Understanding SIR-type epidemic behaviors through set-based dynamic analysis

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October 10, 2024
03:30 pm

Pandemics: Cases and Deaths from COVID-19 pandemic in US

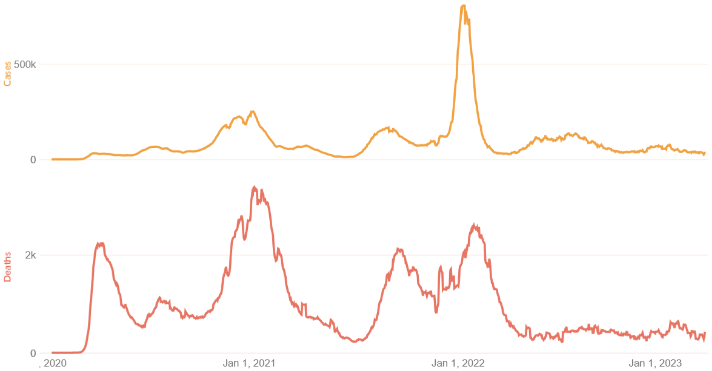

Figure 1: COVID-19 Data Repository by the Center for Systems Science and Engineering at Johns Hopkins University [1].

Pandemics: The further waves of infections scenario

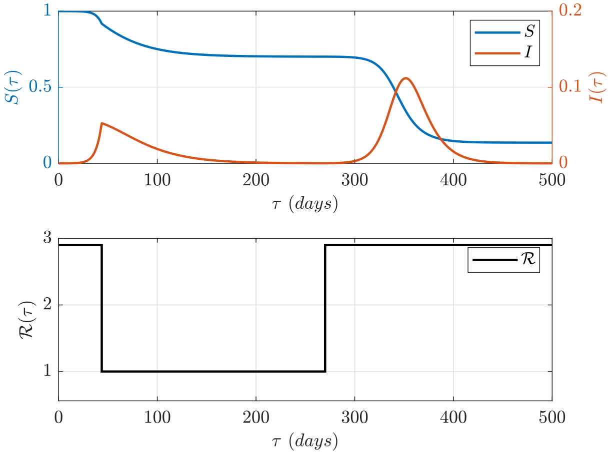

Figure 2: Second wave effect on the basic SIR model proposed by Kermack & McKendrick, (1927).

Pandemics: References from literature

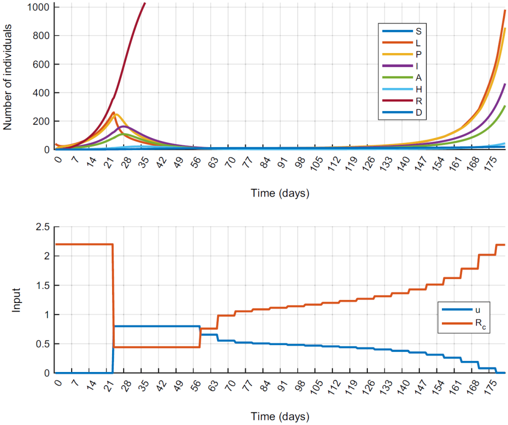

Figure 3: Second wave effect across several optimal control proposals in the Literature, (Péni, 2020).

Pandemics: References from literature

$$
\begin{aligned}
J &= \sum_{i=0}^{M} u_{k+i|k}^2 + w_H H_{M_k} + w_D D_{M_k} + w_\varepsilon \varepsilon, \\
H_{k+i+1|k} &\leq \overline{H} + \varepsilon, \quad 0 \leq \varepsilon, \quad 0 \leq u_{k+i|k} \\
&\leq u_{\max}, \quad \forall i = 0 \ldots M-1.
\end{aligned} \tag{14}
$$

Figure 4: Typical optimal control problem formulation, (Péni, 2020).

