

Model cont...

0.1 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 [Susceptibles Infected \(SI\)](#) model now becomes

$$\frac{dS}{dt} = -\beta S(I + u_\tau I) \quad (1)$$

$$\frac{dI}{dt} = \beta S(I + u_\tau I) - \mu I \quad (2)$$

Our objective is to;

$$\min_{u_\tau} \int_{t_0}^T \beta S_{[u_\tau]} I_{[u_\tau]} dt \quad (3)$$

subject to the SI Model (1)-(2), $T = \inf\{t | I_{[u_\tau]}(t) = 0.5\}$, $u_\tau(t) \in [0, u_{max}]$ for all $t \in [0, T]$ and subject to the resource constraint;

$$\int_{t_0}^T u_\tau I_{[u_\tau]} dt \leq z_{max} \quad (4)$$

Theorem 0.1.1. (*Optimal Travel Restrictions Policy*) *There exists $\hat{t} \in [t_0, T]$ such that the optimal travel restrictions policy for problem 2 is*

$$u_{\tau}^*(t) = \begin{cases} u_{max}, & \text{if } t \in [t_0, \hat{t}) \\ 0, & \text{if } t \in [\hat{t}, T] \end{cases} \quad (5)$$

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

The conclusion drawn from Theorem 0.1.1 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 [51]. This is exemplified by scenarios where the impact of travel restrictions is minimal due to the limited contribution of imported cases to local transmission [46]. Hence, it is significant that policymakers should consider the local incidence of COVID-19, 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:

$$\frac{dS}{dt} = -\beta S(I + u_{\tau} I) \quad (6)$$

$$\frac{dI}{dt} = \beta S(I + u_{\tau} I) - \mu I \quad (7)$$

$$\frac{dz}{dt} = u_{\tau} \tau \quad (8)$$

Next, we formulate Problem 2 Sec.0.1 as a maximization problem and apply the Pontryagin's Maximum Principle (PMP); we derive the necessary conditions for the optimal

control model and the associated adjoint variables. The Hamiltonian is

$$H(t) = -\lambda_0\beta SI - \lambda_S\beta S(I + u_\tau\tau) + \lambda_I\beta S(I + u_\tau\tau) - \lambda_I\mu I + \lambda_z u_\tau\tau \quad (9)$$

$$= -\lambda'_I I + (\lambda_I - \lambda_S)\beta S u_\tau\tau = -\lambda'_S S - \lambda_I\mu = 0 \quad (10)$$

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

$$\lambda'_S = -(\lambda_I - \lambda_0 - \lambda_S)\beta I + (\lambda_S - \lambda_I)\beta u_\tau\tau \quad (11)$$

$$\lambda'_I = -(\lambda_I - \lambda_0 - \lambda_S)\beta S + \lambda_I\mu \quad (12)$$

$$\lambda'_z = 0 \quad (13)$$

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:

$$u_\tau^* = \begin{cases} u_{max}, & \text{if } \lambda_I > \lambda_S \\ ?, & \text{if } \lambda_I = \lambda_S \\ 0, & \text{if } \lambda_I < \lambda_S \end{cases} \quad (14)$$

From (14), we show that if $\lambda_I = \lambda_S$ cannot be sustained over an interval of time but occurs only at finitely many points, then the control u_τ^* is purely bang-bang. If $\lambda_I = \lambda_S$ on some interval of time, then u_τ^* is singular. We show that u_τ^* is not singular. Suppose by contradiction that $\lambda_I = \lambda_S$ on some interval \mathbb{J} . The adjoint equation (11) now becomes

$$\lambda'_S = \lambda_0\beta I \quad (15)$$

This implies that

$$\lambda_S(T) = \lambda_S(t_0) + \lambda_0 \beta \int_{t_0}^T I \, dt \quad (16)$$

Moreover, according to equations (11) - (12), once u_τ^* reaches singularity, it remains singular throughout the entire duration, meaning $T \in \mathbb{J}$. Given that $T \in \mathbb{J}$, the expression on the right-hand side of equation (16) is obligated to fulfill the transversality condition $\lambda_S(T) = 0$. However, it is observed that $\lambda_0 \beta \int_{t_0}^T I \, dt$ does not equal zero, leading to a contradiction. As the transversality condition cannot be met, the optimal control must follow a bang-bang pattern [22]. Therefore, the control characterization is given as

$$u_\tau^*(t) = \begin{cases} u_{max}, & t \in [t_0, \hat{t}) \\ 0, & t \in [\hat{t}, T] \end{cases} \quad (17)$$

