Control of disease and pest dynamics

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Conference Trends in Mathematical Sciences,
Friedrich-Alexander-Universität Erlangen-Nürnberg, June 2024

SEXTOU!

“IT HAS *FRIDAYED*!”

“ES HAT *GEFREITAGT*!”

Scope of this talk

- Present some models for disease and crop pest control and apply different control techniques: classical optimal control, continuous-time and impulsive feedback stabilization, optimal control on networks, etc.

- Comment on difficulties when dealing with control-affine problems and other challenges.

Joint work with:
Y. Dumont (CIRAD, France), L. Moschen (U. Paris-Sorbonne, France)

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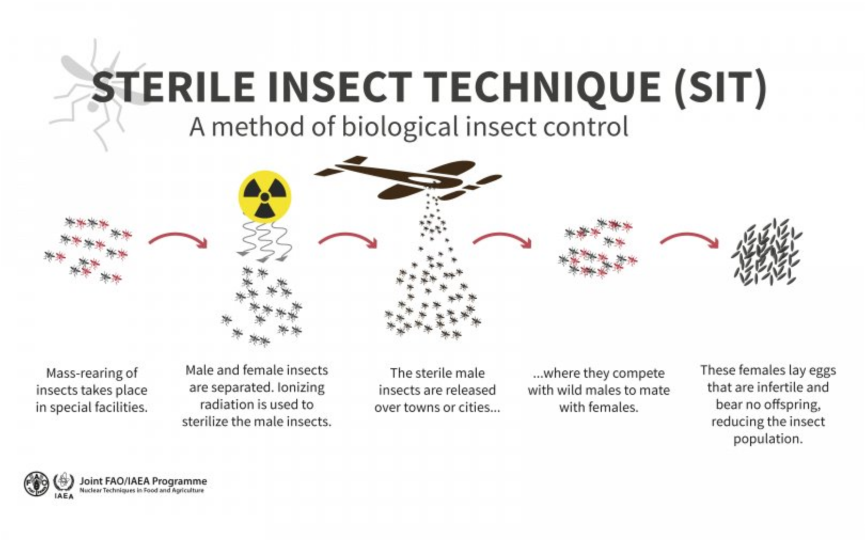
Introduction

Sterile Insect Technique (SIT)

- Use of radiation to generate sterile male adult insects, followed by release of sterile males into the wild
- In the wild, the females that mate with sterile male produce **no or less** offspring
- The aim of the process is reducing the size of the insect population



Source: International Atomic Energy Agency

Some SIT projects around the world

- SIT trials started in the 50s against many species of insects for population reduction or eradication. Some target species: screw-worm fly, *Aedes* mosquito, *Culex* mosquito, *Anopheles* mosquito, Tsetse fly.

- La Réunion, France: SIT against *Aedes albopictus "TIS 2B project"* & SIT against the damaging fruit fly *Bactrocera dorsalis* project *"GEMDOTIS"*.

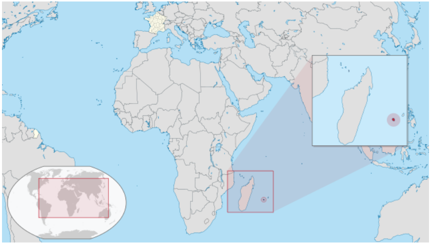


Figure: La Réunion Island

Some considerations

On SIT:

- In general, **high radiation** is required to achieve **full sterility**
- **High radiation has an impact in competitiveness/fitness** of the irradiated males, that have to compete against wild males
- **Lower radiation** has a reduced impact in fitness, but may generate **partially fertile males**

Goal of this work:

- Propose a model for SIT implementation that takes into account partial sterility of to-be-released males
- Evaluate possible SIT release strategies and analytically establish their effectiveness/failure

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The model with sterile insects (SIT)

M, F: male and female wild fertile insects; M_S: sterile male

$$\frac{dM}{dt}(t) = r\rho F(t)\frac{M(t)}{M(t)+\gamma M_S(t)}e^{-\beta(M(t)+F(t))} - \mu_M M(t)$$

$$\frac{dF}{dt}(t) = (1-r)\rho F(t)\frac{M(t)}{M(t)+\gamma M_S(t)}e^{-\beta(M(t)+F(t))} - \mu_F F(t)$$

$$\frac{dM_S}{dt}(t) = \Lambda(t) - \mu_S M_S(t)$$

Parameter	**Description**
$r \in (0,1)$	sex ratio
ρ	mean number of viable eggs by female per day
μ_M, μ_F	death rates
β	characteristic of the competition effect per individual
μ_S	death rate for sterile insects: $\mu_S \geq \mu_M$
$\gamma \in (0,1]$	competitiveness index of sterile male mosquitoes
$\Lambda(t)$	sterile male release rate

