

Chapter 1

Introduction

In the field of life sciences, we frequently come across complex systems whose actions we aim to comprehend and exert an impact on. In this context, we need help with choices concerning devising interventions that yield optimal results while working within resource constraints. Decision makers responsible for managing policy for epidemics have faced difficult choices in balancing the competing claims of saving lives and the high economic cost of control strategies. Despite significant progress in prevention and control, containing and mitigating infectious illnesses remains a challenging task in the modern day due to their complicated spreading patterns and increasing speed of spread [13].

Many efforts to curb a disease attempt to cut the transmission path or control it at its source. For example, the COVID-19 pandemic led many countries to implement social distancing and travel restrictions to prevent the spread of the disease. Effectual measures are imperative to control its transmission and alleviate its impact on public health and society. While these measures have proven effective as a control strategy in some countries, they come with substantial economic and social drawbacks and are frequently met with opposi-

tion during implementation. Additionally, it is challenging to ascertain the ideal duration and extent of implementing controls, as these considerations hinge on various factors, such as preparedness for epidemics and pandemics, the transmission rate, healthcare system capacity, population density and the public's adherence to preventive measures.

The COVID-19 pandemic led many countries to introduce extensive economic and social control measures to limit the spread of the disease. While these measures are costly, they successfully stopped the epidemic's growth in most regions where they were applied relatively early and with sufficient stringency [45].

Some balance has to be struck between saving lives and the economic (and social) cost of implementing control strategies. This paper will present a simple model, with both economic and epidemiological content, to help assess the options.

Modelling techniques help us understand the observed epidemiological patterns and predict the consequences of introducing intervention measures to contain disease spread. Lin et al. (2021) developed the model of Dirk Brockmann and Dirk Helbing (2013) [13] to theoretically explain the impact mechanism of prevention and control measures (mobility restrictions and non-pharmaceutical interventions) on the spread of the epidemic. They discovered that although both measures play a good role in controlling the development of the epidemic, the effect shows significant differences in different regions, and both measures had no significant impact in low-risk regions. Further, they demonstrated that measures taken in a low-risk region are mainly against imported cases. In contrast, a high-risk region has to defend against both imported cases and spread from within [39]. Russel et al. (2021) also demonstrated that the impact of travel restrictions is minimal due to the limited contribution of imported cases to local transmission [58].

However, as a disease becomes more prevalent, one issue of practical concern is the limited

resources available to prevent people from being infected by a particular virus or to treat those infected. Significant progress has been made by proposing mathematical models, which offer valuable information for decision-making in global health [27], [76], [79], [75], [80], [61], [74], [14], [52], [3], [60], [72].

One common aim when modelling resource constraints is to describe how changes in intervention measures will affect the characteristics of the infection dynamics and consequently affect disease control. Many control programs, such as isolation and vaccination, have been modelled [27], [2], [47].

Hansen and Day (2011) provided optimal control policies for an isolation-only model, a vaccination-only model and a combined isolation–vaccination model, with analytic solutions for the controls that minimize the infectious burden under the assumption that there are limited control resources [27].

This work extends that of Hansen and Day (2011) by examining the dynamic phenomena influenced by the variation of the control methods. Specifically, we consider an isolation-only model, a travel restrictions-only model, and a combined isolation-travel restriction model. We also seek to characterize how these novel phenomena in our targeted model affect disease control. We start our model at an early stage of the epidemic. We explore a pragmatic and efficient strategy rooted in optimal control theory to minimize cost and curb disease transmission. We answer the question of “when” and “how” control measures can be implemented within resource constraints.

1.1 Basic Fundamental Properties of Ordinary Differential Equations (ODEs)

We state some basic characteristics of the solutions to ordinary differential equations, including existence, uniqueness, continuous dependence on initial conditions, and continuous dependence on parameters. The state equation

$$\dot{x} = f(t, x, \cdot) \tag{1.1}$$

cannot function as a practical mathematical representation of a physical system without these characteristics. A deterministic system is expected to yield the same trajectory and state if the experiment were to be repeated exactly. For the mathematical model to predict the system's future state from its current state, the initial value problem [Initial-Value Problem \(IVP\)](#)

$$\dot{x} = f(t, x, \cdot); \quad x(t_0) = x_0, \tag{1.2}$$

must have a unique solution. We establish this question of existence and uniqueness in the next section.

1.1.1 Existence and Uniqueness of Solutions to ODEs

The first goal of this section is to establish the local existence and uniqueness of solutions. Models that arise in applications typically depend on a set of parameters Θ and are often time-dependent. Thus, we are interested in solutions to the differential equations [\(1.3\)](#) below that appear to take a more general form. Let $\mathbb{I} \subset \mathbb{R}^n$ an interval of time, $U \subset \mathbb{R}^n$

and $\Theta \subset \mathbb{R}^m$ be open sets and let $f : \mathbb{I} \times U \times \Theta \rightarrow \mathbb{R}^n$ be a continuous function. We focus on solutions to the initial value problem

$$\dot{x} = f(t, x, \theta), \quad x(t_0) = x_0, \quad (1.3)$$

that is, the existence of a solution $x : \mathbb{I} \rightarrow U$ such that $t_0 \in \mathbb{I}$, $\theta \in \Theta$ and $x(t_0) = x_0$.

It is known from the theory of ordinary differential equations that under certain regularity assumptions, a (nonlinear) differential equation (1.3) has a unique solution passing through x_0 at $t = t_0$. The regularity conditions are

1. $f(t, x, \cdot)$ is a continuous function.
2. $f(t, x, \cdot)$ satisfies a global Lipschitz condition.

Definition 1.1.1. Consider metric spaces (X, d_X) (Y, d_Y) . A function $f : X \rightarrow Y$ is Lipschitz if there exists a real constant $K \geq 0$ such that, for all $x_1, x_2 \in X$

$$d_Y(f(x_1), f(x_2)) \leq K d_X(x_1, x_2)$$

The smallest K satisfying this inequality is denoted by $\text{Lip}(f) := K$ and is called the Lipschitz constant of f .

The corresponding existence and uniqueness theorem is as follows. The proofs can be found in [28], [43], [68].

Theorem 1.1.2. Let $\mathbb{I} \subset \mathbb{R}$, $U \subset \mathbb{R}^n$ and $\Theta \subset \mathbb{R}^m$ be open sets, and assume $f : \mathbb{I} \times U \times \Theta \rightarrow \mathbb{R}^n$ is a Lipschitz function. If $(t_0, x_0, \theta_0) \in \mathbb{I} \times U \times \Theta$, then there exists an open neighbourhood of the form $\mathbb{I}_0 \times U_0 \times \Theta_0$ of (t_0, x_0, θ_0) and a Lipschitz continuous function $\varphi : \mathbb{I}_0 \times U_0 \times \Theta_0 \rightarrow \mathbb{R}^n$ such that for every $(t_0, x_0, \theta_0) \in \mathbb{I}_0 \times U_0 \times \Theta_0$

$$\varphi(\cdot, t_0, x_0, \theta_0) : \mathbb{I}_0 \rightarrow \mathbb{R}^n$$

is a solution to the initial value problem

$$\dot{x} = f(t, x, \theta_0), \quad x(t_0) = x_0. \quad (1.4)$$

Furthermore, if $\psi(\cdot, t_0, x_0, \theta_0)$ is another solution to the initial value problem (1.4), then $\psi(t) = \varphi(t)$ on the intersection of their domains of definition.