Remarks 0.1.2. *For a function to be identically zero on some measurable interval, it is necessary that the function and all its derivatives be zero on that interval.*

Claim 0.1.3. *The control $u_\tau \equiv 0$ is not an optimal solution for Problem 2.*

Proof: If $u_\tau^* \equiv 0$, then λ_I is constrained by $\lambda_I \leq \lambda_S$. Additionally, when $u_\tau^* \equiv 0$, it signifies that none of the available resources are utilized for maximum travel restrictions, implying $\lambda_z = 0$. Consequently, this indicates that $\lambda_S \geq 0$. Furthermore, according to equation (10), if $u_\tau^* \equiv 0$, it implies $\lambda_I' \equiv 0$. By rearranging equation (11) and substituting $t = T$, we obtain $\lambda_I(\beta S(T) - \mu) = \lambda_0 \beta S(T)$. This results in two possible scenarios:

1. If $\lambda_0 = 0$, it follows that $\lambda_I \equiv 0$. Since $\lambda_S(T) = 0$ as well, this implies that we have a zero adjoint vector at $t = T$. Consequently, this scenario is not feasible.

2. If $\lambda_0 = 1$, then $\lambda_I < 0$ due to the condition $S(T) < \frac{\mu}{\beta}$. Consequently, this implies, according to equation (10), that $\lambda'_S > 0$. Therefore, as $\lambda_S(T) = 0$, it necessitates that $\lambda_S(t) < 0$ for all $t < T$. However, this contradicts the fact that when $u_\tau^* \equiv 0$, it implies $\lambda_S \geq 0$.

0.2 Problem 3: Mixed Policy (General Problem)

Theorem 0.2.1. (Optimal Mixed Policy) *There exists $\hat{t} \in [t_0, T]$ such that the optimal mixed policy for problem 3 has one of the following forms:*

1.

$$(u_i^*(t), u_\tau^*(t)) = \begin{cases} (u_{max}, u_{max}), & \text{if } t \in [t_0, \hat{t}] \\ (0, u_\tau^*(t)), & \text{if } t \in (\hat{t}, T] \end{cases} \quad (18)$$

where $\int_{t_0}^{\hat{t}} u_{max} I_{[u_{max}, u_{max}]} dt = w_{max}$ if $\hat{t} < T$ or

2.

$$(u_i^*(t), u_\tau^*(t)) = \begin{cases} (u_{max}, u_{max}), & \text{if } t \in [t_0, \hat{t}] \\ (u_i^*(t), 0), & \text{if } t \in (\hat{t}, T] \end{cases} \quad (19)$$

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

Remarks 0.2.2. *In Equation (18), when $t > \hat{t}$, $u_\tau^*(t)$ signifies the optimal control specific to the travel restriction-only model. In other words, for $t > \hat{t}$, the solution to Problem 2 is represented by $u_\tau^*(t)$. Similarly, in Equation (19), if $t > \hat{t}$, $u_i^*(t)$ denotes the optimal control for the isolation-only model. Hence, for $t > \hat{t}$, the solution to Problem 1 is given by $u_i^*(t)$.*

Proof: The model for the mixed policy with limited resources is described by the system of ordinary differential equations:

$$\frac{dS}{dt} = -\beta S(I + u_\tau I) \quad (20)$$

$$\frac{dI}{dt} = \beta S(I + u_\tau I) - (\mu + u_i)I \quad (21)$$

$$\frac{dw}{dt} = u_i I \quad (22)$$

$$\frac{dz}{dt} = u_\tau \tau \quad (23)$$

Next, we formulate Problem 3 Sec.0.2 as a maximization problem and apply the [PMP](#); we derive the necessary conditions for the optimal control model and the associated adjoint variables. The Hamiltonian is

$$H(t) = -\lambda_0 \beta S I - \lambda_S \beta S(I + u_\tau \tau) + \lambda_I \beta S(I + u_\tau \tau) - \lambda_I (\mu + u_i) I + \lambda_w u_i I + \lambda_z u_\tau \tau \quad (24)$$

$$= -\lambda'_I I + (\lambda_I - \lambda_S) \beta S u_\tau \tau = -\lambda'_S S + (\lambda_w - \lambda_I) u_i I - \lambda_I \mu I = 0 \quad (25)$$