The model with SIT and ϵ-residual fertility

M, F: male and female wild fertile insects; M_S: sterile male

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\begin{aligned}
\frac{dM}{dt} &= r\rho F \frac{M + \epsilon\gamma M_S}{M + \gamma M_S} e^{-\beta(M+F)} - \mu_M M \\
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\frac{dM_S}{dt} &= \Lambda - \mu_S M_S
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Parameter	Description
ϵ	residual fertility

Outline

Time continuous closed-loop strategies

Proposition (Continuous-time nonlinear feedback)

Let $\theta > 0$ *be such that*

$$\theta + \epsilon < \mathcal{N}_F^{-1}.$$

If M_S *satisfies*

$$M_S(t) \geq \kappa\big(M(t) + F(t)\big)M(t),$$

where

$$\kappa(x) := \frac{1}{\gamma}\frac{e^{-\beta x} - (\mathcal{N}_F^{-1} - \theta)}{(\mathcal{N}_F^{-1} - \theta) - \epsilon e^{-\beta x}},$$

then every solution of the closed-loop system for (M, F) *converges exponentially to* $(0, 0)$*; and* F *approaches 0 with rate* $(1 - r)\rho\theta$*.*

Impulsive closed-loop strategies

Theorem

Let $\theta > 0$ *be such that*

$$\theta + \epsilon < \mathcal{N}_F^{-1}.$$

Choose release quantities Λ_n *per unit time satisfying*

$$\tau\Lambda_n \geq \max\left\{\kappa_{imp}\left(M(n\tau) + F(n\tau)\right) - M_S(n\tau), 0\right\} \quad \text{for all } n \in \mathbb{N},$$

where κ_{imp} *is a nonlinear function of* $M(n\tau)$ *and* $F(n\tau)$*.*

Then, every solution of the system (M, F) *with* **releases**

$$\tau\Lambda_n = M_S(n\tau^+) - M_S(n\tau),$$

converges exponentially to $(0, 0)$*, with decay rate proportional to* θ *(decay rate =* $(1-r)\rho\theta$*). Additionally,* $\sum_{n\in\mathbb{N}} \Lambda_n < +\infty$*.*

We extended previous result for: **releases at** $t = n\tau$, and **measurements at** $t = np\tau$, for some fixed p.

Impulsive closed-loop strategies

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Choose release quantities Λ_n *per unit time satisfying*

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Aedes Albopictus parameters

Par.	Value	Description
ρ	6.66	Number of viable eggs a female can deposit per day
r	0.5	$r:(1-r)$ expresses the primary sex ratio among offsprings
σ	0.05	Regulates the larvae development into adults under density dependence and larval competition
K	165.21	Carrying capacity in the rainy season (per hectare)
μ_M	1/13	Mean mortality rate of wild adult male mosquitoes
μ_F	1/15	Mean mortality rate of wild adult female mosquitoes
μ_S	1/8.5	Mean mortality rate of sterile adult male mosquitoes
γ	0.91	Competitiveness index of sterile male mosquitoes

Then $\mathcal{N}_F \approx 49.95, \quad \mathcal{N}_M \approx 43.29.$

We need $\epsilon < \mathcal{N}_F^{-1}$, then $\epsilon < 2\%$

The equilibrium $E^* = (M^*, F^*)$ verifies $M^* = 6,000$ and $F^* \approx 6,923$ individuals per hectare.