By solving the relevant differential equation, we can use Gronwall's inequality to constrain a function known to meet a particular differential inequality. It offers a comparison theorem, which can be utilized to demonstrate the uniqueness of a solution to the initial value problem (1.4).

Theorem 1.1.3. (The Gronwall's Inequality) Let $\alpha, \beta : (a, b) \rightarrow [0, \infty)$ be continuous functions. Assume

$$\alpha(t) \leq C + \left| \int_{t_0}^t \alpha(s)\beta(s)ds \right|, \quad t_0, t \in (a, b)$$

for some constant $C \geq 0$. Then,

$$\alpha(t) \leq C \exp \left(\left| \int_{t_0}^t \beta(s)ds \right| \right)$$

Applying the Gronwall's inequality to our initial value problem (1.4), let $\alpha(t) := \|\varphi(\cdot, x_0) - \psi(\cdot, y_0)\|$, $C = \|x_0 - y_0\|$ and $\beta(t) = K$. We obtain the proposition below.

Proposition 1.1.4. Let $U \subset \mathbb{R}^n$ be an open set and assume $f : U \rightarrow \mathbb{R}^n$ is a Lipschitz continuous function with $\text{Lip}(f) = K$. If $\varphi(\cdot, x_0) : \mathbb{I}_{x_0} \rightarrow \mathbb{R}^n$ and $\psi(\cdot, y_0) : \mathbb{I}_{y_0} \rightarrow \mathbb{R}^n$ are solutions to the initial value problem (1.4) with $x(t_0) = x_0$ and $x(t_0) = y_0$, respectively, then

$$\|\varphi(t, x_0, \theta_0) - \psi(t, y_0, \theta_0)\| \leq \|x_0 - y_0\| e^{K|t-t_0|} \quad (1.5)$$

for all $t \in \mathbb{I}_{x_0} \cap \mathbb{I}_{y_0}$.

Remarks 1.1.5. *Proposition 1.1.4 guarantees the existence and uniqueness of solutions. To show that two solutions to the same initial value problem (1.4) agree on the intersection of their domains of definition, we let $\varphi : \mathbb{I}_0 \rightarrow \mathbb{R}^n$ and $\psi : \mathbb{I}_1 \rightarrow \mathbb{R}^n$ denote two solutions to the initial value problem (1.4). Given that $x(t_0) = x_0 = y_0$, from equation (1.5) for all $t \in \mathbb{I}_0 \cap \mathbb{I}_1$,*

$$\|\varphi(t) - \psi(t)\| = 0,$$

which establishes the uniqueness of the solution to the initial value problem (1.4).

1.2 Pontryagin's Maximum Principle (PMP)

The Pontryagin Maximum Principle is a fundamental mathematical principle in the field of optimal control theory. It provides necessary conditions that an optimal control and corresponding state trajectory must satisfy for a wide class of optimal control problems. [50].

The PMP is applied to problems where the objective is to maximize a certain performance criterion or cost, typically expressed as the integral of a given performance index over a specified time interval. The principle states that, under certain regularity conditions, an optimal control strategy and the corresponding state trajectory must satisfy a set of differential equations known as the canonical equations [38].

The canonical equations involve the system dynamics, the costate variables (Lagrange multipliers), and the partial derivatives of the Hamiltonian, which is a function combining the system dynamics and the cost function. The optimal control is determined by maximizing the Hamiltonian over the set of feasible controls.

The Pontryagin Maximum Principle is widely used to analyze and solve optimization problems, where the goal is to find the best control strategy for a dynamic system.

The basic optimal control problem for ordinary differential equations consists of finding a piecewise control $u(t)$ and the associated state variable $x(t)$ to maximize the given objective functional below,

$$\max J = \int_{t_0}^T L(t, x(t), u(t)) dt \quad (1.6)$$

$$\text{subject to } \dot{x} = f(t, x(t), u(t)), \quad x(t_0) = x_0. \quad (1.7)$$

where equation (1.7) models the system dynamics, and the term $L(t, x(t), u(t))$ is referred to as the integral cost. In solving the optimal control problem above (1.6)-(1.7), the first step is to form the Hamiltonian. The Hamiltonian is defined as

$$H(t, x(t), u(t), \lambda(t)) = L(t, x(t), u(t)) + \lambda f(t, x(t), u(t)) \quad (1.8)$$

Theorem 1.2.1. (*PMP*) *If $u^*(t)$ and $x^*(t)$ are the optimal solution of the control problem, then there exist piecewise differentiable adjoint variables $\lambda(t)$ such that*

$$H(t, x^*(t), u(t), \lambda(t)) \leq H(t, x^*(t), u^*(t), \lambda(t)) \quad (1.9)$$

for all controls u at each time t , where H is the Hamiltonian and

$$\dot{\lambda}(t) = \frac{\partial H(t, x^*(t), u^*(t))}{\partial x} \quad (1.10)$$

$$\lambda(T) = 0 \quad (1.11)$$

are the costate and transversality conditions, respectively.

We focus on the application of the *PMP* theorem, excluding detailed proof. We refer [4], [50] for the proof.

Theorem 1.2.2. *Suppose that $f(t, x, u)$ and $g(t, x, u)$ are continuously differentiable functions in their three arguments and concave in u . Suppose u^* is an optimal control with associated state x^* , and λ a piecewise differentiable function with $\lambda(t) \geq 0 \forall t$. Suppose for all $t_0 \leq t \leq T$*

$$0 = H_u(t, x^*(t), u^*(t), \lambda(t)). \quad (1.12)$$

Then for all controls u and each $t_0 \leq t \leq T$, we have

$$H(t, x^*(t), u(t), \lambda(t)) \leq H(t, x^*(t), u^*(t), \lambda(t)) \quad (1.13)$$

The same essential conditions are derived through similar reasoning when the problem involves minimizing rather than maximizing. In a minimization problem, we are minimizing the Hamiltonian pointwise, and the inequality in [PMP](#) is reversed [\[77\]](#). Indeed, for a minimization problem with f and g being convex in u , we can derive

$$H(t, x^*(t), u(t), \lambda(t)) \geq H(t, x^*(t), u^*(t), \lambda(t)) \quad (1.14)$$

by the same argument as in [Theorem 1.2.2](#)

This concludes our elementary derivation of the Pontryagin maximum principle.

Chapter 2

Mathematical Model

We formulate a mathematical model capable of simulating infectious disease propagation and assessing the most effective management of travel restrictions and isolation as control measures across various scenarios. The model will account for the disease transmission dynamics and how these measures influence its spread.

2.1 Disease Dynamics: SI Model

We incorporate the widely used epidemiological compartmental model, [Susceptibles Infected \(SI\)](#) model. It will consider the movement of individuals between the compartments, encompassing those who are susceptible and infected. Here, the [SI](#) model captures the importation (infected non-resident travellers). Within the system, each of the two compartments represents a specific population group, and as time progresses, individuals transition through each category on the path toward recovery. Our model and analysis follow closely from Hansen and Day (2011) [\[27\]](#).

$$\frac{dS}{dt} = -\beta S(I + u_\tau \tau) \quad (2.1)$$

$$\frac{dI}{dt} = \beta S(I + u_\tau \tau) - (\mu + u_i)I \quad (2.2)$$

with $S(t_0) > 0, I(t_0) \geq 0, \beta, \mu, \tau \geq 0$, where S is the number of susceptibles, I is the number of infected hosts, β is the transmission rate per unit time, μ is the per capita loss rate of infected individuals (per unit time) through both mortality and recovery, τ is the baseline number of infected non-resident travellers per unit time, u_τ is the rate of travel restrictions (per unit time) and u_i is the rate of isolation (per unit time).

