UNIVERSIDAD DE COSTA RICA
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MAESTRIA PROFESIONAL EN METODOS MATEMATICOS Y APLICACIONES

THESIS PROPOSAL
Development and analysis of human adaptive behavior in a model with non-linear relapse

PROPUESTA DE TESIS
Desarrollo y análisis del comportamiento humano adaptivo en un modelo con relapso no lineal

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1. INTRODUCTION

Epidemiological models serve as a important tool to understand disease dynamics. Many examples through history yield insightful results on how initial conditions and parameters alter the progression of an epidemic outbreak (see [3]); key concepts developed in this setting, as the R_0 reproductive number, work as threshold indicators for disease behavior. Modern epidemiological mathematics makes heavy use of bread-and-butter SIR models, as described in [1], for example. However, a drawback with classical models is their treatment of contact rates among individuals of different health statuses. Often the assumption consists of a homogeneous behavior in each compartment (for example among susceptible and infected individuals), by means of establishing constant or proportional contact rates. This approach hides the inherent characteristics and responses of different individuals towards the disease progress.

Multiple efforts for dealing with this problem have accumulated for some time now. A first approach consists of specifying non-linear incidence rates by constructing functions that reflect the impact of the state of the model into the contact rates through time, examples include [11, 12, 19] for models without relapse, and [15, 20] for models with non-linear relapse rates. Common examples of this include functions of the form

$$g_{\kappa,\nu}(\cdot)I = \frac{\kappa I^p}{1+\nu I^q},$$

for positive constants κ, ν, p, q and with $I = I(t)$ the infected population size in time. Within relapse phenomena, very similarly, [15] proposes

$$g_{\kappa,\nu}(\cdot) = \frac{\kappa}{1+\nu\frac{\widetilde{S}}{N}}, \tag{1.1}$$

where $\widetilde{S} = \widetilde{S}(t)$ is the size of the recovered (with possibility of reinfection) population, and N is the total population size. As we can see, with this approach modelers usually specify functions that decrease when epidemic burden is high, so that they depend inversely on sizes of infected or recovered populations in time. The analysis is commonly focused on the impact of the model's hyper-parameters (constants as κ, ν in the non-linear functions) on the behavior of the system.

Key analytical results can be obtained using this approach and they can tackle the problem of different behaviors among health classes: the *epidemiological heterogeneity* of agents involved in the disease progress. However, in recent years more interest is placed on the *economical heterogeneity* of individuals. Hence, there has been significant effort in researching how to add the utilitarian adaptive decisions individuals make within the development of the epidemic scenario.

The main contribution from [7], consists of devising a process in which contact rates for individuals in each health class can be updated simultaneously as the state of disease changes. The idea consists of modelling the individuals as decision agents who take into account the status of their environment and their personal utility to decide optimal contact rates throughout time. This approach tries to bring in the economical considerations individuals have when deciding how many contacts should they engage in, at each time period. A detailed review of other types of proposals that attempt to add these types of decision making behavior can be found in [8], in general these efforts can be found under the umbrella of economical epidemiology studies.

This recent technique allows the computation of contact rates alongside the progress of the disease, by means of an optimization decision process performed by each individual. We call this procedure the *adaptive setting*. This has proved useful to create epidemiological models closer to the actual decision making processes made by individuals within the development of an epidemic, and has been applied to create more realistic settings and to compare them with the classical formulation ([18, 6, 5]). Analytical comparisons and conjectures can be found in [13], for the non-relapse case.

The adaptive setting is not detached from the first approach. In order to compute contact rates adaptively, we must first define non-linear incidence rate functions that will use these contact rates. The formulation of non-linear incidence rate functions in the adaptive setting is commonly expressed like this:

$$g(S, I, \widetilde{S}) = \frac{C^s C^i N}{S C^s + I C^i + \widetilde{S} C^{\widetilde{s}}}, \tag{1.2}$$

where C^h are the contact rates for each health status individual (where $h \in \{s, i, \widetilde{s})$ and N is the total population size. In this case, these are the parameters that are computed *adaptively* throughout the disease dynamics, as opposed to the first approach, where they are kept constant.