Impulsive feedback for different values of the residual fertility

$\tau = 1$ (day)

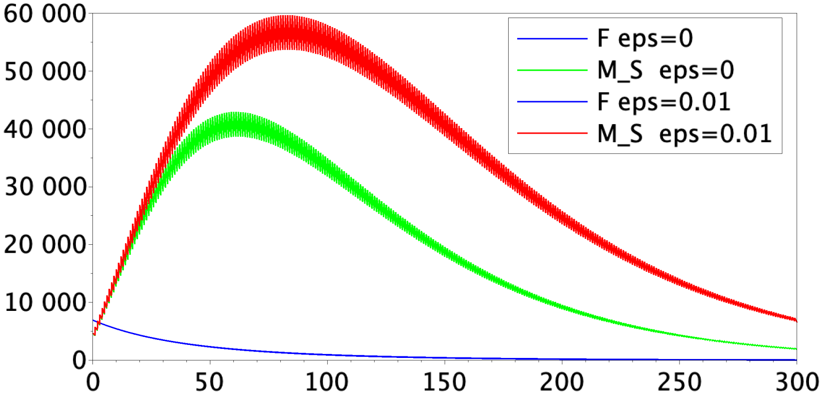

Figure: Comparison for $\varepsilon = 0$ vs. $\varepsilon = 0.01$

Long-term strategies for practical implementation

For periodic constant impulsive releases

$$M_S(n\tau^+) = M_S(n\tau) + \tau\Lambda,$$

gives periodic solution $M_{S,\mathrm{per}}$. The resulting impulsive system is bounded from above by the autonomous system

$$\frac{dM}{dt} = r\rho\frac{F(M+\epsilon\gamma M_{S,\Lambda})}{M+\gamma M_{S,\Lambda}}e^{-\beta F} - \mu_M M,$$
$$\frac{dF}{dt} = (1-r)\rho\frac{F(M+\epsilon\gamma M_{S,\Lambda})}{M+\gamma M_{S,\Lambda}}e^{-\beta F} - \mu_F F.$$

where $M_{s,\Lambda} > 0$ is a lower bound of $M_{S,\mathrm{per}}(t)$.

For $0 < \Lambda < \Lambda^{\varepsilon}_{\mathrm{crit}}$, the system above possesses the ordered equilibria equilibria: $0 < \mathbf{E_1} < \mathbf{E_2}$.

It is easy to check that latter system is **monotone cooperative** in the subset

$$[\mathbf{0}, \mathbf{E}_1[:= \{(F,M) \in I\!R^2_+ : \mathbf{0} < (F,M) < \mathbf{E}_1\}.$$

Associated optimal control problem

$u(t)$: release rate of sterile insects

$$\min \int_0^T u(t)dt$$

$$\frac{dM}{dt} = r\rho \frac{F(M + \epsilon\gamma M_s)}{M + \gamma M_s} e^{-\beta(M+F)} - \mu_M M,$$

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$$\frac{dM_S}{dt} = -\mu_S M_S(t) + u(t)$$

$$M(0) = M_0, \quad F(0) = F_0, \quad M_S(0) = 0,$$

$$M(T) \leq M_T, \quad F(T) \leq F_T, \quad \text{desired final values}$$

with admissible controls $u\colon [0,T] \to \mathbb{R}_0^+$ measurable.

Optimal vs. closed-loop impulsive strategies

Set $p = 1, \tau = 6$, which means releases and measurements every 6 days.