The set of admissible controls is given by

$U_{ad} = \{u = (u_i, u_\tau) \text{ such that } (u_i, u_\tau) \text{ measurable; } (u_i(t), u_\tau(t)) \in [0, u_{max}] \times [0, u_{max}]\};$ being a compact convex subset of \mathbb{R}^m and the controls are bounded and Lebesgue measurable. Thus, all possible set u must be contained in the set of admissible controls U_{ad} .

2.2 General Problem (Optimal Control Problem)

Let $z(t)$ denote the total number of restricted non-resident infected travellers, and $w(t)$ denote the total number of isolated individuals.

$S_{[u_i, u_\tau]}, I_{[u_i, u_\tau]}, z_{[u_i, u_\tau]}, w_{[u_i, u_\tau]}$ denote that the actual number of the state variables (S, I, z, w) which depend on the choice of the controls u_i and u_τ .

The aim is to reduce the overall cost of infections over a specified duration while adhering to the epidemic dynamics described by the system of differential equations (2.1)-(2.2). The variables we seek to optimize are denoted as u_τ, u_i , the control variables.

The current optimal control challenge within our SI model (2.1)-(2.2) is to determine the values of u_τ and u_i that minimize cumulative infections.

Fixing $w_{max} \geq 0$ and $z_{max} \geq 0$, our optimal control for the general problem is formulated as:

$$\min J = \int_{t_0}^T \beta S_{[u_i, u_\tau]} I_{[u_i, u_\tau]} dt \quad (2.3)$$

subject to equations (2.1)-(2.2), $T = \inf\{t | I_{[u_i, u_\tau]}(t) = 0.5\}$, $(u_i(t), u_\tau(t)) \in [0, u_{max}] \times [0, u_{max}]$ for all $t \in [0, T]$, $u_{max} \in (0, \infty)$, and subject to the resource constraints;

$$\int_{t_0}^T u_i I_{[u_i, u_\tau]} dt \leq w_{max} \quad (2.4)$$

and

$$\int_{t_0}^T u_\tau \tau_{[u_i, u_\tau]} dt \leq z_{max} \quad (2.5)$$

The selection of the terminal time T is one possible issue with optimal control [27]. The concept behind our choice of T is straightforward. Given the limited resources at our disposal, a large selection of T may result in varying infection peaks since we are likely to run out of resources and be unable to control the disease. Another argument is that since we cannot predict when an epidemic will cease, we have established a threshold $I(t) = I_{min} = 0.5$ to verify that the disease has died out. In other words, our terminal time is the instant at which we can get from a given initial state to a specified final state in the shortest possible time using the controls and resources available.

2.2.1 Existence of Optimal Controls

The [PMP](#) only provides necessary conditions for optimality, and the fulfilment of necessary conditions alone does not guarantee optimality. Application of the necessary conditions for optimality is only possible if the optimal solution exists. Tonelli (1915) introduced the first theorem of the existence of a solution in the minimization of an integral functional [\[69\]](#). For an optimal control to exist, we want to have compactness of feasible solution sets. We provide a result stating the existence of at least one optimal solution to the optimal control problem [\(2.3\)-\(2.5\)](#) under some appropriate compactness and convexity assumptions. Precisely, we follow the standard Filippov's approach [\[20\]](#). Filippov's existence theorem is a result of the theory of differential inclusions, which are generalizations of ordinary differential equations that allow for multiple possible trajectories at a single point in the state space. Filippov's existence theorem addresses the existence of solutions for differential inclusions [\[19\]](#), [\[20\]](#).

Theorem 2.2.1. (*Filippov's existence theorem*) *Consider an optimal control problem defined by a differential inclusion $\dot{x} \in F(t, x, u)$, where $F : [t_0, T] \times \mathbb{R}^n \times \mathbb{R}^m \rightarrow \mathbb{R}^n$ is a set-valued mapping representing the dynamics, t is time, x is the state variable and u is the control input. Assume that the set-valued map F is upper semicontinuous in x and continuous in u for each fixed t . If the optimal control problem has nonempty, compact, and convex solution sets for all t , then an optimal control exists for almost every initial point in \mathbb{R}^n .*

To establish the existence of the optimal control, we rely on findings presented in [\[21\]](#) and [\[42\]](#). Initially, we address the boundedness of the state variables in the system [\(2.1\)-\(2.2\)](#). By summing up all the equations in the model [\(2.1\)-\(2.2\)](#), we obtain $N(t) \leq N(t_0)$. Considering the characteristics of the infectious disease model, for $\mu \geq 0$, it is evident that

$0 \leq S(t), I(t) \leq N(t_0)$. In other words, the state variables of the system are bounded. The assurance of the existence of an optimal control solution is ensured by satisfying the following conditions.

- (a) The set of control variables and corresponding state variables is not empty.
- (b) The admissible control set U_{ad} is compact and bounded.
- c) The vector function $f(t, x, u)$ is continuous.

By examining the control set U_{ad} , it becomes apparent that the system state equation's solution remains continuous and bounded for every permissible control function. Therefore, condition (a) and (b) are satisfied. The function $f(t, x, u)$, as described in (2.1)-(2.2), adheres to the Lipschitz condition concerning the state variables, ensuring the existence of the model's solution. The system's (2.1)-(2.2) solution is evidently continuous, thereby fulfilling condition (c).

Next, we apply the PMP on our optimal control problem (2.3)-(2.5). We begin by forming the system state equations for the general problem described in Section 2.2.

$$\frac{dS}{dt} = -\beta S(I + u_\tau \tau) \quad (2.6)$$

$$\frac{dI}{dt} = \beta S(I + u_\tau \tau) - (\mu + u_i)I \quad (2.7)$$

$$\frac{dw}{dt} = u_i II \quad (2.8)$$

$$\frac{dz}{dt} = u_\tau \tau I \quad (2.9)$$

Next, we form the Hamiltonian H

$$H = \lambda_0 \beta SI - \lambda_S [\beta S(I + u_\tau \tau)] + \lambda_I [\beta S(I + u_\tau \tau) - (\mu + u_i)I] + \lambda_w u_i I + \lambda_z u_\tau \tau \quad (2.10)$$

The adjoint variables, $\lambda_S, \lambda_I, \lambda_w, \lambda_z$, correspond to the states S, I, w and z respectively such that;

$$\dot{\lambda}_S = -\frac{\partial H}{\partial S} = -(\lambda_0 - \lambda_S + \lambda_I)\beta I + (\lambda_S - \lambda_I)\beta u_\tau \tau \quad (2.11)$$

$$\dot{\lambda}_I = -\frac{\partial H}{\partial I} = -(\lambda_0 - \lambda_S + \lambda_I)\beta S + (\lambda_I - \lambda_w)u_i + \lambda_I \mu \quad (2.12)$$

$$\dot{\lambda}_w = -\frac{\partial H}{\partial w} = 0 \quad (2.13)$$

$$\dot{\lambda}_z = -\frac{\partial H}{\partial z} = 0 \quad (2.14)$$

The transversality conditions are $(\lambda_0, \lambda_S(T), \lambda_I(T), \lambda_w, \lambda_z) = (\lambda_0, 0, \lambda_I(T), q, p)$ where $p, q \leq 0$. The optimality conditions are

$$\frac{\partial H}{\partial u_i} = (\lambda_w - \lambda_I)I \quad (2.15)$$

$$\frac{\partial H}{\partial u_\tau} = (\lambda_I - \lambda_S)\beta S\tau + \lambda_z\tau \quad (2.16)$$