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

$$\lambda'_S = -(\lambda_I - \lambda_0 - \lambda_S) \beta I - (\lambda_I - \lambda_S) \beta u_\tau \tau \quad (26)$$

$$\lambda'_I = -(\lambda_I - \lambda_0 - \lambda_S) \beta S - (\lambda_w - \lambda_I) u_i + \lambda_I \mu \quad (27)$$

$$\lambda'_w = 0 \quad (28)$$

$$\lambda'_z = 0 \quad (29)$$

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

The control characterization is given as:

$$u_\tau^* = \begin{cases} u_{max}, & \text{if } \lambda_I > \lambda_S \\ ?, & \text{if } \lambda_I = \lambda_S \\ 0, & \text{if } \lambda_I < \lambda_S \end{cases} \quad (30)$$

and

$$u_i^* = \begin{cases} u_{max}, & \text{if } \lambda_w > \lambda_I \\ ?, & \text{if } \lambda_w = \lambda_I \\ 0, & \text{if } \lambda_w < \lambda_I \end{cases} \quad (31)$$

Claim 0.2.3. *If u_τ is singular on some interval \mathbb{J} , then u_i is not singular on \mathbb{J} and $u_i = 0$.*

Proof: Let assume by contradiction that u_i is singular on \mathbb{J} . Then $\lambda_I' = 0$, $\lambda_w = \lambda_I$ and consequently, $\lambda_I' = \lambda_S' = 0$. Now u_i and u_τ being singular implies from (30) and (31) that $\lambda_S = \lambda_I = \lambda_w$. Since $T \in \mathbb{J}$ and $\lambda_S(T) = 0$, it implies that $\lambda_S = \lambda_I = \lambda_w = 0$ on the interval. Furthermore, given that $\lambda_I' = 0$, we have from (27) that $\lambda_0 = 0$ and obviously $\lambda_z = 0$. This solution leads to a zero adjoint vector on the interval \mathbb{J} . Since we cannot have a zero adjoint vector, it implies that u_i cannot be singular, a contradiction to our assumption.

On the other hand, if u_i is not singular, then $\lambda_S = \lambda_I \neq \lambda_w$. We have that $\lambda_I' = 0$. From (25), we have $\lambda_I = \lambda_w \frac{u_i}{u_i + \mu}$. But $\lambda_w \neq 0$, if $\lambda_w = 0$, then $\lambda_I = 0$, which leads to the contradiction, hence it must be that $\lambda_w < 0$ which implies that $\lambda_w < \lambda_I$. Therefore, from (31), $u_i = 0$.

Claim 0.2.4. *If u_i is singular on \mathbb{J} , then $u_\tau = 0$ on \mathbb{J} .*

Proof: If u_i is singular on \mathbb{J} , then $\lambda_I' = 0$.

From (25), this implies that $(\lambda_I - \lambda_S)\beta S u_\tau \tau = 0$. So either u_τ is singular ($\lambda_I = \lambda_S$) or $u_\tau = 0$. But we just proved in claim 0.2.3 that u_i and u_τ cannot be singular at the same time; therefore, it must be that $u_\tau = 0$ on \mathbb{J} .

Claim 0.2.5. *If there exists a $\hat{t} \geq 0$ such that $u_i(t) = 0$ is constant for all $t \in (\hat{t}, T]$, then $u_\tau(t) = u_\tau^*(t)$ for all $t \in (\hat{t}, T]$.*

Proof: Once $t > \hat{t}$ the mixed isolation–travel restrictions model becomes a travel restrictions-only model, and therefore, the optimal u_τ is the optimal control for the travel restrictions-only model with parameters $\tilde{t}_0 = \hat{t}$, $\tilde{z}_{max} = z_{max} - \int_{\hat{t}_0}^{\hat{t}} u_\tau \tau \, dt$.

Claim 0.2.6. *If there exists a $\hat{t} \geq 0$ such that $u_\tau(t) = 0$ is constant for all $t \in (\hat{t}, T]$, then $u_i(t) = u_i^*(t)$ for all $t \in (\hat{t}, T]$.*

Proof: Once $t > \hat{t}$ the mixed isolation–travel restrictions model becomes an isolation-only model, and therefore, the optimal u_i is the optimal control for the isolation-only model with parameters $\tilde{t}_0 = \hat{t}$, $\tilde{w}_{max} = w_{max} - \int_{\hat{t}_0}^{\hat{t}} u_i I \, dt$.