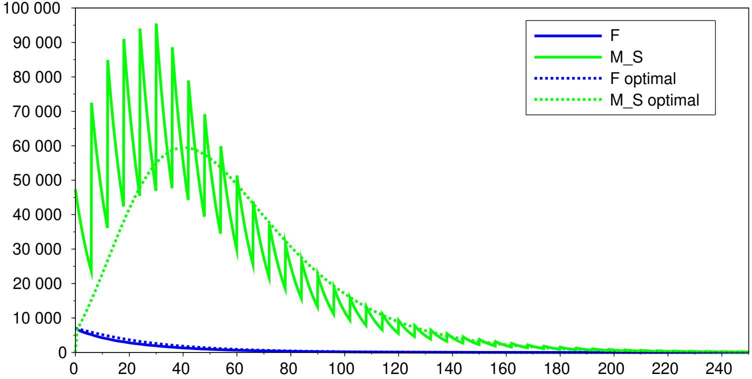

Figure: Female and sterile male

Optimal vs. closed-loop impulsive costs

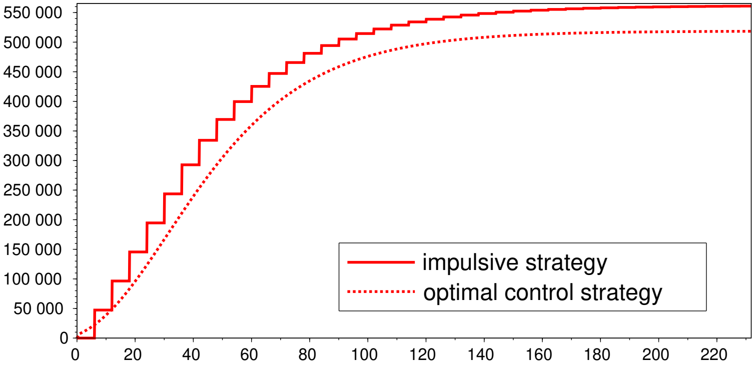

Figure: Cost (accumulated sterile insects)

Outline

Concluding remarks for the SIT problem

What we did:

- Proposed impulsive strategies in feedback form that converge analytically to 0.
- Constructed long-term strategies based on monotone properties of the system.
- Compared (numerically) to optimal cost.

Ongoing and future work:

- Add cost to each intervention: this gives a mixed continuous-discrete optimal control problem.
- Optimize impulsive control.
- Extend theoretical resultados for control-affine problems in general formulations with vector control and constraints: feedback formula for singular control, sufficient optimality conditions, others.

Outline

Metropolitan region

Metropolitan region: a central city and its surrounding areas, tightly linked by economic and social activities, forming a densely populated area.

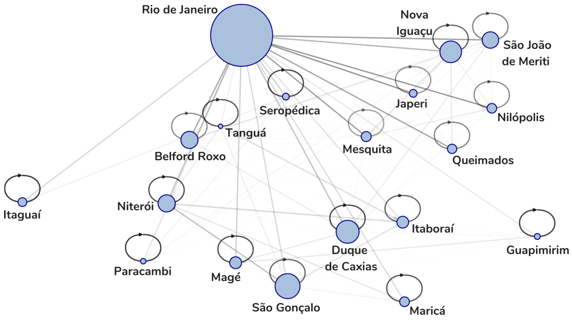

Figure: Graph representation of the Rio de Janeiro metropolitan region.

In Rio de Janeiro metropolitan area (13 million), over **2 million work in a different city than they live**. Most of them commute to the capital.

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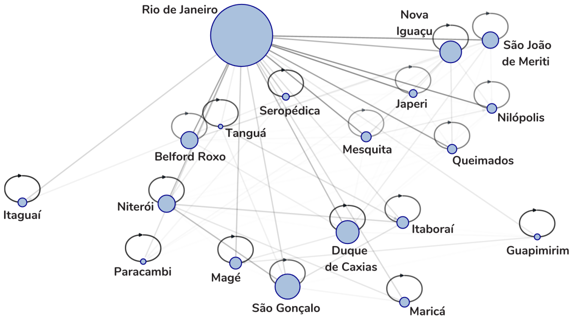

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Our research question and tools

- Which are efficient (or optimal) vaccination strategies in metropolitan regions?
- How and when should vaccines be distributed among cities?
- Should the capital receive vaccines earlier and in larger quantities?

Our tools:

- SIR model on a general network of interconnected cities,
- expression for the *basic reproduction number* $\mathcal{R}_0$;
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Modelling commuting [1]

The effective population in i during working hours is $P_i^{\text{eff}} = \sum_{j=1}^{K} p_{ji} n_j$.

The proportion of infectious people in i is $I_i^{\text{eff}} = \frac{1}{P_i^{\text{eff}}} \sum_{j=1}^{K} p_{ji} I_j n_j$