There is not combination of the *weighting factors* that prevent us for the second wave effect

Dynamical Analysis

SIR-type model: dynamic analysis

SIR Kermack & McKendrick

$$\begin{aligned}
\dot{S}(t) &= -\frac{\beta}{N} I(t) S(t) \\
\dot{I}(t) &= -\frac{\beta}{N} I(t) S(t) - \gamma I(t) \\
\dot{R}(t) &= \gamma I(t)
\end{aligned}$$

SIR dimensionless

$$\dot{S}(\tau) = -\mathcal{R}(\tau) S(\tau) I(\tau), \tag{1a}$$

$$\dot{I}(\tau) = \mathcal{R}(\tau) S(\tau) I(\tau) - I(\tau), \tag{1b}$$

SIR-type model: dynamic analysis

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Parameters β y γ stand for the infection and remove (recovery/death) rate of the virus. $\mathcal{R}(\cdot) := \beta(\cdot)/\gamma$, stand for the time-varying reproduction number. The state space is restricted by the following set:

$$\mathcal{X} := \{(S, I) \in \mathbb{R}^2 : S \in [0, 1], I \in [0, 1], S + I \leq 1\},$$

SIR-type model: dynamic analysis

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we consider $\mathcal{R}(\tau)$ as a control action, under the following condition:

$$\Omega_{\mathcal{R}} := \{\mathcal{R}(\cdot) : \mathbb{R}_{\geq 0} \to \mathbb{R}_{\geq 0} : \mathcal{R}(\tau) \in [\underline{\mathcal{R}}, \overline{\mathcal{R}}], \text{ for } \tau \in [\tau_i, \tau_f], \\ \text{and } \mathcal{R}(\tau) = \overline{\mathcal{R}}, \text{ for } \tau \in [0, \tau_i) \text{ and } \tau \in (\tau_f, \infty)\},$$

SIR-type model: dynamic analysis

The equilibrium set of System (1), with $\mathcal{R}(\tau) \equiv \overline{\mathcal{R}}$ and initial conditions $(S(\tau_0), I(\tau_0)) \in \mathcal{X}$, is given by $\mathcal{X}_s := \{(\bar{S}, \bar{I}) \in \mathcal{X} : \bar{S} \in [0, S(\tau_0)], \bar{I} = 0\}$. The following theorem defines the asymptotic stability of a subset of $\mathcal{X}_s$.

SIR-type model: dynamic analysis

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Theorem 1.1 (Asymptotic Stability of $\mathcal{X}_s^{st}$)

Consider System (1) with $\mathcal{R}(\tau)\equiv\overline{\mathcal{R}}$ and constrained by $\mathcal{X}$. Then, the set

$$\mathcal{X}_s^{st} := \{(\bar{S}, \bar{I}) \in \mathcal{X} : \bar{S}\in[0, S^*], \bar{I}=0\},$$

is the unique asymptotically stable (AS) set of System (1), with a domain of attraction given by $\mathcal{X}$. S^* stand for the **herd immunity** *value define as* $S^* := \min\{1, 1/\overline{\mathcal{R}}\}$.

SIR-type model: dynamic analysis

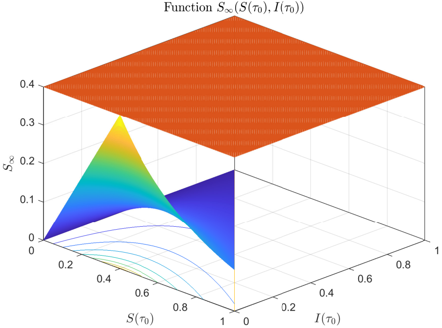

Figure 5: Function $S_\infty(\mathcal{R}, S_0, I_0)$.