When $\frac{\partial H}{\partial u_i} = 0$ and $\frac{\partial H}{\partial u_\tau} = 0$, we are not able to find a characterization of the controls u_i, u_τ respectively. Therefore, we define $\psi_i(t)$ and $\psi_\tau(t)$ called the switching functions

$$\psi_i(t) = (\lambda_w - \lambda_I)I \quad (2.17)$$

$$\psi_\tau(t) = (\lambda_I - \lambda_S)\beta S\tau + \lambda_z\tau \quad (2.18)$$

2.3 Bang-Bang Optimal Controls

We shift our focus to a particular scenario frequently encountered in practical applications. More precisely, we concentrate on scenarios characterized by linearity in the controls. Johnson and Gibson [24] defined the linear optimization problem as that class of optimal control

problems in which the control function appears only linearly. In these cases, optimal solutions often incorporate discontinuities in the control variables. Notice that equations (2.11) - (2.14) and the integrand in (2.3) are both linear functions of the controls u_i, u_τ . Thus, the Hamiltonian (2.10) is also a linear function of the controls; hence, the optimality condition contains no information on the controls. The PMP, when applied to bounded control problems that are linear in the control variable, explicitly defines the bang-bang control. However, the bang-bang control is undefined when the switching function is identically zero. The consequence of this problem is that we are not able to find a characterization of the optimal controls. We define switching functions $\psi_i(t)$, $\psi_\tau(t)$, and then our controls are characterized by the control input switching between two extreme values, typically denoted as u_{max} and u_{min} . In our case $u_{min} = 0$.

$$u_i^*(t) = \begin{cases} u_{max}, & \text{if } \psi_i(t) > 0 \\ ?, & \text{if } \psi_i(t) = 0 \\ 0, & \text{if } \psi_i(t) < 0 \end{cases} \quad (2.19)$$

$$u_\tau^*(t) = \begin{cases} u_{max}, & \text{if } \psi_\tau(t) > 0 \\ ?, & \text{if } \psi_\tau(t) = 0 \\ 0, & \text{if } \psi_\tau(t) < 0 \end{cases} \quad (2.20)$$

If $\psi_i = 0, \psi_\tau = 0$ does not exist in a finite time interval but occurs only at the finite points, then we refer to the control as bang-bang control.

If $\psi_i(t) \equiv 0, \psi_\tau(t) \equiv 0$ on some interval of time, we say the controls u_i^*, u_τ^* are singular on that interval. This property gives rise to the possibility of other controls existing which

satisfy the [PMP](#). Consequently, before solving the linear optimization problem, it must be shown to be non-singular, or all the singular controls must be found. Johnson and Gibson [\[24\]](#) were the first researchers to show that for certain linear optimization problems, there do exist controls other than the bang-bang control for which the [PMP](#) can be satisfied. They termed these controls the singular controls and the corresponding linear optimization problem the singular problem.

2.4 Problem 1: Isolation Only ($z_{max} = 0, u_\tau = 0$)

The derivation and proof of the theorems of Problem 1 is a direct result of the work of Hansen and Day 2011 [\[27\]](#).

Considering isolation as the only control in the model, our model now becomes;

$$\frac{dS}{dt} = -\beta SI \quad (2.21)$$

$$\frac{dI}{dt} = \beta SI - (\mu + u_i)I \quad (2.22)$$

Our objective is;

$$\min J = \int_{t_0}^T \beta S_{[u_i]} I_{[u_i]} dt \quad (2.23)$$

subject to equations [\(2.21\)](#)-([2.22](#)), $T = \inf\{t | I_{[u_i]}(t) = 0.5\}$, $u_i(t) \in [0, u_{max}]$ for all $t \in [0, T]$ and subject to the resource constraint;

$$\int_{t_0}^T u_i I_{[u_i]} dt \leq w_{max} \quad (2.24)$$

From Eq. (2.21), we have

$$dS = \beta SI \, dt \quad (2.25)$$

integrating both sides, we get

$$\int_{t_0}^T dS = - \int_{t_0}^T \beta SI \, dt \quad (2.26)$$

$$S(T) - S(t_0) = - \int_{t_0}^T \beta SI \, dt \quad (2.27)$$

$$S_0 - S(T) = \int_{t_0}^T \beta SI \, dt \quad (2.28)$$

on the other hand, rearranging Eq. (2.21), we get

$$\frac{1}{S} dS = -\beta I \, dt \quad (2.29)$$

Taking integral on both sides, we have

$$\int_{t_0}^T \frac{1}{S} dS = -\beta \int_{t_0}^T I \, dt \quad (2.30)$$

$$-\frac{1}{\beta} \ln \left(\frac{S(T)}{S_0} \right) = \int_{t_0}^T I \, dt \quad (2.31)$$

We observe from equations (2.28) and (2.31) that the terms on the right-hand side are both minimized by maximizing $S(T)$ since S_0 is a fixed quantity.

Theorem 2.4.1. (Optimal Isolation Policy) *If $w_{u_{max}}(T) \leq w_{max}$, then the optimal isolation policy for Problem 1 is $u_i^* = u_{max}$. If $w_{u_{max}}(T) > w_{max}$, then the optimal policy u_i^* is any control u_i such that $w_{u_{max}}(T) = w_{max}$.*

Proof: Following equations (2.21), (2.22) and (2.24), the isolation model with limited resources is described by the system of ordinary differential equations:

$$\frac{dS}{dt} = -\beta SI \quad (2.32)$$

$$\frac{dI}{dt} = \beta SI - (\mu + u_i)I \quad (2.33)$$

$$\frac{dw}{dt} = u_i I \quad (2.34)$$

Next, we formulate Problem 1 Sec.2.4 as a maximization problem and apply the [PMP](#).

The objective now becomes

$$\max J = - \int_{t_0}^T \beta S_{[u_i]} I_{[u_i]} dt \quad (2.35)$$

We derive the necessary conditions for optimality and the associated adjoint variables. The Hamiltonian is

$$H(t) = -\lambda_0 \beta SI - \lambda_S \beta SI + \lambda_I \beta SI - \lambda_I (\mu + u_i) I + \lambda_w u_i I \quad (2.36)$$

$$= -\dot{\lambda}_I I = -\dot{\lambda}_S S - \lambda_I \mu + (\lambda_w - \lambda_I) u_i I = 0 \quad (2.37)$$

There are associated adjoint variables, $\lambda_S, \lambda_I, \lambda_w$, which correspond to the states S, I , and w respectively such that;

$$\dot{\lambda}_S = -\frac{\partial H}{\partial S} = -(\lambda_I - \lambda_0 - \lambda_S) \beta I \quad (2.38)$$

$$\dot{\lambda}_I = -\frac{\partial H}{\partial I} = -(\lambda_I - \lambda_0 - \lambda_S) \beta S - (\lambda_w - \lambda_I) u_i + \lambda_I \mu \quad (2.39)$$

$$\dot{\lambda}_w = -\frac{\partial H}{\partial w} = 0 \quad (2.40)$$

and the optimality condition is obtained as:

$$\frac{\partial H}{\partial u_i} = \psi_i(t) = (\lambda_w - \lambda_I) I \text{ at } u_i^* \quad (2.41)$$

with the boundary conditions $(\lambda_0, \lambda_S(T), \lambda_I(T), \lambda_w) = (\lambda_0, 0, \lambda_I(T), q)$ known as the transversality conditions, where $q \leq 0$. Equations (2.36)-(2.63) form the necessary conditions that an optimal control must satisfy. The adjoint variables are the marginal variations in the objective function with respect to the respective state variables at every time t , and this helps to determine what sign (positive or negative) to expect from an adjoint variable.