$\alpha \in [0, 1]$: night-time proportion

For each city $i = 1, \ldots, K$,

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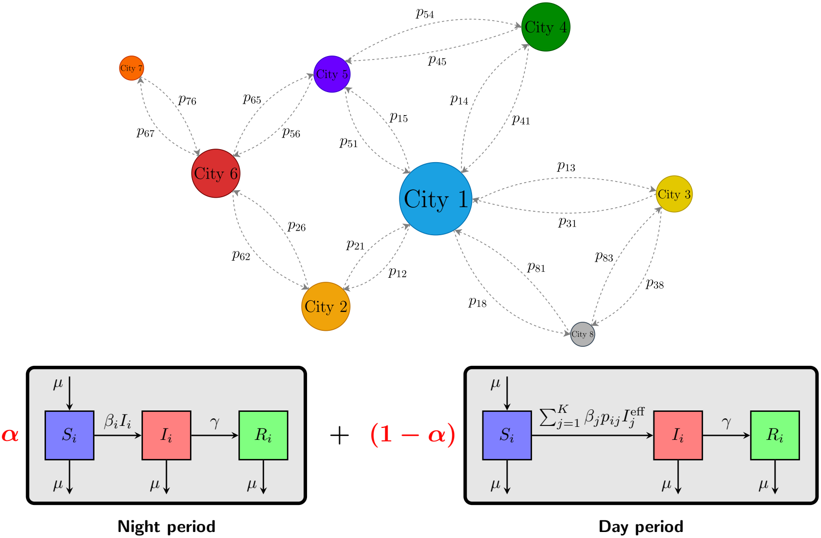

Outline

Basic reproduction number $\mathcal{R}_0$

$\mathcal{R}_0$: epidemic threshold

We consider the parameters that correspond to the **case of isolated cities:**

$$\mathcal{R}_0^i = \frac{\beta_i}{\gamma + \mu}, \qquad i = 1, \ldots, K.$$

Starting from the calculation approach in [Van den Driessche & Watmough (2002)][2], we get:

Theorem (Bounds for $\mathcal{R}_0$)

One has

$$\min_{1 \le i \le K} \left(\alpha \mathcal{R}_0^i + (1-\alpha) \sum_{k=1}^{K} p_{ik} \mathcal{R}_0^k \right) \le \mathcal{R}_0 \le \max_{1 \le i \le K} \left(\alpha \mathcal{R}_0^i + (1-\alpha) \sum_{k=1}^{K} p_{ik} \mathcal{R}_0^k \right).$$

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Simulations for $\mathcal{R}_0$ bounds

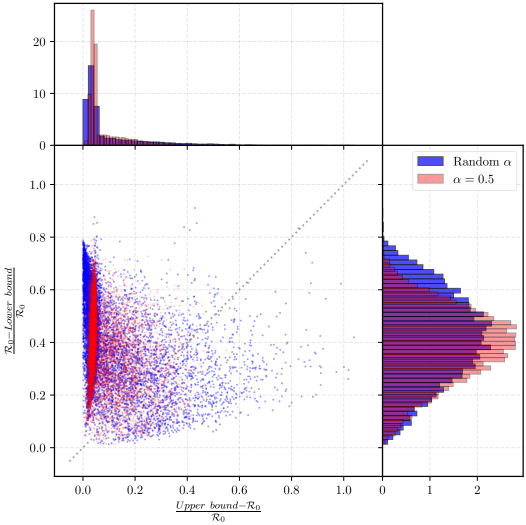

Figure: Analysis of $\mathcal{R}_0$ bounds using $10,000$ random samples for parameters β, P and α (in blue) in the case of 5 cities. Red is for $\alpha = 0.5$.

Outline

Introducing vaccination

Population of city i is vaccinated at a rate u_i, leading to

$$S_i' = \mu - \alpha\beta_i S_i I_i - (1-\alpha) S_i \sum_{j=1}^{K} \beta_j p_{ij} I_j^{\text{eff}} - u_i S_i - \mu S_i$$

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$$R_i' = \gamma I_i + u_i S_i - \mu R_i$$

$$V_i' = u_i S_i$$

$V_i(t)$: vaccinated until time t

Setting:

$$\mathcal{R}_{0,i}^{\text{vac}} := \frac{\mu}{\mu + u_i} \frac{\beta}{\gamma + \mu},$$

we get analogous inequalities for $\mathcal{R}_0^{\text{vac}}$:

$$\min_i \left(\alpha \mathcal{R}_{0,i}^{\text{vac}} + (1-\alpha) \sum_{k=1}^{K} p_{ik} \mathcal{R}_{0,k}^{\text{vac}} \right) \le \mathcal{R}_0^{\text{vac}} \le \max_i \left(\alpha \mathcal{R}_{0,i}^{\text{vac}} + (1-\alpha) \sum_{k=1}^{K} p_{ik} \mathcal{R}_{0,k}^{\text{vac}}, \right).$$

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Impact of vaccination rates on $\mathcal{R}_0^{\mathrm{vac}}$