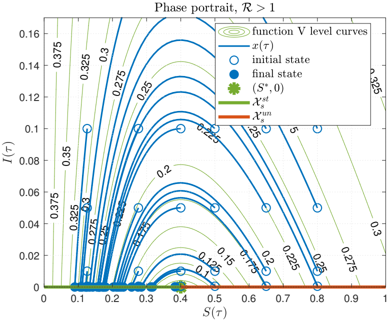

Figure 6: Phase portrait for SIR-type System (1).

Epidemiological severity indexes

Performance indexes

Performance indexes

1. **Infected Peak Prevalence** (IPP)

The first epidemic-severity index, the IPP, is defined as:

$$IPP := \max_{t\in[0,\infty)} I(t).$$

A high IPP, could overwhelm the healthcare capacity.

Performance indexes

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A high IPP, could overwhelm the healthcare capacity.

2. **Epidemic Final Size** (EFS)
The second epidemic-severity index, the EFS, is defined as:

$$EFS := 1 - S_\infty.$$

A high EFS means a high total number of infected individuals at the end of the epidemic.

Performance indexes

3. **Social Distancing Index** (SDI)

The third epidemic-severity index, the SDI, is defined as:

$$SDI := \int_0^\infty (\overline{\mathcal{R}} - \mathcal{R}(t))dt = \int_{t_s}^{t_f} (\overline{\mathcal{R}} - \mathcal{R}(t))dt.$$

A high SDI means longer and harder interventions, causing social fatigue and economic issues.

Control objectives

Considering the epidemiological indexes presented above, the *control* objectives are established as follows:

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Definition (Epidemiological control objective (ECO))

Bringing the EFS *as near as possible to* $(1 - S^*)$*, while maintaining* $IPP \leq I_{\max}$.

Control objectives

Considering the epidemiological indexes presented above, the *control* objectives are established as follows:

Definition (Epidemiological control objective (ECO))

Bringing the EFS *as near as possible to* $(1 - S^*)$*, while maintaining* $IPP \leq I_{\max}$.

Definition (Socio-Economic Control Objective (SECO))

Minimizing SDI*, provided that the Epidemic Control Objective was achieved.*

A road path to a well-posed Optimal Control Problem

Open-loop SD strategies (1)

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Definition (Goldilocks Single-interval strategy)

The goldilocks single-interval intervention is defined by a starting time, τ_s^g, fulfilling condition:

$$\mathcal{R}_{si}^g := \mathcal{R}_{si}^*(S^*, \tau_s^g) = \hat{\mathcal{R}}_{si}(I_{\max}, \tau_s^g).$$

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Theorem 1.2 (Goldilocks Single-interval)

Consider System (1) *with initial conditions* $(S(0), I(0)) = (1-\epsilon, \epsilon)$*, where* $0 < \epsilon \ll 1$*, and* $\mathcal{R}(0) = \overline{\mathcal{R}}$ *such that* $S(0) > S^*$*. Consider a given* $I_{\max}$ *and consider also that* $\mathcal{R}(\cdot) \in \Omega_{\mathcal{R}}$*. Then, if for* S^* *and* $I_{\max}$ *there exists a goldilocks single-interval intervention, it is the only one that arbitrarily approaches the ECO, as* $\tau_f \to \infty$*.*

SD strategy: goldilocks single-interval

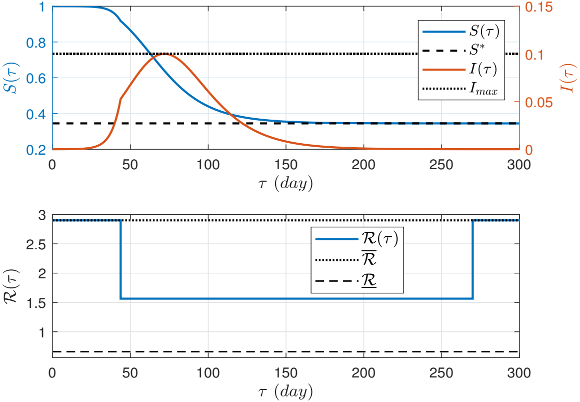

Figure 7: S, I y $\mathcal{R}$ temporal evolution (left), phase portrait (right). Single interval intervention with $\mathcal{R}^{g}_{si} = 1.565$, $S^* = 0.35$ y $I_{\max} = 0.1$.