Obtaining analytical results in the adaptive setting proves to be challenging due to the way these contact rates are evolving through time. When they are presumed constant -thus, following the first approach discussed above- the situation might be more manageable.

Our purpose for this research project will be to extend this analysis, by examining conditions for the existence of equilibria points for a relapse model using (1.2) as the bases for incidence rate calculation. This thesis aims at formulating and examining an epidemiological model with non-linear relapse employing the adaptive technique. An initial objective is to formulate the model and create a computational implementation of it, in order to develop simulations and obtain concrete insights on its nature and behavior.

Another key objective is to study the analytical impact of spreading contact rates using (1.2) and the repercussions on how to interpret these models. Consequently, this thesis proposes the study of the effect of computing said contact rates with the adaptive setting and compare equilibrium states found with both approaches, in order to find analytical relationships between modelling systems with both proposals. (The constant non-linear contact rates, and the adaptive setting).

The value of this research lies within the constant academic need to make epidemiological models appear to be closer to the real behavior of disease dynamics. We expand on the need for these proposals in the next section.

2. JUSTIFICATION

The inclusion of specific decision making in epidemiological models aims at solving two major problems within classical proposals: 1. the different responses that individuals can provide towards the disease depending on their health status and 2. the socio-economical factors that lead

agents to engage (or reframe from engaging) in contacts with others. The main problem according to [7] is that the classical literature mixes the biological and behavioral aspects that go into the development of an epidemic.

For this reason, increasing effort exists in recent years in order to incorporate the utilitarian decisions agents make within the progress of a disease. This effort is considered to be part of the *epi-economic* literature. The advantages of this new proposal reside in their closer inspiration on reality and the economical considerations of individuals, as [7] mentions: *Mechanistic understanding of contact functions and tradeoffs can improve the cost effectiveness of disease control and help health authorities avoid unintended consequences*. This technique has been applied to show its power in current situations. For example in [5], the adaptive behavior was used to justify and project, mathematically, the effect of asymptomatic individuals in epidemic sizes, specially applied for COVID-19 scenarios.

The incorporation of the adaptive technique to more complex phenomena such as non-linear relapse rates (as proposed in this thesis) or others (for example two-patch compartments scenarios as developed in [4]) yields an opportunity to bring classical models in these areas closer to the individual's decision behavior that occurs in reality, and thus providing more validity to models developed to study these situations.

3. Background

The adaptive method for epidemiological models was originally introduced by [7], where a simple SIR model without relapse is studied and the adaptive scheme is made only on the susceptible agents, because the absence of relapse means that infected and recovered individuals are not forced to great utilitarian considerations with respect to their number of contacts. Using this formulation, we have some applications ([18, 6, 5]) to more specialized problems, such as: adaptive behavior in influenza epidemics, analysis of the effect of obedience to distancing measures

by (non)compliant individuals, and the effect of adaptive behavior of asymptomatic populations, among others.

In these cases, and also since the original formulation, the progress of the different models has been observed to differ substantially by incorporating adaptive behavior, in comparison to the classical setting. This has important repercussions on the final outcome of the disease, the existence and value of endemic breakpoints, and the prevalence of the disease over time. In many cases, the simulations suggest that the classical model overestimates the epidemic burden of the disease, by ignoring the different decision factors faced by the agents of the process.

The incorporation of the adaptive method in epidemiological models is very recent. Until now, research efforts have been aimed at developing the model and corresponding simulations, but its analysis has not been developed in detail. The reason for this is the great difficulty that this new technique presents for obtaining analytical results. The simple fact that the system adapts and reconfigures itself at each time step makes classical analysis insufficient. Also, relapse behavior hasn't been properly studied so far with the adaptive setting and conditions for epidemic equilibria in that case are, to this moment, unknown. This offers an opportunity for research, which this thesis aims at fulfilling.

4. Problem Statement

For this thesis project, we propose the following research question.

What are the main analytical properties of a non-linear relapse model with the use of human adaptive behavior techniques?

Main Objective: Analyze the analytical properties of non-linear relapse models that use the human adaptive behavior techniques.