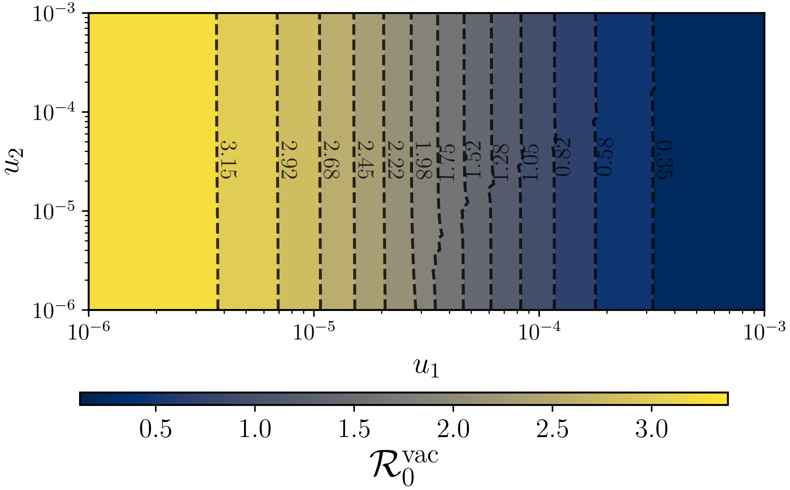

Figure: $\mathcal{R}_0^{\mathrm{vac}}$ as a function of **constant** vaccination rates

Outline

The Optimal Control Problem

Dynamics

$$S_i' = \mu - \alpha\beta_i S_i I_i - (1-\alpha) S_i \sum_{j=1}^{K} \beta_j p_{ij} I_j^{\text{eff}} - u_i S_i - \mu S_i$$

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$$R_i' = \gamma I_i + u_i S_i - \mu R_i$$

$$V_i' = u_i S_i$$

Constraints

- Vaccine availability *(shipments):* $\sum_{i=1}^{K} V_i(t) n_i \leq D(t)$.
- Vaccination capacity: $u_i(t) S_i(t) \leq v_i^{\max}$.
- $u_i(t) \geq 0$, a.e. $t \in [0, T]$.

Cost

$$\min c_v \sum_{i=1}^{K} n_i V_i(T) + c_h \int_0^T r_h n_i I_i \, dt$$

The Optimal Control Problem in abstract form

$$
\begin{aligned}
&\min \int_0^T f_0(x(t))\,dt + \Psi(x(T)),\\
\text{s.t.}\quad & x'(t) = f(x(t)) + h(x(t))u(t), \quad \text{a.e. } t \in [0,T]\\
& g(t, x(t)) \le 0, \quad \text{for all } t \in [0,T]\\
& m(x(t), u(t)) \le 0, \quad \text{a.e. } t \in [0,T]\\
& u(t) \in U, \quad \text{a.e. } t \in [0,T]\\
& x(0) = x_0.
\end{aligned}
$$

Theoretical results for the Optimal Control Problem

- The optimal control problem has a global minimum: derived from classical results from [Cesari, 1965][3]

- Optimality conditions of first order (in the form of a Pontryagin Maximum Principle): derived from [Boccia et al., 2016][4]

- The optimal solution for $K = 1$ (one city) does not have singular arcs, that is, there is no interval such that

$$0 < u_1^*(t) S_1^*(t) < v_1^{\max}.$$

Some progress for the case $K > 1$. Numerically, the assertion holds for the general case, this is,

$$u_i^*(t) S_i^*(t) \in \{0, v_i^{\max}\}, \quad \text{for a.e. } t \in [0, T],\ i = 1, \dots, K.$$

[3] Cesari, L. "Existence theorems for optimal solutions in Pontryagin and Lagrange problems". J. SIAM Control (1965)

[4] Boccia, A., Pinho, M. D. R. de, and Vinter, R. B. "Optimal control problems with mixed and pure state constraints". SIAM J Control and Optim. (2016)

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Outline

Metropolitan region assumption

The capital is the **largest and most densely populated city, people from the surroundings, either work in the capital or in their own cities:**

$$\beta_1 > \max_{i=2,\dots,K} \beta_i, \quad N_1 > \max_{i=2,\dots,K} N_i.$$

Transition matrix structure:

$$P = \begin{bmatrix} 1 & 0 & 0 & \cdots & 0 \\ p_{21} & p_{22} & 0 & \cdots & 0 \\ p_{31} & 0 & p_{33} & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ p_{K1} & 0 & 0 & \cdots & p_{KK} \end{bmatrix}$$

Numerical simulations are done under this assumption or an approximation of it.