SD strategy: goldilocks single-interval

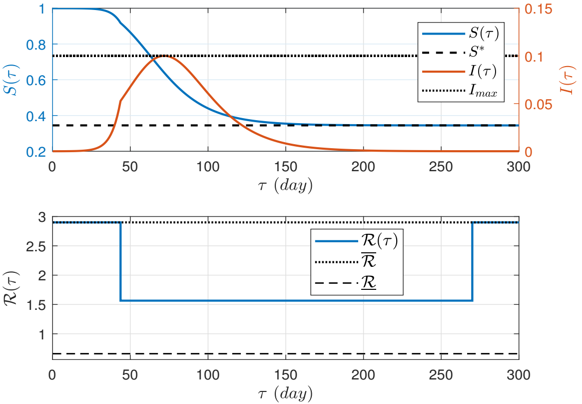

Figure 7: S, I y $\mathcal{R}$ temporal evolution (left), phase portrait (right). Single interval intervention with $\mathcal{R}_{si}^g = 1.565$, $S^* = 0.35$ y $I_{\max} = 0.1$.

Performance indexes: $\mathrm{EFS} = 0.660$, $\mathrm{IPP} = 0.100$, $\mathrm{SDI} = 301.710$.

SD strategy: goldilocks single-interval

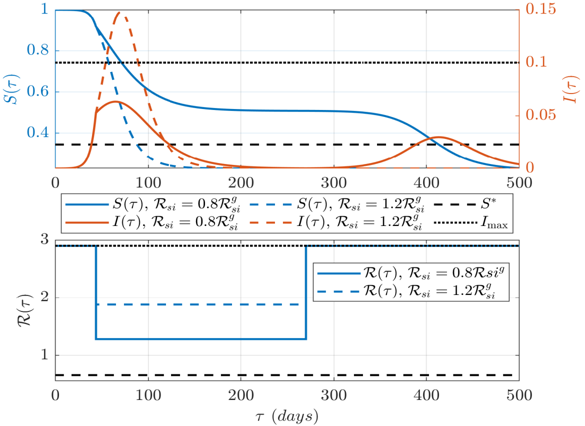

Figure 8: S, I y $\mathcal{R}$ temporal evolution. when a wrong goldilocks single interval SD is applied, $\mathcal{R}_{si} = \mathcal{R}_{si}^g \pm 0.2\mathcal{R}_{si}^g$.

Open-loop SD strategies (2)

Definition ("Wait, Maintain, Suspend" strategy)

It is defined as follow:

$$\mathcal{R}(\tau) := \begin{cases} \overline{\mathcal{R}} & \textit{for} \quad \tau \in [0, \tau_s), \\ \frac{1}{S(\tau)} & \textit{for} \quad \tau \in [\tau_s, \tau_1), \\ \mathcal{R}^*_{si} & \textit{for} \quad \tau \in [\tau_1, \tau_f], \\ \overline{\mathcal{R}} & \textit{for} \quad \tau \in (\tau_f, \infty). \end{cases} \tag{2}$$

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Theorem 1.3 ("Wait, Maintain, Suspend" strategy)

Consider System (1) *with initial conditions* $(S(0), I(0)) = (1 - \epsilon, \epsilon)$, *where* $0 < \epsilon \ll 1$, *and* $\mathcal{R}(0) = \overline{\mathcal{R}}$ *such that* $S(0) > S^*$. *Consider a given* $I_{\max}$ *and consider also that* $\mathcal{R}(\cdot) \in \Omega_{\mathcal{R}}$. *Then, there exist some* $0 \le \tau_i < \tau_1^* < \tau_f$ *such that the "wait, maintain, suspend" strategy given by* (2), *achieves the ECO,* $S_\infty \approx S^*$ *and* $I(\tau) \le I_{\max}$ $(\tau_f \to \infty)$.