Specific Objectives:

- Formulate a model with non-linear relapse which uses the adaptive human behavior setting.
- Implement computationally the model with non-linear relapse which uses the adaptive human behavior setting, in order to perform simulations and obtain concrete insights.
- Examine the existence and determination of equilibria points and other analytical results in the model with non-linear relapse which uses the adaptive human behavior setting. First, using constant contact rates for each health compartment and then incorporating the adaptive technique and performing the corresponding comparison.

5. THEORY

In this section we describe the fundamentals of epidemiological models and the technique of adaptive behavior. We also strengthen the adaptive setting's theory with a brief presentation on Markov Decision Processes (MDP). This theory acts as the basis of the adaptive formulation.

5.1. **Adaptive Behavior in Epidemiological Models.**

We describe the new modeling technique presented in [7], which gives an adaptive approach to the construction of an epidemiological system. The classical approach for a system with no relapse, is taking the quintessential SIR system:

$$\begin{aligned} \frac{dS}{dt} &= -g(\cdot)\beta\frac{SI}{N}, \\ \frac{dI}{dt} &= g(\cdot)\beta\frac{SI}{N} - \gamma I, \\ \frac{dZ}{dt} &= \gamma I, \end{aligned} \tag{5.1}$$

where:

- A population of N individuals is divided in three compartments: $N = S + I + R$. Here S, I, R denote the susceptible, infected and recovered individuals, respectively.
- β represents the likelihood that contact with an infected individual yields infection.
- γ is the rate of recovery.

- $g(\cdot)$ is the rate that susceptible contact infected, which means that $g(\cdot)\beta$ is the rate that susceptible individuals become infected.

In the classical setting, either $g(\cdot) = c$ (contacts are constant) or $g(\cdot) = cN$ (contacts are proportional to N). In the adaptive setting, the idea is that $g(\cdot)$ depends on the incentives different individuals have to vary their number of contacts. The costs and benefits of individual contact vary across health status.

The proposal is then to divide the individuals by health type. Let $Y = \{s, i, z\}$. For $h \in Y$ denote C^h the expected number of contacts made by an individual of type h. For $m, n \in Y$ we define the rate of contact between individuals of types m and n as

$$C^{mn}(\cdot) = C^m C^n N/(SC^s + IC^i + ZC^z).$$

Here, C^m **is a choice** made by individuals of type m. In the classical model $g(\cdot) = C^{si}(\cdot)$, using $C^s = C^i = C^z$.

People engage in contacts because there is a certain utility to gain from them. The adaptive approach models the utility for an individual of type $h \in Y$ depending on the current time, therefore we have the utility function $u_t^h = u_t^h(C_t^h)$, for engaging in C_t^h contacts for an individual of type h at time t. The utility function should be concave, it should have a single peak with respect to the number of contacts and should decrease with infection.

An example of a commonly used utility function is

$$u_t^h = (b^h C_t^h - (C_t^h)^2)^\gamma - a^h,$$

where γ, b^h, a^h are fixed parameters, with $b^s = b^z \geq b^i \geq 0$, $a^z = a^s = 0$, $\gamma > 0$, $a^i > 0$. **Intuitively, this means that during the infection period, the utility has a term that pauses it's increment. Note that each state utility has a peak with respect to C_t^h.**

Recovered (and Immune) and Infected individuals: If the individual doesn't think that a change in their contacts will affect their health status, then for a given time t, the best thing would

be to choose C_t^h such that u_t^h is maximized. This happens with individuals of types i and z. The optimal choice is $C_h^{t*} = 0.5b^h$.

Susceptible individuals: The number of contacts a susceptible individual engages in might affect their health status, so the optimal choice of contacts C_t^{s*} is subjected to planning towards the future. Here is where the adaptive decision comes in, as a factor of future utility.

Let P_t^i the probability that an s-type individual becomes infected at time t. This depends on the current state of things and the selection of C_t^s, as

$$P_t^i = 1 - e^{-\beta I_t C_t^s C_t^{i*}/(S_t C_t^{s*} + I_t C_t^{i*} + Z_t C_t^{z*})}, \tag{5.2}$$

where C_t^{s*} is the optimal choice of other susceptible individuals the present susceptible individual might encounter.