Optimal control: 2 cities

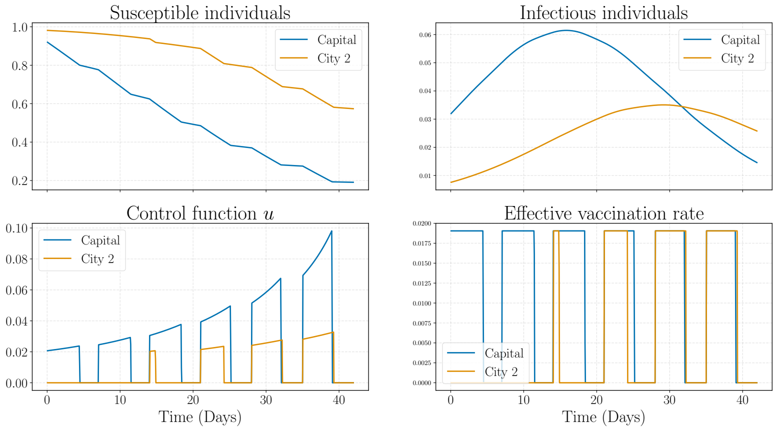

Figure: **Optimal trajectories and control for two-city interaction**: The fourth subplot illustrates the variables $u_i(t)S_i(t) \in \{0, v_i^{\max}\}$, $i = 1, 2$. The settings for this experiment are: $\beta = (0.25, 0.18)$, $\alpha = 0.64$, $p_{21} = 0.2$, $n_1 = 10^6$ and $n_2 = 10^5$.

Optimal control: 5 cities

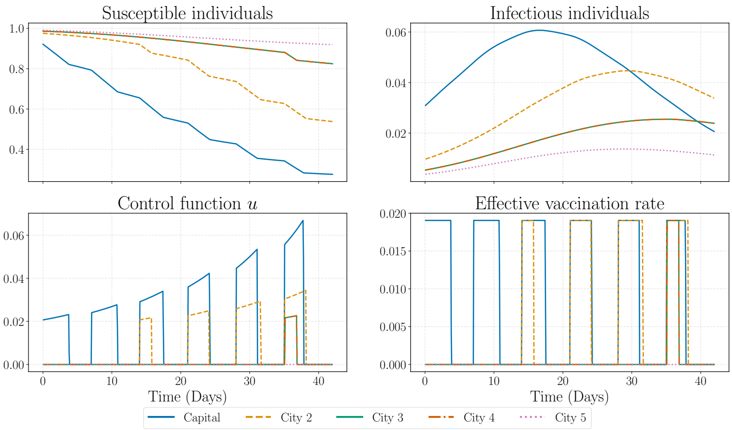

Figure: **Optimal trajectories and control functions for 5 cities**
$\beta = (0.4, 0.3, 0.15, 0.15, 0.1)$, $\alpha = 0.64$, $p_{k1} = 0.2$ for each city $k > 1$, and $n = 10^5(50, 10, 10, 1, 1)$ is the vector of population sizes.

Outline

Transition matrix of the Rio de Janeiro metropolitan area

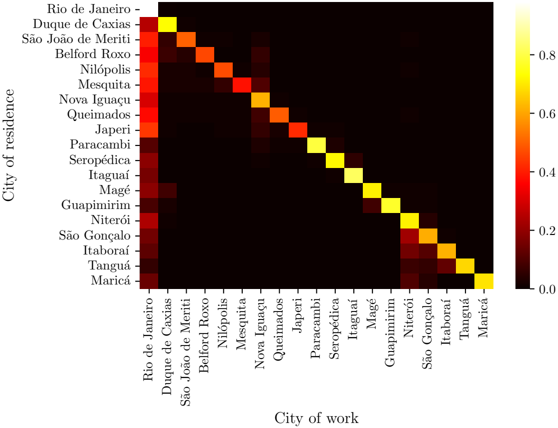

Figure: Heatmap showing the matrix P in the case of Rio de Janeiro metropolitan area