SD strategy: "Wait, Maintain, Suspend"

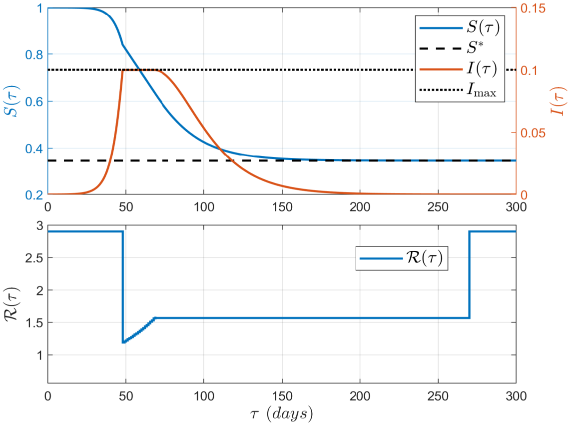

Figure 9: S, I y $\mathcal{R}$ temporal evolution. "Wait, Maintain, Suspend" strategy with $\mathcal{R}_{si}^* = 1.5654$, $S^* = 0.35$ y $I_{\max} = 0.1$.

SD strategy: "Wait, Maintain, Suspend"

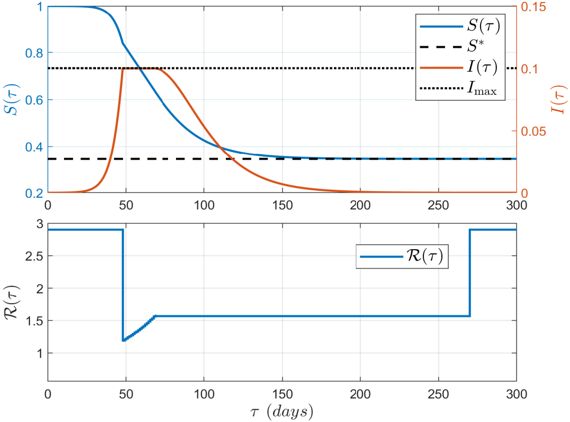

Figure 9: S, I y $\mathcal{R}$ temporal evolution. "Wait, Maintain, Suspend" strategy with $\mathcal{R}_{si}^* = 1.5654$, $S^* = 0.35$ y $I_{\max} = 0.1$.

Performance indexes: EFS$= 0.6596$, IPP$= 0.0998$, SDI$= 298.8647$.

SD strategy: "Wait, Maintain, Suspend"

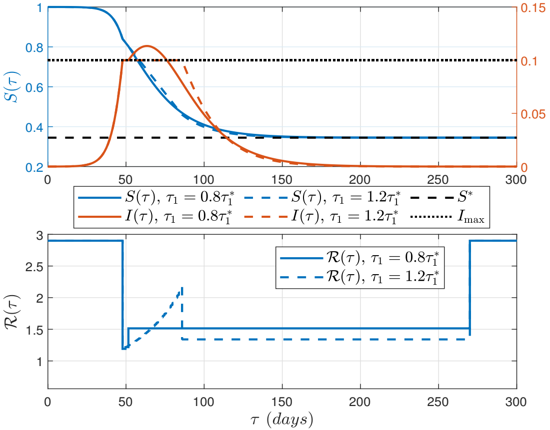

Figure 10: S, I y $\mathcal{R}$ temporal evolution. When a wrong "Wait, Maintain, Suspend" control sequence is applied. If τ_1 is too small, then the ECO is not achieved. If τ_1 is too large, the ECO are still achieved, but with a large SDI$= 336.9136$.

