# Convex Optimization of the Basic Reproduction Number

Francesco Bullo

Center for Control,
Dynamical Systems & Computation

University of California at Santa Barbara

http://motion.me.ucsb.edu

Tutorial Session: Modeling, Estimation, and Control of COVID-19
Modeling, Estimation and Control Conference (MECC 2021)
Online, Oct 24-27, 2021

Kevin D. Smith
PhD student, Electrican & Computer Engineering
UC Santa Barbara

- K. D. Smith and F. Bullo. Convex optimization of the basic reproduction number. *IEEE Transactions on Automatic Control*, October 2021. URL: https://arxiv.org/abs/2109.07643

# Basic Reproduction Number

*Basic Reproduction Number* ($R_0$): "Typical" number of secondary infections that arise in a completely susceptible population.

| Disease | Outbreak | $R_0$ |
|---|---|---|
| Spanish Flu | Spring 1918 | 1.5 |
| Spanish Flu | Fall 1918 | 3.8 |
| H1N1 | 2009, S. Africa | 1.3 |
| Ebola | 2014, Guinea | 1.5 |
| COVID-19 | 2020 | $\sim 3$ |
| COVID-19 ($\delta$) | 2021 | 5–9 |

U.S. | THE NUMBERS

**The Numerical Language of Covid-19: A Primer**

Understanding terms like R0, R and herd immunity is vital to understanding spread of pandemic

*The Wall Street Journal, 3/15/20*

THE INTERPRETER

***R0, the Messy Metric That May Soon Shape Our Lives, Explained***

'R-naught' represents the number of new infections estimated to stem from a single case. You may be hearing a lot about this.

*The New York Times, 4/23/20*

# Outline

1. Mathematical definition of $R_0$
2. Useful new characterization of $R_0$
3. Optimal resource allocation with $R_0$
4. Santa Barbara County Case Study

# Basic Reproduction Number

Dynamics of infected ($x \in \mathbb{R}^n_{\geq 0}$) and non-infected ($y \in \mathbb{R}^m_{\geq 0}$) compartments:

$$\dot{x} = \underbrace{f(x, y)}_{\text{new infections}} + \underbrace{v(x, y)}_{\text{(re)moved infections}}$$

$$\dot{y} = g(x, y)$$

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, 1990.

doi:10.1007/BF00178324

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$\longrightarrow$

Infected subsystem decouples from $y$ when linearized about equilibrium $(\mathbb{0}_n, y^*)$:

$$\dot{x} \approx \Bigg( \underbrace{F}_{\geq 0} + \underbrace{V}_{\text{Hurwitz + Metzler}} \Bigg) x$$

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Estimate secondary infections by

$$x_1 = \int_0^\infty F e^{Vt} x_0 \, dt = \underbrace{-FV^{-1}}_{NGM} x_0$$

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**Definition (Basic Reproduction Number)**

$$R_0 = \rho(FV^{-1})$$

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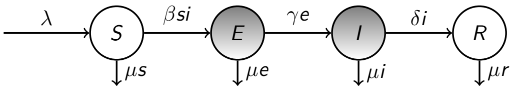
# Example: SEIR Model




Infected subsystem:

$$\begin{bmatrix} \dot{e} \\ \dot{i} \end{bmatrix} = \begin{bmatrix} \underbrace{\beta s i}_{f} - \underbrace{(\gamma+\mu)e}_{v} \\ \underbrace{\gamma e - (\delta+\mu) i}_{v} \end{bmatrix} \approx \begin{bmatrix} -(\gamma+\mu) & \beta s^* \\ \gamma & -(\delta+\mu) \end{bmatrix} \begin{bmatrix} e \\ i \end{bmatrix}$$

Computation of $R_0$:

$$F = \begin{bmatrix} 0 & \beta s^* \\ 0 & 0 \end{bmatrix}, \qquad V = \begin{bmatrix} -(\gamma+\mu) & 0 \\ \gamma & -(\delta+\mu) \end{bmatrix}, \qquad R_0 = \rho(FV^{-1}) = \frac{\beta\gamma s^*}{(\gamma+\mu)(\delta+\mu)}$$