References

- [1] Stability Theory of Dynamical Systems: 161 (Grundlehren der mathematischen Wissenschaften) - Bhatia, N.P.; Szegö, G.P.: 9783540051121 - AbeBooks.
- [2] John Alongi and Gail Nelson. *Recurrence and Topology*, volume 85 of *Graduate Studies in Mathematics*. American Mathematical Society, Providence, Rhode Island, July 2007.
- [3] 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.
- [4] 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.
- [5] 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.

- [6] Sergey M Aseev and Vladimir M Veliov. MAXIMUM PRINCIPLE FOR INFINITE-HORIZON OPTIMAL CONTROL PROBLEMS WITH DOMINATING DISCOUNT.
- [7] 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.
- [8] Nam Parshad Bhatia and George Philip Szegő. *Stability Theory of Dynamical Systems*. Springer, 1st edition edition, January 1970.
- [9] 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.
- [10] 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.
- [11] 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.
- [12] 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.
- [13] 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.
- [14] 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.
- [15] A. F. Filippov. *Differential Equations with Discontinuous Righthand Sides: Control Systems*. Springer Science & Business Media, September 1988. Google-Books-ID: KBDyZSwpQpQC.
- [16] 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.
- [17] 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.
- [18] Charlie Giattino. How epidemiological models of COVID-19 help us estimate the true number of infections, July 2020.

- [19] John Gibson and Carroll Johnson. Singular Solutions in Problems of Optimal Control. *Department of Electrical and Computer Engineering Technical Reports*, August 1963.
- [20] 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.
- [21] 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.
- [22] Elsa Hansen and Troy Day. Optimal control of epidemics with limited resources. *Journal of Mathematical Biology*, 62(3):423–451, March 2011.
- [23] 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.
- [24] 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.
- [25] 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.
- [26] 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.
- [27] Hem Raj Joshi, Suzanne Lenhart, Sanjukta Hota, and Folashade Augusto. OPTIMAL CONTROL OF AN SIR MODEL WITH CHANGING BEHAVIOR THROUGH AN EDUCATION CAMPAIGN.
- [28] 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.
- [29] David I Ketcheson. Optimal control of an SIR epidemic through finite-time non-pharmaceutical intervention.
- [30] Thomas Kruse and Philipp Strack. Optimal Control of an Epidemic through Social Distancing, April 2020.
- [31] 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.
- [32] 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.
- [33] Jessica S Lugo. Numerical Simulations for Optimal Control of a Cancer Cell Model With Delay.

- [34] DL LUKES. DIFFERENTIAL EQUATIONS: CLASSICAL TO CONTROLLED. *DIFFERENTIAL EQUATIONS: CLASSICAL TO CONTROLLED*, 1982.
- [35] 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.
- [36] 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.
- [37] 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.
- [38] Vinicius Piccirillo. Nonlinear control of infection spread based on a deterministic SEIR model. *Chaos, Solitons, and Fractals*, 149:111051, August 2021.
- [39] 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 I.W. Neustadt edition, 1986. OCLC: 467924324.
- [40] W. F. Powers. On the order of singular optimal control problems. *Journal of Optimization Theory and Applications*, 32(4):479–489, December 1980.
- [41] 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.

- [42] 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.
- [43] 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.
- [44] Garrett Robert Rose. Numerical Methods for Solving Optimal Control Problems.
- [45] 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.
- [46] 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.
- [47] 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.
- [48] 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.

- [49] 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.
- [50] Jesse Aeden Sharp. Numerical methods for optimal control and parameter estimation in the life sciences.
- [51] Wei Shi, Yun Qiu, Pei Yu, and Xi Chen. Optimal Travel Restrictions in Epidemics. 2022.
- [52] 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.
- [53] 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.
- [54] Leonida Tonelli. Sur une méthode directe du calcul des variations. *Rendiconti del Circolo Matematico di Palermo (1884-1940)*, 39(1):233–264, December 1915.
- [55] 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.
- [56] 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.

- [57] 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.
- [58] Suzanne Lenhart Workman, John T. *Optimal Control Applied to Biological Models*. Chapman and Hall/CRC, New York, May 2007.
- [59] Tunde Tajudeen Yusuf and Francis Benyah. Optimal control of vaccination and treatment for an SIR epidemiological model. 8(3), 2012.