Well-posed Optimal Control Problem (3)

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Definition (Optimal control strategy)

$\mathcal{P}_{opt}(S(0), I(0), S^*, I_{\max}; \mathcal{R}(\cdot))$:

$$\min_{\mathcal{R}(\cdot)} \quad J(\mathcal{R}(\cdot)) = \int_0^T \overline{\mathcal{R}} - \mathcal{R}(t)dt$$

s.a.

$$\begin{aligned} &\dot{S}(\tau) = -\mathcal{R}(\tau)S(\tau)I(\tau), && \tau \in [0,T], \\ &\dot{I}(\tau) = \mathcal{R}(\tau)S(\tau)I(\tau) - I(\tau), && \tau \in [0,T], \\ &(S(\tau), I(\tau)) \in \mathcal{X}, \; I(\tau) \leq I_{\max}, && \tau \in [0,T], \\ &S(T) = S^*, \;\; \mathcal{R}(\cdot) \in \Omega_{\mathcal{R}}, \end{aligned} \tag{3}$$

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&(S(\tau), I(\tau)) \in \mathcal{X}, \ I(\tau) \leq I_{\max}, && \tau \in [0, T],\\
&S(T) = S^*, \ \ \mathcal{R}(\cdot) \in \Omega_{\mathcal{R}},
\end{aligned} \tag{3}$$

Theorem 1.4 (Optimal control strategy)

Consider System (1) *with initial conditions* $(S(0), I(0)) = (1 - \epsilon, \epsilon)$, *where* $0 < \epsilon \ll 1$, *and* $\mathcal{R}(0) = \overline{\mathcal{R}}$ *with* $S(0) > S^*$. *Consider a given* $I_{\max}$ *and consider also that* $\mathcal{R}(\cdot) \in \Omega_{\mathcal{R}}$. *Then, the solution of Problem* $\mathcal{P}_{opt}$, *denoted as* $\mathcal{R}^{opt}$, *produces* $(S(\tau), I(\tau))$ *for all* $\tau \geq 0$, *such that* $S_\infty \approx S^*$ *and* $I(\tau) \leq I_{\max}$, *while minimize the SDI, which constitutes the SECO.*

Optimal control strategy

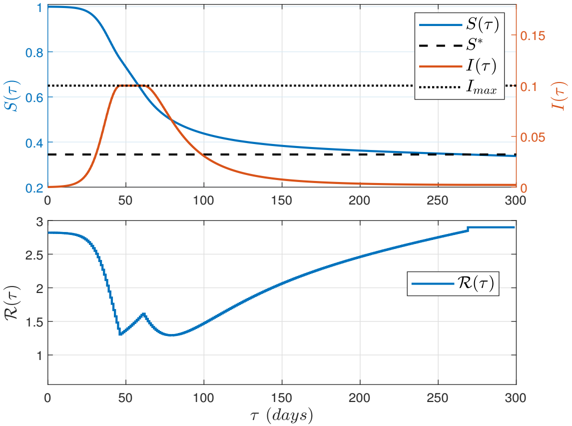

Figure 11: S, I and $\mathcal{R}$ temporal evolution. Optimal control formulation $\mathcal{R}^{opt}$. $S^* = 0.35$ and $I_{\max} = 0.1$.

Optimal control strategy

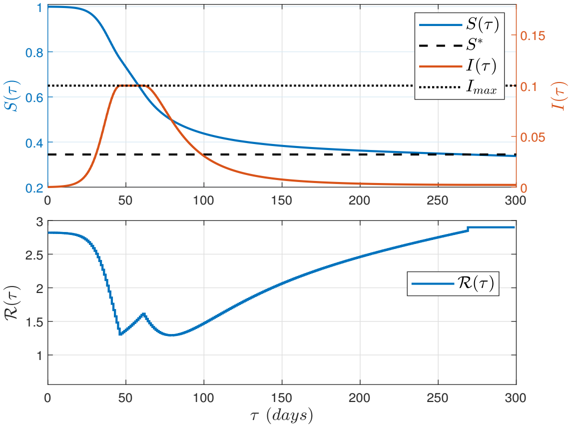

Figure 11: S, I and $\mathcal{R}$ temporal evolution. Optimal control formulation $\mathcal{R}^{opt}$. $S^* = 0.35$ and $I_{\max} = 0.1$.