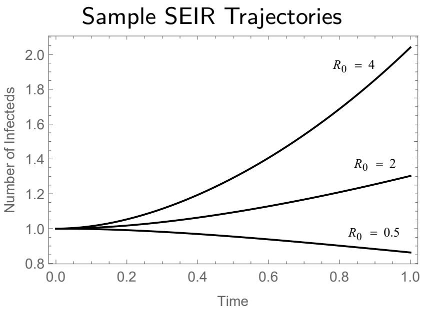
# Basic Reproduction Number

**Theorem (Epidemic Threshold)**

1. *The equilibrium* $(\mathbb{0}_n, y^*)$ *is locally asymptotically stable*
2. *the spectral abscissa of* $F + V$ *is negative*
3. $R_0 < 1$

P. Van den Driessche and J. Watmough. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 180(1):29–48, 2002.

doi:10.1016/S0025-5564(02)00108-6



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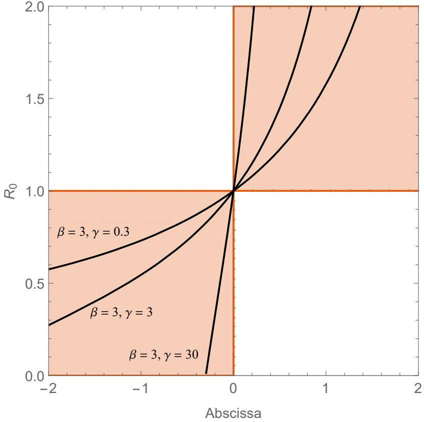
Realizable Absicssa, $R_0$ Pairs in the SEIR Model



# Basic Reproduction Number

$R_0$ is the solution to a convex optimization problem:

**Theorem (GP Characterization of $R_0$)**

*Decompose $V = V_{od} - V_d$ into its off-diagonal and diagonal part, respectively. Then $R_0$ is the infimum of the following geometric program:*

$$\begin{aligned} \textit{minimize}: &\quad r \\ \textit{variables}: &\quad r > 0,\ w > \mathbb{0}_n \\ \textit{subject to}: &\quad (F + rV_{od})w \leq rV_d w \end{aligned}$$

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# Basic Reproduction Number

- $R_0 =$ "typical" number of secondary infections
- Widely-known parameter reflecting epidemic spreading rate
- Distinct from the spectral abscissa
- Equivalent mathematical definitions:

$$R_0 = \rho(FV^{-1}) = \underbrace{\inf_{r>0, w>\mathbb{0}_n} \{r : (F + rV_{od})w \leq rV_d w\}}_{\text{Geometric Program}}$$

# Resource Allocation

**Problem**: allocate limited resources $\theta \geq \mathbb{0}_k$, including...

- distribution of limited pharmaceuticals: vaccines, antivirals
- NPI: lockdowns, closures, distancing measures with social / economic impact

Choose $\theta$ to balance epidemic mitigation against cost $c(\theta)$

**Typical approach**: Minimize spectral abscissa $\alpha(F + V)$


- C. Nowzari, V. M. Preciado, and G. J. Pappas. Optimal resource allocation for control of networked epidemic models.
  *IEEE Transactions on Control of Network Systems*, 4:159–169, 2017.
  doi:10.1109/TCNS.2015.2482221
- A. R. Hota, J. Godbole, and P. E. Paré. A closed-loop framework for inference, prediction, and control of SIR epidemics on networks.
  *IEEE Transactions on Network Science and Engineering*, 8(3):2262–2278, 2021.
  doi:10.1109/TNSE.2021.3085866

# Resource Allocation

**Proposal**: minimize $R_0$ instead of the spectral abscissa

- easier objective to communicate with the public
- reflects spreading rate more directly

Can our geometric program characterization of $R_0$ be extended into a resource allocation program?

# Optimizing $R_0$

Intuitive GP transcriptions for resource allocation problems:

**Budget-Constrained Allocation**

$$\begin{aligned} \text{minimize}: &\quad R_0(\theta) \\ \text{variables}: &\quad \theta \in \Theta \\ \text{subject to}: &\quad c(\theta) \le c_{\max} \end{aligned}$$

$\overset{?}{\Longleftrightarrow}$

**GP Formulation**

$$\begin{aligned} \text{minimize}: &\quad r \\ \text{variables}: &\quad r > 0,\ w > \mathbb{0}_n,\ \theta \in \Theta \\ \text{subject to}: &\quad (F(\theta) + rV_{od}(\theta))w \le rV_d(\theta)w \\ &\quad c(\theta) \le c_{\max} \end{aligned}$$

**$R_0$-Constrained Allocation**

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$\Longleftrightarrow$ $\epsilon \to 0$