To find the optimal C_t^{s*} we maximize the value function

$$V_t(s) = \max_{C^s \in X} \left\{ u_t^s(C_t^s) + \delta \left[(1 - P_t^i) V_{t+1}(s) + P_t^i V_{t+1}(i) \right] \right\}, \tag{5.3}$$

where X is the range of possible contacts, δ is a discount factor, $V_{t+1}(s)$ is the present value of expected utility if the individual remains susceptible and $V_{t+1}(i)$ the present value of expected utility if the individual becomes infected.

Solving equation (5.3) gives the first order condition:

$$\frac{\partial u_t}{\partial C_t^s} = \delta (V_{t+1}(s) - V_{t+1}(i)) \left(\frac{\partial P_t^i}{\delta C_t^s} \right). \tag{5.4}$$

The idea on how to select the optimal C_t^{s*} at time t depends on the current state of things and the previsions the individual does for the future. The adaptive approach proposes a continuous update of the selection made across time.

For each $t < \tau - 1$, the individual will solve (5.3). For that they will need to solve (5.4). This requires knowledge of $V_{t+1}(i)$, which is modeled like:

$$V_{t+1}(i) = u_t^z(C_t^{z*}) \left[\left(\frac{1-\delta^{\tau+1}}{1-\delta} \right) - \left(\frac{1-(\delta(1-P^z))^{\tau+1}}{1-\delta(1-P^z)} \right) \right], \tag{5.5}$$

where τ is the **planning period** and $P^z = 1 - e^{-\gamma}$ is the probability of recovery.

5.2. **Incorporating Relapse.** Relapse (the phenomenon in which individuals become recovered but they can re-infect) adds a series of complexities to the system. Simple relapse models have been proposed using standard relapse behavior ([16, 17]). An initial step to incorporate the relapse phenomenon is to modify the SIR system in (5.1) to get a system of the form:

$$\begin{aligned} \frac{dS}{dt} &= -g(\cdot)\beta\frac{SI}{N} + \mu N - \mu S, \\ \frac{dI}{dt} &= g(\cdot)\beta\frac{SI}{N} + \phi\frac{\widetilde{S}I}{N} - (\gamma+\mu)I, \\ \frac{d\widetilde{S}}{dt} &= \gamma I - \phi\frac{I\widetilde{S}}{N} - \mu\widetilde{S}. \end{aligned} \tag{5.6}$$

This includes a rate of reinfection γ and a population control parameter μ. The main purpose of this research project is **to study what are the main analytical behaviors that can be obtained in this model, when we introduce an adaptive computation of $g(\cdot)$ in the relapse case.**

5.3. **Markov Decision Processes towards explaining adaptive behavior.** In order to get a clearer idea behind the adaptive algorithm for obtaining the contact rates C^h, we recall the theoretical roots for these adaptive algorithms. We take as references [10] and [14] for this section.

These are embedded inside the theory of **Markov Decision Processes**, a topic within a branch of Machine Learning called **Reinforcement Learning**.

Definition 5.1. A Markov Decision Process is an abstraction used to model a process of decision making by an individual or agent. It consists of the following:

- A space of **states** $\mathcal{S}$.
- A space of possible **actions** $\mathcal{A}$.
- A **progression over a time axis** t, where, for each t, there is a state S_t and the need to make a decision to take an action A_t in order to move to the next time stage.
- An **immediate award** $u_t^h : \mathcal{A} \to \mathbb{R}$ for each state h, that gives the reward/utility of choosing action a at time t if the current state is h.
- For each time stage t and for each states $h, h' \in \mathcal{S}$, there is a **probability of transition** $p_{hh'}^t : \mathcal{A} \to [0, 1]$, where $p_{hh'}^t(a)$ denotes *the probability that at time* $t + 1$ *the state of the system becomes* h' *if at the current time the state is* h *and the agent takes decision* a *to move forward.*
- A **planning horizon** τ, decisions are made for $t = 0, 1, \cdots, \tau$.

These are the settings of a Markov Decision Process, the actual decision that the agent makes is what is known as a policy.

Definition 5.2. Let $(\mathcal{S}, \mathcal{A}, p_{hh'}^t)$ a Markov Decision Process (MDP). a **deterministic policy** is a series of functions $\{\pi^t : \mathcal{S} \to \mathcal{A}\}$, that for each time t give the agent what action to take if depending of the state of the system.