Performance indexes: EFS$= 0.6725$, IPP$= 0.1$, SDI$= 192.4838$.

well-posedness of Problem $\mathcal{P}_{opt}$

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Let consider the objective function given by:

$$V(\mathcal{R}(\cdot)) = \int_0^T \alpha_I I(t) + \alpha_{\mathcal{R}}(\overline{\mathcal{R}} - \mathcal{R}(t))dt, \tag{4}$$

where α_I and $\alpha_{\mathcal{R}}$ are penalization weights that handle the relative importance of each term. Consider also that constraints $I(\tau) \leq I_{max}$, $\tau \in [0, T]$ and $S(T) = S^*$ are removed from Problem $\mathcal{P}_{opt}$.

Trade-off objective function

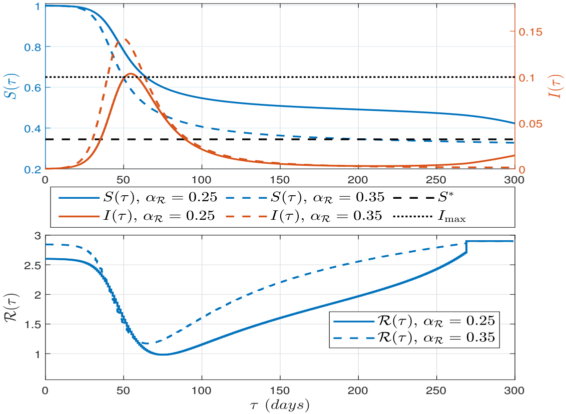

Figure 12: S, I and $\mathcal{R}$ temporal evolution. System (1) with $S^* = 0.35$ and $I_{\max} = 0.1$ when objective function (4) is used for the optimal control problem $\mathcal{P}_{opt}$, and constraints $I(\tau) \leq I_{max}$, $\tau \in [0, T]$ and $S(T) = S^*$ are removed.

Trade-off objective function

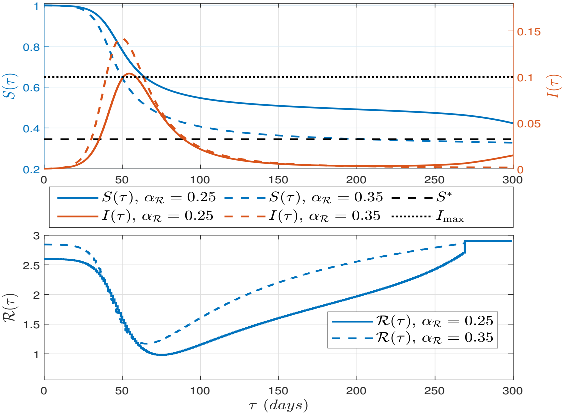

Figure 12: S, I and $\mathcal{R}$ temporal evolution. System (1) with $S^* = 0.35$ and $I_{\max} = 0.1$ when objective function (4) is used for the optimal control problem $\mathcal{P}_{opt}$, and constraints $I(\tau) \leq I_{max}$, $\tau \in [0, T]$ and $S(T) = S^*$ are removed.

There is no combination of α_I and $\alpha_{\mathcal{R}}$ that achieves the ECO.

Conclusions

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- No matter how long or even how strong the SD is, if you stay en the unstable region you will obtain a further wave of infections.