Remarks 2.4.2. *Pontryagin defines the Hamiltonian with two co-state variables λ_0 and λ_x (x represents the state variables). Hence, λ_x represents the adjoint variable with respect to the state variables. Subsequently, λ_0 turns out to be constant in time; its value is determined in the Pontryagin theory as follows:*

$\lambda_0 = -1$ if $u(t)$ is feasible and the objective functional (2.35) is to be minimized.

$\lambda_0 = +1$ if $u(t)$ is feasible and the objective functional (2.35) is to be maximized.

$\lambda_0 = 0$ if $u(t)$ is unfeasible.

For our simplified problem, we have shown that all admissible controls are feasible, and we are to look for a maximum of the objective function, thus $\lambda_0 = +1$.

We now summarize the control characterization as:

$$u_i^* = \begin{cases} u_{max}, & \text{if } \lambda_w > \lambda_I \\ ?, & \text{if } \lambda_w = \lambda_I \\ 0, & \text{if } \lambda_w < \lambda_I \end{cases} \quad (2.42)$$

which follows from equation (2.19).

From Eq.(2.37), we observe that $\dot{\lambda}_I = 0$ and therefore the optimal control is either $u_i^* \equiv 0$, $u_i^* \equiv u_{max}$ or u_i^* is singular.

We observe that without the constraint Eq. (2.24), Problem 1 (2.4) becomes an unconstrained optimal control problem, and its solution is $u_i^* \equiv u_{max}$.

Claim 2.4.3. *The Optimal control for Problem 1 with $w_{max} = \infty$ is $u_i^* \equiv u_{max}$.*

Proof: substituting equation (2.38) into (2.39) with $\lambda_w = 0$ and making $\dot{\lambda}_S$ the subject gives,

$$\dot{\lambda}_S = \dot{\lambda}_I \frac{I}{S} - \lambda_I (\mu + u_i) \frac{I}{S} \quad (2.43)$$

We show that the optimal control is purely bang-bang (no singular components).

Since by Eq.(2.37), λ_I is a constant, if u_i is singular then it must be singular on the entire interval $[0, T]$. This implies, from Eq.(2.43), that λ_S is constant and since $\lambda_S(T) = 0$, it must be that $\lambda_S \equiv 0$. Equation (2.38) then gives $\lambda_0 = 0$. this contradicts the assumption that $(\lambda_0, \lambda_I(t), \lambda_S(t))$ must be nonzero for all $t \in [0, T]$. Therefore, u_i^* cannot be singular. The optimal control will be determined once the sign of λ_I is determined. To determine the sign of λ_I , we use the transversality condition $\lambda_S(T) = 0$. Since λ_I is a constant, Eq(2.39) gives

$$\lambda_I = \frac{(\lambda_0 + \lambda_S)\beta S}{\beta S - u_i - \mu} = \frac{(\lambda_0)\beta S(T)}{\beta S(T) - u_i(T) - \mu} \quad (2.44)$$

This implies that $\text{sign}(\lambda_I) = \text{sign}\left(S(T) - \frac{u_i(T) + \mu}{\beta}\right)$. From Eq.(2.1)-(2.2), λ_I is negative if and only if $\frac{dI}{dt} < 0$. Since T is the smallest time that $I = 0.5$ and $I(0) > 0.5$, it must be that $\frac{dI}{dt}$ is negative. Therefore, $u_i^* \equiv u_{max}$.

Our second observation is that the total number of isolated individuals can be calculated as

From Eq(2.32), we can write $-\dot{S} = \beta SI$ and $I = -\frac{\dot{S}}{\beta S}$. Substituting these two expressions into Eq.(2.33) gives;

$$\dot{I} = -\dot{S} + \frac{\mu}{\beta} \frac{\dot{S}}{S} - u_i I. \quad (2.45)$$

Rearranging Eq.(2.45) and integrating from t_0 to T , we obtain:

$$\int_{t_0}^T u_i I \, dt = S_0 - S(T) + I_0 - I(T) + \frac{\mu}{\beta} \ln \left(\frac{S(T)}{S_0} \right) \quad (2.46)$$

Equation (2.46) shows that the constraint value $w_{[u_i]}(T) = \int_{t_0}^T u_i I_{[u_i]} \, dt$ depends only on $S_{[u_i]}(T)$.

Again, the cost function can be rewritten as

$$\int_{t_0}^T \beta I_{[u_i]} S_{[u_i]} \, dt = S_0 - S_{[u_i]}(T) \quad (2.47)$$

and therefore minimizing the cost function is equivalent to maximizing $S_{[u_i]}(T)$.

Now to determine the optimal control when $w_{[u_{max}]}(T) > w_{max}$, we rewrite Eq(2.46) as

$$\frac{\mu}{\beta} \ln(S_{[u_i]}(T)) - S_{[u_i]}(T) = I_{[u_i]}(T) - I_0 - S_0 + \frac{\mu}{\beta} \ln(S_0) + w_{[u_i]}(T). \quad (2.48)$$

There are two possible scenarios:

1. If $w_{[u_{max}]}(T) > w_{max}$ and $S_{[u_{max}]}(T) < \frac{\mu}{\beta}$, then as long as $w_{[u_i]}(T) \leq w_{max} < w_{[u_{max}]}(T)$, the function $S_{[u_i]}(T)$ shows an upward trend concerning $w_{[u_i]}(T)$. This implies that any control strategy u_i^* utilizing the entire available resource set will be optimal.

2. If $w_{[u_{max}]}(T) > w_{max}$ and $S_{[u_{max}]}(T) > \frac{\mu}{\beta}$, considering the convex downward function $f(S) = \frac{\mu}{\beta} \ln(S) - S$ with a maximum at $S = \frac{\mu}{\beta}$, for any u_i with $w_{[u_i]}(T) < w_{max}$, it implies that $S_{[u_i]}(T) < \frac{\mu}{\beta}$. Consequently, $S_{[u_i]}(T)$ increases with $w_{[u_i]}(T)$ for any $w_{[u_i]}(T) < w_{max}$. Thus, u_i^* denotes any control strategy utilizing all available resources. This concludes the proof of Theorem 2.4.1.

2.5 Problem 2: Travel Restrictions Only ($w_{max} = 0, u_i = 0$)

In Problem 2, we consider travel restrictions as the only control in the model; our model now becomes

$$\frac{dS}{dt} = -\beta S(I + u_\tau I) \quad (2.49)$$

$$\frac{dI}{dt} = \beta S(I + u_\tau I) - \mu I \quad (2.50)$$

Our objective is;

$$\min J = \int_{t_0}^T \beta S_{[u_\tau]} I_{[u_\tau]} dt \quad (2.51)$$

subject to equations (2.49)-(2.50), $T = \inf\{t | I_{[u_\tau]}(t) = 0.5\}$, $u_\tau(t) \in [0, u_{max}]$ for all $t \in [0, T]$ and subject to the resource constraint;

$$\int_{t_0}^T u_\tau I_{[u_\tau]} dt \leq z_{max} \quad (2.52)$$

Theorem 2.5.1. (Optimal Travel Restrictions Policy) *There exists $\hat{t} \in [t_0, T]$ such that the optimal travel restrictions policy for problem 2 is*

$$u_{\tau}^*(t) = \begin{cases} u_{max}, & \text{if } t \in [t_0, \hat{t}) \\ 0, & \text{if } t \in [\hat{t}, T] \end{cases} \quad (2.53)$$

where $\int_{t_0}^{\hat{t}} u_{max} \tau dt = z_{max}$ if $\hat{t} < T$.