**GP Formulation**

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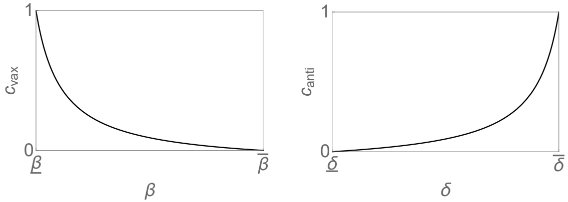
# Santa Barbara County COVID-19 Case Study

- **Cost-constrained allocation** of:
  vaccines (reduce local transmission rates $\beta_i$)
  antivirals (increase local recovery rates $\delta_i$)
- Cost models:

$$c(\beta,\delta) = \sum_{i=1}^{N} c_{\mathrm{vax,i}}(\beta_i) + c_{\mathrm{anti,i}}(\delta_i)$$

$$c_{\mathrm{vax,i}}(\beta_i) = \frac{\beta_i^{-1} - \overline{\beta}_i^{-1}}{\underline{\beta}_i^{-1} - \overline{\beta}_i^{-1}}$$

$$c_{\mathrm{anti,i}}(\delta_i) = \frac{(\tilde{\delta}_i - \delta_i)^{-1} - (\tilde{\delta}_i - \underline{\delta}_i)^{-1}}{(\tilde{\delta}_i - \overline{\delta}_i)^{-1} - (\tilde{\delta}_i - \underline{\delta}_i)^{-1}}$$

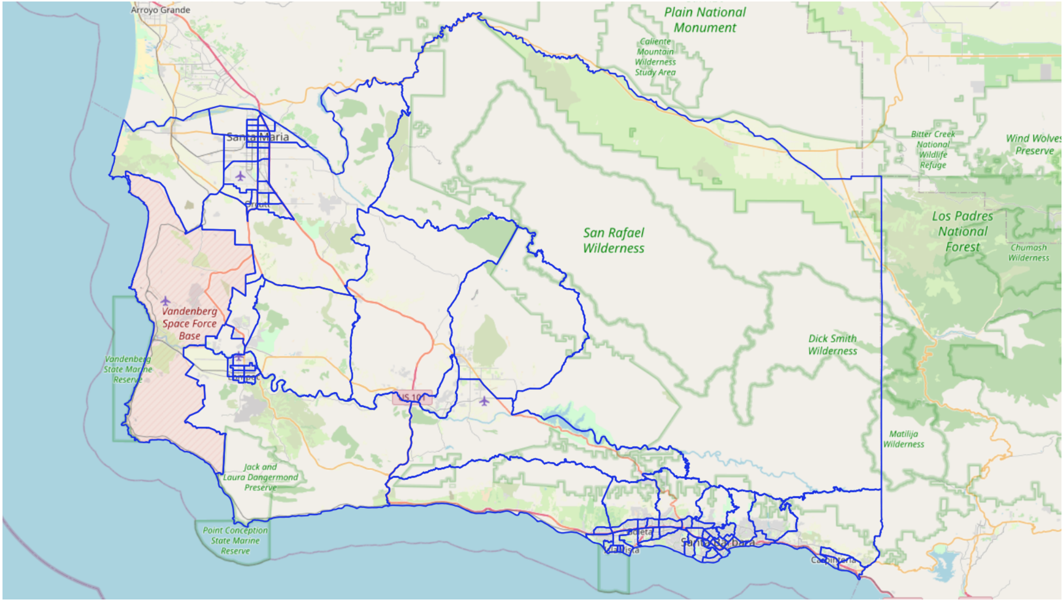




V. M. Preciado, M. Zargham, C. Enyioha, A. Jadbabaie, and G. J. Pappas. Optimal resource allocation for network protection against spreading processes.
*IEEE Transactions on Control of Network Systems*, 1(1):99–108, 2014.

doi:10.1109/TCNS.2014.2310911

# 87 census tracts in Santa Barbara County

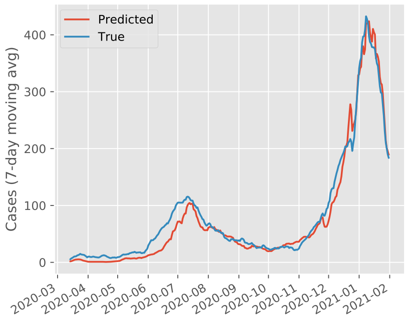


# Santa Barbara County COVID-19 Case Study

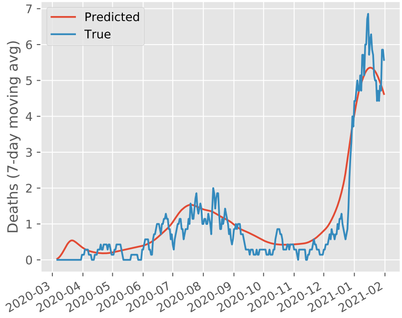
Model:

