout the period of study and thereby proves to be widely effective in patch 1. Its effect in patch 2 is, however noticeable only after 9 weeks. We can thus conclude that the controls are feasible and effective, which indicates that more effort should be devoted to both the systems in implementation when such a scenario arises.



Similar observations that were conclusive from the numerical simulation are as follows –

- When the migration is equal between the patches, control u_1 becomes effective only after 14 weeks whereas control u_2 becomes effective as early as 2 weeks. Nevertheless, the propagation of disease is higher even with control u_2. Hence more resources should be made use at the 2nd patch than the 1st patch.
- When the migration is higher from the 1^{st} patch to the 2^{nd}, control u_1 is necessary only in later stages, while control u_2 is always at its maximum value implying that more efforts are required in the 2^{nd} patch.

Comments

In the phase where no drugs or vaccines were available, the existence of such models proves beneficial. Hence, it was indispensable to find all possible ways to control and subsidize the spread of EVD. One such possible mechanism would be to spread awareness about the transmission possibilities, and this is precisely what was tested by Mhlanga in this model. The case where the rate of migration of the susceptible class is higher from the 2^{nd} patch to the 1^{st} implied that the reproductive number is higher in the first patch than the second, while both the values were greater than 1. This specific scenario promised great results in both the sub-populations, although it required solid efforts on control system throughout the runtime.

In fact, in a place such as Western Africa, it was furthermore important to venture out on campaigns that taught the general public about safe burial practices, proper hygiene at the hospital, social distancing and self-isolation. The possibilities of such an idea were tested by this model.

What can be improved?

"All models are wrong, but some are useful"

Going by the above phrase, the model developed by Mhlanga was very useful in identifying ways to reduce the spread of EVD, but certain factors such as the following would help build a more, realistic model that might offer a few more insights.

- Having a separate class for health workers who are in contact with the infected, longer than other susceptible people.
- The density of population in each patch could be perturbed to observe changes in the patterns.