The conclusion drawn from Theorem 2.5.1 is that the most effective approach for travel restrictions is to exert maximum effort at the initial stages of the pandemic, maintaining these restrictions for as long as feasible, either until all resources are depleted or the pandemic comes to an end. An intriguing insight from the theorem is that, in specific situations, stringent restrictions might be inefficient, leading to unnecessarily high costs [65]. This is exemplified by scenarios where the impact of travel restrictions is minimal due to the limited contribution of imported cases to local transmission [58]. Hence, it is significant that policymakers consider the local incidence of the disease, the growth of local epidemics, and the volume of travel before implementing such restrictions.

Proof: The travel restrictions-only model with limited resources is described by the system of ordinary differential equations:

$$\frac{dS}{dt} = -\beta S(I + u_{\tau}I) \quad (2.54)$$

$$\frac{dI}{dt} = \beta S(I + u_{\tau}I) - \mu I \quad (2.55)$$

$$\frac{dz}{dt} = u_{\tau} \tau \quad (2.56)$$

Next, we formulate Problem 2 Sec.2.5 as a maximization problem and apply the PMP.

Our objective now becomes;

$$\max J = - \int_{t_0}^T \beta S_{[u_\tau]} I_{[u_\tau]} dt \quad (2.57)$$

We derive the necessary conditions for optimality and the associated adjoint variables. The Hamiltonian is

$$H(t) = -\lambda_0 \beta S I - \lambda_S \beta S (I + u_\tau \tau) + \lambda_I \beta S (I + u_\tau \tau) - \lambda_I \mu I + \lambda_z u_\tau \tau \quad (2.58)$$

$$= -\dot{\lambda}_I I + (\lambda_I - \lambda_S) \beta S u_\tau \tau = -\dot{\lambda}_S S - \lambda_I \mu = 0 \quad (2.59)$$

There are associated adjoint variables, $\lambda_S, \lambda_I, \lambda_z$, which correspond to the states S, I , and z respectively such that;

$$\dot{\lambda}_S = -(\lambda_I - \lambda_0 - \lambda_S) \beta I + (\lambda_S - \lambda_I) \beta u_\tau \tau \quad (2.60)$$

$$\dot{\lambda}_I = -(\lambda_I - \lambda_0 - \lambda_S) \beta S + \lambda_I \mu \quad (2.61)$$

$$\dot{\lambda}_z = 0 \quad (2.62)$$

and the optimality condition is obtained as:

$$\frac{\partial H}{\partial u_\tau} = \psi_\tau(t) = (\lambda_I - \lambda_S) \beta S \tau + \lambda_z \tau \text{ at } u_i^* \quad (2.63)$$

The transversality conditions are $(\lambda_0, \lambda_S(T), \lambda_I(T), \lambda_z) = (\lambda_0, 0, \lambda_I(T), p)$ where $p \leq 0$.

The control characterization is given as:

$$u_\tau^* = \begin{cases} u_{max}, & \text{if } \lambda_z > (\lambda_S - \lambda_I) \beta S \\ ?, & \text{if } \lambda_z = (\lambda_S - \lambda_I) \beta S \\ 0, & \text{if } \lambda_z < (\lambda_S - \lambda_I) \beta S \end{cases} \quad (2.64)$$

which follows from equation (2.20).

References

- [1] Stability Theory of Dynamical Systems: 161 (Grundlehren der mathematischen Wissenschaften) - Bhatia, N.P.; Szegő, G.P.: 9783540051121 - AbeBooks.
- [2] Andris Abakuks. Optimal Immunisation Policies for Epidemics. *Advances in Applied Probability*, 6(3):494–511, 1974. Publisher: Applied Probability Trust.
- [3] Ahmed Abdelrazec, Jacques Bélair, Chunhua Shan, and Huaiping Zhu. Modeling the spread and control of dengue with limited public health resources. *Mathematical Biosciences*, 271:136–145, January 2016.
- [4] Andrei A. Agrachev and Yuri L. Sachkov. *Control Theory from the Geometric Viewpoint*, volume 87 of *Encyclopaedia of Mathematical Sciences*. Springer Berlin Heidelberg, Berlin, Heidelberg, 2004.
- [5] John Alongi and Gail Nelson. *Recurrence and Topology*, volume 85 of *Graduate Studies in Mathematics*. American Mathematical Society, Providence, Rhode Island, July 2007.
- [6] Suwardi Annas, Muh. Isbar Pratama, Muh. Rifandi, Wahidah Sanusi, and Syafruddin Side. Stability analysis and numerical simulation of SEIR model for pandemic COVID-19 spread in Indonesia. *Chaos, Solitons, and Fractals*, 139:110072, October 2020.

- [7] Julien Arino, P. Driessche, James Watmough, and Jianhong Wu. A final size relation for epidemic models. *Mathematical biosciences and engineering : MBE*, 4:159–75, May 2007.
- [8] Sergei M. Aseev and Arkady V. Kryazhimskiy. The Pontryagin Maximum Principle and Transversality Conditions for a Class of Optimal Control Problems with Infinite Time Horizons. *SIAM Journal on Control and Optimization*, 43(3):1094–1119, January 2004.
- [9] Sergey M Aseev and Vladimir M Veliov. MAXIMUM PRINCIPLE FOR INFINITE-HORIZON OPTIMAL CONTROL PROBLEMS WITH DOMINATING DISCOUNT.
- [10] M. T. Barlow, N. D. Marshall, and R. C. Tyson. Optimal shutdown strategies for COVID-19 with economic and mortality costs: British Columbia as a case study. *Royal Society Open Science*, 8(9):202255.
- [11] Nam Parshad Bhatia and George Philip Szegő. *Stability Theory of Dynamical Systems*. Springer, 1st edition edition, January 1970.
- [12] Michelangelo Bin, Peter Y. K. Cheung, Emanuele Crisostomi, Pietro Ferraro, Hugo Lhachemi, Roderick Murray-Smith, Connor Myant, Thomas Parisini, Robert Shorten, Sebastian Stein, and Lewi Stone. Post-lockdown abatement of COVID-19 by fast periodic switching. *PLoS Computational Biology*, 17(1):e1008604, January 2021.
- [13] Dirk Brockmann and Dirk Helbing. The Hidden Geometry of Complex, Network-Driven Contagion Phenomena. *Science*, 342(6164):1337–1342, December 2013. Publisher: American Association for the Advancement of Science.