There are many possibilities for policies to take, however there's an optimal one.

Definition 5.3. The **optimal policy** for a MDP process is obtained through a process of backwards induction. For each state $h \in \mathcal{S}$, we define the value function $V_t(h)$ at time t. The optimal $a \in \mathcal{A}$ to choose at time t when state is h (this is $\pi^t(h)$) is computed using the **Bellman Equation** for

$V_t(h)$:

$$V_t(h) = \max_{a \in \mathcal{A}} \left\{ u_t^h(a) + \delta \sum_{h' \in \mathcal{S}} p_{hh'}^t(a) V_{t+1}(h') \right\}, \tag{5.7}$$

where δ is a *discount factor*.

This is computed using a process of backwards induction by means of the planning horizon. We start with an initial vector $(V_{t+\tau+1}(h), h \in \mathcal{S})$ and move back to find $V_t(h)$.

Remark 5.4 (**How the adaptive model is actually a Markov Decision Process**). In the case of epidemiological models, our adaptive model is actually an example of an MDP, with the following parameters:

- The state space $\mathcal{S} = \{s, i, z\}$, the possible states for an individual at the epidemic system.
- The action state $\mathcal{A} = [0, C_{\max}]$, an interval of possible contact rates that can be made by an individual per time period.
- The immediate rewards $u_t^h(a) = (b^h a - a^2)^\gamma - a^h$, concave functions with a maxima.
- The transition probabilities, in this case they are

$$\begin{pmatrix} p_{ss}^t(a) & p_{si}^t(a) & p_{sz}^t(a) \\ p_{is}^t(a) & p_{ii}^t(a) & p_{iz}^t(a) \\ p_{zs}^t(a) & p_{zi}^t(a) & p_{zz}^t(a) \end{pmatrix} = \begin{pmatrix} 1 - p_{si}^t(a) & p_{si}^t(a) & 0 \\ 0 & 1 - p_{iz}^t(a) & p_{iz}^t(a) \\ 0 & p_{zi}^t(a) & 1 - p_{zi}^t(a) \end{pmatrix}$$

Important: when there's no reinfection, $p_{zi}^t \equiv 0$. (this is the case with the model in [7]). In this case, p_{si}^t is given by equation (5.2), or what we called P_t^i (here a is C^s) and p_{iz}^t is the probability of recovery, given by $p_{iz}^t = P^z = 1 - e^{-\gamma}$, as mentioned before.

Here, Bellman's equation is given by

$$\begin{aligned} V_t(s) &= \max_{C^s \in \mathcal{A}} \left\{ u_t^s(C^s) + \delta [p_{ss}^t(C^s) V_{t+1}(s) + p_{si}^t(C^s) V_{t+1}(i)] \right\} \\ &= \max_{C^s \in \mathcal{A}} \left\{ u_t^s(C^s) + \delta [(1 - p_{si}^t(C^s)) V_{t+1}(s) + p_{si}^t(C^s) V_{t+1}(i)] \right\} \end{aligned} \tag{5.8}$$

which is the same equation we have in (5.3).

6. METHODOLOGY

To advance with the project we propose a continuous research process with the constant advise of the thesis committee and other researchers interested, for example, one author of [6, 5] -Dr. Baltazar Espinoza from the Biocomplexity Institute and Initiative at the University of Virginia- has shown interest in this research, as it relates to his own.

Here we propose a general timeline for the progress of this research project.

General Timeline for the Thesis Research Project	
Time Period	Activity
August 2022 - September 2022	Study bibliography on adaptive techniques for epidemiological models. Develop computational implementations.
October 2022 - November 2022	Examine analytical conditions for relapse models with non-linear relapse rates with constant contact rates.
December 2022 - January 2022	Continue with simulations. Write draft of first paper with findings at the constant rates case.
February 2022 - June 2022	Research analytical conditions in relapse models with adaptive behavior. Other possible research steps could be the development of two patch relapse models with adaptive behavior and computational results.

This is a general timeline for this project and is subject to new results and progress of the investigation efforts. Rows in green have been completed when this proposal was written (December 2022). Rows with yellow are currently work in progress.

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