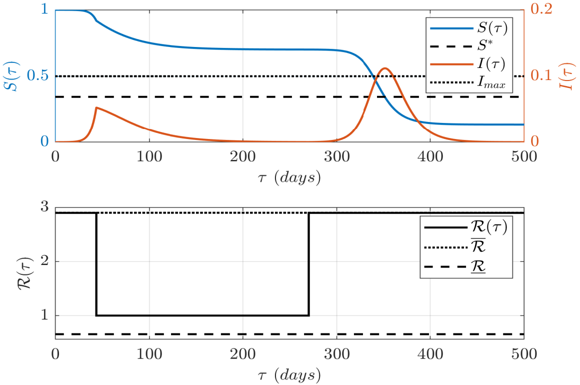

Figure 13: Long term isolation

Conclusions

- This equilibrium set analysis also include more sophisticate and complex models like the SIDARTHE model.

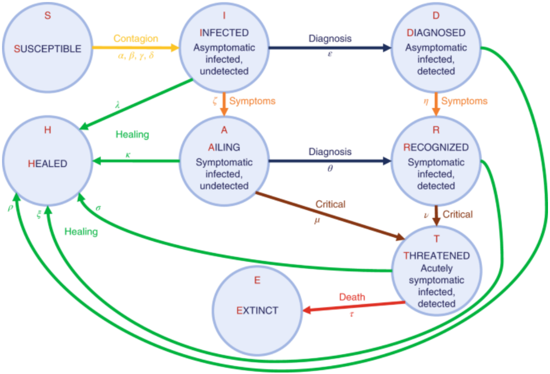

Figure 14: SIDARTHE model (Giordano, G., et al. *Nature Medicine*. 2020).

Perspectives

- Further investigations need to be done in order to define how this equilibrium analysis could change when consider Pharmaceutical Actions: Vaccines are especially important because they could help us to bring to the stable region.

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Perspectives

- Further investigations need to be done in order to define how this equilibrium analysis could change when consider Pharmaceutical Actions: Vaccines are especially important because they could help us to bring to the stable region.
- On the contrary, new strains of the pathogen could bring us out of the stable region, thus creating further waves of infections.
- Complex model networks and population behavior could also play a key role in the temporal evolution of an epidemic.

Thank you
questions?

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[1] Center for Systems Science and Engineering at Johns Hopkins University. COVID-19, cases and deaths data from jhu csse. *Johns Hopkins Coronavirus Resource Center, accessed October 10, 2024*, 2022.

[2] Giulia Giordano et al. Modelling the COVID-19 epidemic and implementation of population-wide interventions in italy. *Nature medicine*, 26(6):855–860, 2020.

[3] William Ogilvy Kermack and Anderson G McKendrick. A contribution to the mathematical theory of epidemics. *Proceedings of the royal society of london. Series A, Containing papers of a mathematical and physical character*, 115(772):700–721, 1927.

[4] Tamás Péni, Balázs Csutak, Gábor Szederkényi, and Gergely Röst. Nonlinear model predictive control with logic constraints for COVID-19 management. *Nonlinear Dynamics*, 102(4):1965–1986, 2020.

[5] JE Sereno, A D'Jorge, EA Hernandez-Vargas, and AH González. Switched NMPC for epidemiological and social-economic control objectives in SIR-type systems. *Annual Reviews in Control*, 56:100901, 2023.

[6] J. E. Sereno, A. Ferramosca, A. H. González, and A. D'Jorge. Impacts of quantifying social distancing measures on MPC performance for SIR-type systems. *Anales del 28° Congreso Argentino de Control Automático 2023*, 2023.

[7] J. E. Sereno Mesa, A. Ferramosca, A. H. González, and A. D'Jorge. Impacts of quantifying social distancing measures on MPC performance for SIR-type systems. *Latin American Applied Research*, 53(4):417–422, 2023.

[8] J. E. Sereno Mesa, A. Ferramosca, A. H. González, and A. D'Jorge. Impacts of quantifying social distancing measures on MPC performance for SIR-type systems. In *2023 Congreso Argentino de Control Automático (AADECA)*, pages 1–6, 2023.