- [14] L. Böttcher, O. Woolley-Meza, N. a. M. Araújo, H. J. Herrmann, and D. Helbing. Disease-induced resource constraints can trigger explosive epidemics. *Scientific Reports*, 5(1):16571, November 2015. Number: 1 Publisher: Nature Publishing Group.
- [15] José M. Carcione, Juan E. Santos, Claudio Bagaini, and Jing Ba. A Simulation of a COVID-19 Epidemic Based on a Deterministic SEIR Model. *Frontiers in Public Health*, 8, 2020.
- [16] Louis Yat Hin Chan, Baoyin Yuan, and Matteo Convertino. COVID-19 non-pharmaceutical intervention portfolio effectiveness and risk communication predominance. *Scientific Reports*, 11:10605, May 2021.
- [17] O. Diekmann, J. A. P. Heesterbeek, and J. A. J. Metz. On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. *Journal of Mathematical Biology*, 28(4):365–382, June 1990.
- [18] Noah S. Diffenbaugh, Christopher B. Field, Eric A. Appel, Ines L. Azevedo, Dennis D. Baldocchi, Marshall Burke, Jennifer A. Burney, Philippe Ciais, Steven J. Davis, Arlene M. Fiore, Sarah M. Fletcher, Thomas W. Hertel, Daniel E. Horton, Solomon M. Hsiang, Robert B. Jackson, Xiaomeng Jin, Margaret Levi, David B. Lobell, Galen A. McKinley, Frances C. Moore, Anastasia Montgomery, Kari C. Nadeau, Diane E. Pataki, James T. Randerson, Markus Reichstein, Jordan L. Schnell, Sonia I. Seneviratne, Deepti Singh, Allison L. Steiner, and Gabrielle Wong-Parodi. The COVID-19 lockdowns: a window into the Earth System. *Nature Reviews Earth & Environment*, 1(9):470–481, September 2020. Number: 9 Publisher: Nature Publishing Group.

- [19] A. F. Filippov. On Certain Questions in the Theory of Optimal Control. *Journal of the Society for Industrial and Applied Mathematics Series A Control*, 1(1):76–84, January 1962. Publisher: Society for Industrial and Applied Mathematics.
- [20] A. F. Filippov. *Differential Equations with Discontinuous Righthand Sides: Control Systems*. Springer Science & Business Media, September 1988. Google-Books-ID: KBDyZSwpQpQC.
- [21] Wendell Fleming and Raymond Rishel. Existence and Continuity Properties of Optimal Controls. In Wendell Fleming and Raymond Rishel, editors, *Deterministic and Stochastic Optimal Control*, Applications of Mathematics, pages 60–79. Springer, New York, NY, 1975.
- [22] Chryssi Giannitsarou, Stephen Kissler, and Flavio Toxvaerd. Waning Immunity and the Second Wave: Some Projections for SARS-CoV-2. *American Economic Review: Insights*, 3(3):321–338, September 2021.
- [23] Charlie Giattino. How epidemiological models of COVID-19 help us estimate the true number of infections, July 2020.
- [24] John Gibson and Carroll Johnson. Singular Solutions in Problems of Optimal Control. *Department of Electrical and Computer Engineering Technical Reports*, August 1963.
- [25] Giulia Giordano, Franco Blanchini, Raffaele Bruno, Patrizio Colaneri, Alessandro Di Filippo, Angela Di Matteo, and Marta Colaneri. Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy. *Nature Medicine*, 26(6):855–860, June 2020. Number: 6 Publisher: Nature Publishing Group.

- [26] T. H. Gronwall. Note on the Derivatives with Respect to a Parameter of the Solutions of a System of Differential Equations. *Annals of Mathematics*, 20(4):292–296, 1919. Publisher: Annals of Mathematics.
- [27] Elsa Hansen and Troy Day. Optimal control of epidemics with limited resources. *Journal of Mathematical Biology*, 62(3):423–451, March 2011.
- [28] Ralph Howard. THE GRONWALL INEQUALITY.
- [29] Amy Hurford, Maria Martignoni, J. Loredó-Ostí, Francis Anokye, Julien Arino, Bilal Husain, Brian Gaas, and James Watmough. Pandemic modelling for regions implementing an elimination strategy. *Journal of Theoretical Biology*, 561:111378, December 2022.
- [30] Amy Hurford, Maria Martignoni, Jesus Loredó-Ostí, Francis Anokye, Julien Arino, Bilal Husain, Brian Gaas, and James Watmough. *Pandemic modelling for regions implementing an elimination strategy*. July 2022.
- [31] Amy Hurford and James Watmough. Don’t Wait, Re-escalate: Delayed Action Results in Longer Duration of COVID-19 Restrictions. pages 235–249. September 2021.
- [32] Morganne Igoe, Renato Casagrandi, Marino Gatto, Christopher M. Hoover, Lorenzo Mari, Calistus N. Ngonghala, Justin V. Remais, James N. Sanchirico, Susanne H. Sokolow, Suzanne Lenhart, and Giulio de Leo. Reframing Optimal Control Problems for Infectious Disease Management in Low-Income Countries. *Bulletin of Mathematical Biology*, 85(4):31, 2023.
- [33] Hem Raj Joshi, Suzanne Lenhart, Sanjukta Hota, and Folashade Augusto. OPTIMAL CONTROL OF AN SIR MODEL WITH CHANGING BEHAVIOR THROUGH AN EDUCATION CAMPAIGN.

- [34] Matt J. Keeling, Glen Guyver-Fletcher, Alex Holmes, Louise Dyson, Michael J. Tildesley, Edward M. Hill, and Graham F. Medley. Precautionary breaks: planned, limited duration circuit breaks to control the prevalence of COVID-19, October 2020. ISSN: 2021-1813 Pages: 2020.10.13.20211813.
- [35] David I Ketcheson. Optimal control of an SIR epidemic through finite-time non-pharmaceutical intervention.
- [36] Thomas Kruse and Philipp Strack. Optimal Control of an Epidemic through Social Distancing, April 2020.
- [37] Samson Lasaulce, Chao Zhang, Vineeth Varma, and Irinel Constantin Morărescu. Analysis of the Tradeoff Between Health and Economic Impacts of the Covid-19 Epidemic. *Frontiers in Public Health*, 9, 2021.
- [38] Andrew D Lewis. The Maximum Principle of Pontryagin in control and in optimal control.
- [39] Ruofei Lin, Shanlang Lin, Na Yan, and Junpei Huang. Do prevention and control measures work? Evidence from the outbreak of COVID-19 in China. *Cities*, 118:103347, November 2021.
- [40] Kailiang Liu. Optimal Control Policy on COVID-19: An Empirical Study on Lock-down and Travel Restriction Measures using Reinforcement Learning. *International Journal of High School Research*, 4(3):60–68, June 2022.
- [41] Jessica S Lugo. Numerical Simulations for Optimal Control of a Cancer Cell Model With Delay.

- [42] DL LUKES. DIFFERENTIAL EQUATIONS: CLASSICAL TO CONTROLLED. *DIFFERENTIAL EQUATIONS: CLASSICAL TO CONTROLLED*, 1982.
- [43] M. Gameiro, J.P. Lessard, J. Mireles James, and K. Mischaikow. Gronwall Inequality - an overview | ScienceDirect Topics.
- [44] Chinwendu E. Madubueze, Sambo Dachollom, and Isaac Obiajulu Onwubuya. Controlling the spread of COVID-19: optimal control analysis. *Computational and Mathematical methods in Medicine*, 2020, 2020. Publisher: Hindawi Limited.
- [45] Imad A. Moosa. The effectiveness of social distancing in containing Covid-19. *Applied Economics*, 52(58):6292–6305, December 2020. Publisher: Routledge .eprint: <https://doi.org/10.1080/00036846.2020.1789061>.
- [46] Dylan H. Morris, Fernando W. Rossine, Joshua B. Plotkin, and Simon A. Levin. Optimal, near-optimal, and robust epidemic control. *Communications Physics*, 4(1):1–8, April 2021. Number: 1 Publisher: Nature Publishing Group.
- [47] R. Morton and K. H. Wickwire. On the Optimal Control of a Deterministic Epidemic. *Advances in Applied Probability*, 6(4):622–635, 1974. Publisher: Applied Probability Trust.
- [48] Samuel Okyere, Joseph Ackora-Prah, Kwaku Darkwah, Francis Oduro, and Ebenezer Bonyah. Fractional Optimal Control Model of SARS-CoV-2 (COVID-19) Disease in Ghana. *Journal of Mathematics*, 2023:25 pages, April 2023.
- [49] Vinicius Piccirillo. Nonlinear control of infection spread based on a deterministic SEIR model. *Chaos, Solitons, and Fractals*, 149:111051, August 2021.