Fonte: SEBRAE. Mobilidade urbana e mercado de trabalho no Rio de Janeiro

Vaccination strategies comparison

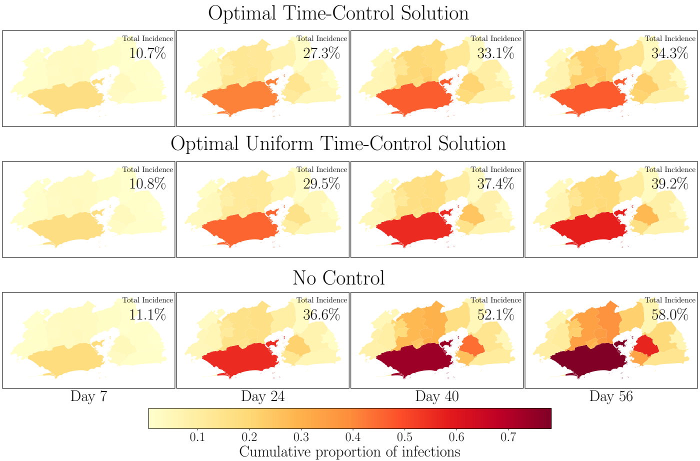

Figure: **Disease Progression in the Rio de Janeiro Metropolitan Area**
The transmission rate β is randomly chosen between 0 and 0.3, and sorted by city population size.

Outline

Optimal vaccination: comments and perspectives

What we did:

- Studied a model for vaccination in a metropolitan region
- Obtained sharp inequalities for $\mathcal{R}_0$
- Proved properties of the associated optimal control problem, which is control-affine (no quadratic cost was considered)
- Theoretical results and numerical tests showed that the epidemic is governed by the capital city (the biggest and most densely populated city)

Ongoing and future work:

- Prove non-existence of singular arcs for the general case of $N > 1$ cities.
- Generalizations of the model: infections in transportation, age-structure or other risk groups, various type of vaccines and doses, etc.

Outline

Other disease/pest control problems

Malaria control through breeding site removal:
Antunes, Aronna & Codeço. *Modeling and control of malaria dynamics in fish farming regions.* SIAM J. Applied Dynam. Systems (2023).
Joint project with FIOCRUZ (Oswaldo Cruz Foundation, Brazil)

Dengue fever control through *Wolbachia* bacteria:
Bliman, Aronna *et al.* *Ensuring successful introduction of Wolbachia in natural populations of Aedes aegypti by means of feedback control.* J. Math. Biology (2018).

Crop pest control through parasitoids (for sugarcane plantation):
work in progress. Joint project with EMBRAPA (Brazilian Agricultural Research Corporation) and Universidade Federal de Pelotas (Brazil).

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Outline

Conclusion and perspectives

• We proposed and studied models for disease and pest control involving different control techniques: feedback stabilization, impulsive feedback stabilization and optimal control.

• In many situations in disease/pest control (and more generally, in many biological systems), it comes natural to model by an optimal control problem with control-affine dynamics and several type of constraints: on the control, on the state and control-state mixed.

Many theoretical questions remain open when it comes to control-affine systems: sufficient optimality conditions, convergence of algorithms, (structure) stability of optimal solutions, etc.

• Work in progress on dealing with uncertainty in the parameters, that may have a significant impact in practice and opens to challenging theoretical questions. This include online parameter estimation and control.

• Work in progress on dealing with impulsive optimal control problems.

Some references

Vaccination part:

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Sterile Insect Technique (SIT) part:

- Aronna, M.S. & Dumont, Y. *"On nonlinear pest/vector control via the Sterile Insect Technique: impact of residual fertility"*. Bull. Mathem. Biol. 2020.
- Bliman, P.A., Cardona-Salgado, D., Dumont, Y., Vasilieva, O. *"Implementation of Control Strategies for Sterile Insect Techniques".* Mathem. Biosc., 2019.

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- Antunes, F. J., Aronna, M. S., & Codeço, C. T. *'Modeling and control of malaria dynamics in fish farming regions".* SIAM J. Applied Dynam. Syst., (2023).
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Universidad de los Andes & Quantil - Colombia

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MORE INFORMATION AND CALL FOR SESSIONS COMING SOON

THANK YOU FOR YOUR ATTENTION!

More talks, slides and references at `sites.google.com/view/aronna`