- 87-group SEIR model, with additional "external group" to model forcing from contact with people outside of SB county
- Time-varying inter-group contact rates estimated from SafeGraph cell phone mobility data

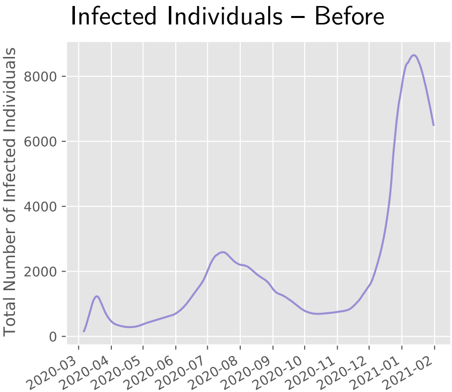
County-Wide Detected Cases

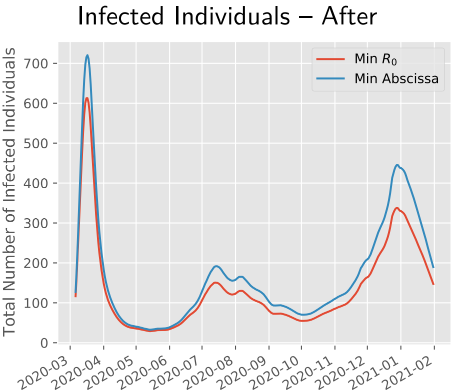



County-Wide Deaths



# Allocation Results




$R_0$-minimizing allocation leads to fewer cases than abscissa-minimizing allocation!

# Conclusions

**Summary:**

- $R_0$ useful metric for epidemic resource allocation
- Compared to spectral abscissa, $R_0$ easier to communicate, more directly reflects spreading rate
- Efficient resource allocation to minimize or constrain $R_0$ via geometric programming

**Future directions:**

- Robust resource allocation with uncertain or dynamic model parameters
- Rigorous performance guarantees when applied to nonlinear model

# Additional Slides

# Geometric Programming

- *Monomial*: Function $f : \mathbb{R}^n_{>0} \to \mathbb{R}_{>0}$ of form

$$f(x) = \alpha x_1^{\beta_1} x_2^{\beta_2} \cdots x_n^{\beta_n}$$

  where $\alpha > 0$ and $\beta_i \in \mathbb{R}$.
- *Posynomial*: Sum of monomials.
- *Geometric program*: Given posynomials $f_i$, $i = 0, 1, 2, \ldots, m$:

$$\begin{aligned} \text{minimize} : &\quad f_0(x) \\ \text{variables} : &\quad x > \mathbb{0}_n \\ \text{subject to} : &\quad f_i(x) \leq 1, \ \forall i = 1, 2, \ldots, m \end{aligned}$$

- Transformed into convex problem with change of variables $x_i \to e^{y_i}$

# Basic Reproduction Number

## GP Characterization: Proof Outline

- Lemma: if $H$ is Hurwitz and Metzler and $E \geq 0$, then $H + E$ is Hurwitz if and only if $\rho(EH^{-1}) < 1$.
- Lemma: if $M$ is Metzler, then $M$ is Hurwitz if and only if $Mw < \mathbb{0}$ for some $w > 0$.
- Recall $R_0 = \rho(FV^{-1})$. Then:

$$\begin{aligned} R_0 &= \inf_{r>0} \left\{ r : \rho(FV^{-1}) < r \right\} \\ &= \inf_{r>0} \left\{ r : \rho(F(rV)^{-1}) < 1 \right\} \\ &= \inf_{r>0} \{ r : F + rV \text{ is Hurwitz} \} \\ &= \inf_{r>0, w>0} \{ r : (F + rV)w < 0 \} \end{aligned}$$

- Relaxing $<$ to $\leq$ is correct (if $F \neq 0$) but nontrivial to prove.