- [50] Lev Semenovich Pontryagin. *L.S. Pontryagin selected works / Volume 4, The mathematical theory of optimal processes ; [with the collab. of] V.G. Boltyanskii, R.V. Gamkrelidze, and E.F. Mishchenko ; transl. from the Russian by K.N. Trirogoff ..* L.S. Pontryagin selected works. Gordon and Breach, New York, facsim. ed., english ed. by l.w. neustadt edition, 1986. OCLC: 467924324.
- [51] W. F. Powers. On the order of singular optimal control problems. *Journal of Optimization Theory and Applications*, 32(4):479–489, December 1980.
- [52] Wenjie Qin, Sanyi Tang, Changcheng Xiang, and Yali Yang. Effects of limited medical resource on a Filippov infectious disease model induced by selection pressure. *Applied Mathematics and Computation*, 283:339–354, June 2016.
- [53] Thomas Rawson, Tom Brewer, Dessislava Veltcheva, Chris Huntingford, and Michael B. Bonsall. How and When to End the COVID-19 Lockdown: An Optimization Approach. *Frontiers in Public Health*, 8, 2020.
- [54] Thomas Rawson, Chris Huntingford, and Michael B. Bonsall. Temporary “Circuit Breaker” Lockdowns Could Effectively Delay a COVID-19 Second Wave Infection Peak to Early Spring. *Frontiers in Public Health*, 8, 2020.
- [55] R. M. Redheffer. The Theorems of Bony and Brezis on Flow-Invariant Sets. *The American Mathematical Monthly*, 79(7):740–747, 1972. Publisher: Mathematical Association of America.
- [56] Garrett Robert Rose. Numerical Methods for Solving Optimal Control Problems.
- [57] Timothy W Russell, Nick Golding, Joel Hellewell, Sam Abbott, Carl A B Pearson, van Zandvoort, Christopher I Jarvis, Hamish Gibbs, Yang Liu, Rosalind M Eggo, W John,

- and Adam J Kucharski. Reconstructing the global dynamics of under-ascertained COVID-19 cases and infections.
- [58] Timothy W Russell, Joseph T Wu, Sam Clifford, W John Edmunds, Adam J Kucharski, and Mark Jit. Effect of internationally imported cases on internal spread of COVID-19: a mathematical modelling study. *The Lancet Public Health*, 6(1):e12–e20, January 2021.
- [59] Kristoffer Rypdal, Filippo Maria Bianchi, and Martin Rypdal. *Intervention fatigue is the primary cause of strong secondary waves in the COVID-19 pandemic*. November 2020.
- [60] Chunhua Shan, Yingfei Yi, and Huaiping Zhu. Nilpotent singularities and dynamics in an SIR type of compartmental model with hospital resources. *Journal of Differential Equations*, 260(5):4339–4365, March 2016.
- [61] Chunhua Shan and Huaiping Zhu. Bifurcations and complex dynamics of an SIR model with the impact of the number of hospital beds. *Journal of Differential Equations*, 257(5):1662–1688, September 2014.
- [62] Jesse A. Sharp, Alexander P. Browning, Tarunendu Mapder, Christopher M. Baker, Kevin Burrage, and Matthew J. Simpson. Designing combination therapies using multiple optimal controls. *Journal of Theoretical Biology*, 497:110277, July 2020.
- [63] Jesse A. Sharp, Kevin Burrage, and Matthew J. Simpson. Implementation and acceleration of optimal control for systems biology. *Journal of The Royal Society Interface*, 18(181):20210241, August 2021. Publisher: Royal Society.
- [64] Jesse Aeden Sharp. Numerical methods for optimal control and parameter estimation in the life sciences.

- [65] Wei Shi, Yun Qiu, Pei Yu, and Xi Chen. Optimal Travel Restrictions in Epidemics. 2022.
- [66] Chengjun Sun and Ying-Hen Hsieh. Global analysis of an SEIR model with varying population size and vaccination. *Applied Mathematical Modelling*, 34(10):2685–2697, October 2010.
- [67] Nasser Sweilam, Seham Al-Mekhlafi, and Dumitru Baleanu. Optimal Control for a Fractional Tuberculosis Infection Model Including the Impact of Diabetes and Resistant Strains. *Journal of Advanced Research*, 17, May 2019.
- [68] Gerald Teschl. Ordinary Differential Equations and Dynamical Systems.
- [69] Leonida Tonelli. Sur une méthode directe du calcul des variations. *Rendiconti del Circolo Matematico di Palermo (1884-1940)*, 39(1):233–264, December 1915.
- [70] Calvin Tsay, Fernando Lejarza, Mark A. Stadtherr, and Michael Baldea. Modeling, state estimation, and optimal control for the US COVID-19 outbreak. *Scientific Reports*, 10(1):10711, July 2020. Number: 1 Publisher: Nature Publishing Group.
- [71] P. van den Driessche and James Watmough. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 180(1):29–48, November 2002.
- [72] Aili Wang, Yanni Xiao, and Robert A. Cheke. Global dynamics of a piece-wise epidemic model with switching vaccination strategy. *Discrete and Continuous Dynamical Systems - B*, 19(9):2915–2940, August 2014. Publisher: Discrete and Continuous Dynamical Systems - B.

- [73] Aili Wang, Yanni Xiao, and Robert Smith. Multiple Equilibria in a Non-smooth Epidemic Model with Medical-Resource Constraints. *Bulletin of Mathematical Biology*, 81(4):963–994, April 2019.
- [74] Aili Wang, Yanni Xiao, and Huaiping Zhu. Dynamics of a Filippov epidemic model with limited hospital beds. *Mathematical biosciences and engineering: MBE*, 15(3):739–764, June 2018.
- [75] Wendi Wang. Backward bifurcation of an epidemic model with treatment. *Mathematical Biosciences*, 201(1):58–71, May 2006.
- [76] Wendi Wang and Shigui Ruan. Bifurcations in an epidemic model with constant removal rate of the infectives. *Journal of Mathematical Analysis and Applications*, 291(2):775–793, March 2004.
- [77] Suzanne Lenhart Workman, John T. *Optimal Control Applied to Biological Models*. Chapman and Hall/CRC, New York, May 2007.
- [78] Tunde Tajudeen Yusuf and Francis Benyah. Optimal control of vaccination and treatment for an SIR epidemiological model. 8(3), 2012.
- [79] Xu Zhang and Xianning Liu. Backward bifurcation of an epidemic model with saturated treatment function. *Journal of Mathematical Analysis and Applications*, 348(1):433–443, December 2008.
- [80] Linhua Zhou and Meng Fan. Dynamics of an SIR epidemic model with limited medical resources revisited. *Nonlinear Analysis: Real World Applications*, 13:312–324, February 2012.