Multigroup SEIR model with $N = 87$ groups (census tracts):

$$\dot{s}_i = -\beta_i s_i \sum_{j=1}^{N} a_{ij} x_j - \beta_i a_{i0} s_i u \qquad \dot{e}_i = \beta_i s_i \sum_{j=1}^{N} a_{ij} x_j + \beta_i a_{i0} s_i u - \gamma_i e_i$$

$$\dot{x}_i = \gamma_i e_i - \delta_i x_i \qquad \dot{r}_i = \delta_i x_i$$

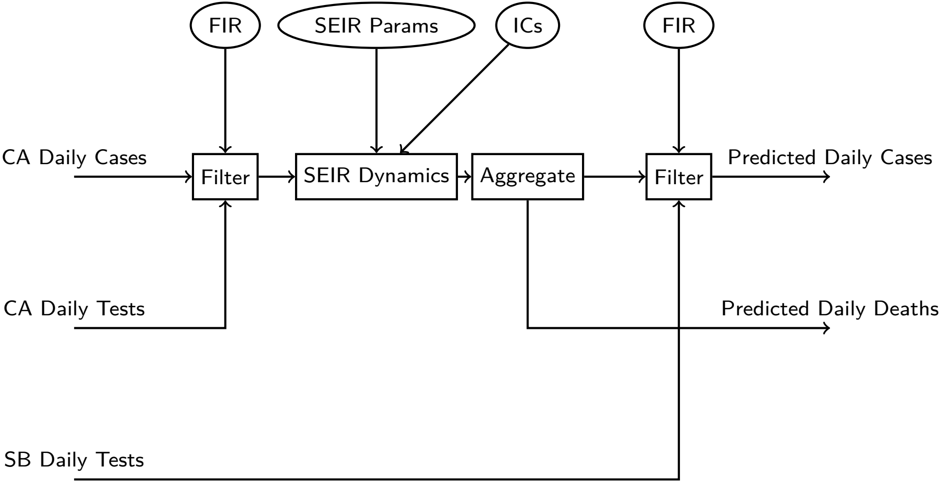
$u(t)$ is estimate of external cases

System Identification:

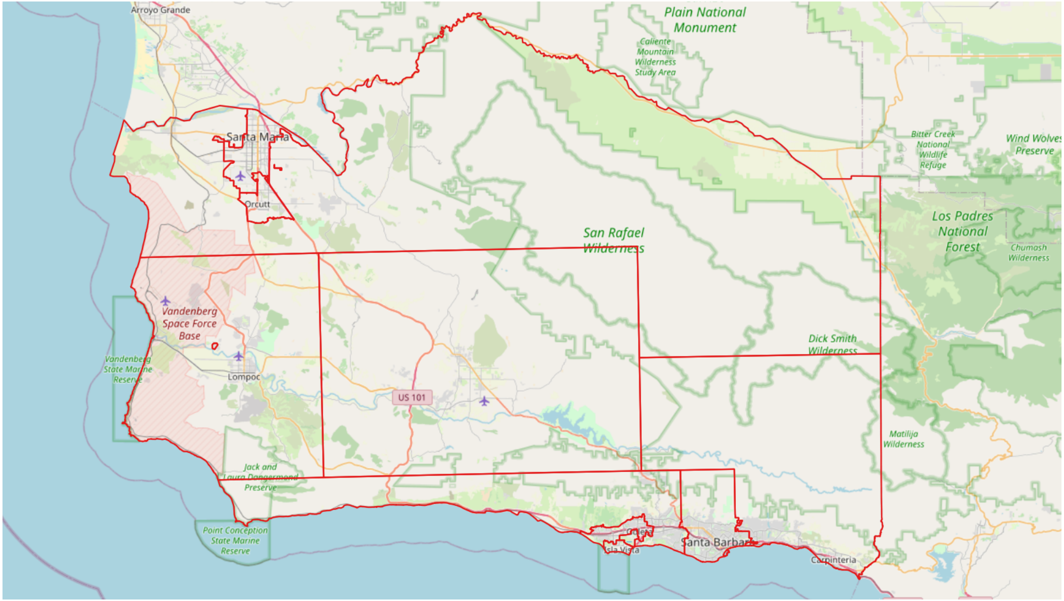
- Time-varying contact rates $a_{ij}(t)$ from cell phone mobility data
- Constant $\beta_i$, $\gamma_i$, $\delta_i$ fit to county data on detected cases + deaths

# Santa Barbara County COVID-19 Case Study

## Learning Architecture



# Results aggregated into 10 reporting areas



# Allocation Results