# How ubiquitous are the reproduction numbers for epidemics processes?

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**STATISTICAL MECHANICS FOR COMPLEXITY**

**A CELEBRATION OF THE 80TH BIRTHDAY OF CONSTANTINO TSALLIS**

**RIO DE JANEIRO, 6 TO 10 NOVEMBER 2023**

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# Café Científico traz Constantino Tsallis a Salvador

8 de novembro de 2013 0 Comentário café científico.ufba

O Café Científico da UFBA traz a Salvador, na próxima sexta-feira, 08 de novembro, o palestrante Constantino Tsallis, pesquisador titular do Centro Brasileiro de Pesquisas Físicas (CBPF), membro da Academia Brasileira de Ciências e líder do Instituto Nacional de Ciência e Tecnologia de Sistemas Complexos. No evento, que será realizado na SaladeArte-Cinema da UFBA, no Canela às 10h, Tsallis abordará o tema "Complexidade em Ciência e Tecnologia". O evento é realizado pela Pró-Reitoria de Extensão Universitária (PROEXT).

# VIII Latin American Workshop on Nonlinear Phenomena (LAWNP'03) - September 28 to October 3rd 2003 – Salvador – Brazil)

# Trends and perspectives in extensive and non-extensive statistical mechanics

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Physica A: Statistical Mechanics and its Applications
Volume 344, Issues 3–4, 15 December 2004, Pages v-vi

## Preface

Hans Herrmann, Marcia Barbosa, Evaldo Curado

Proceedings of the International Workshop on "Trends and perspectives in extensive and non-extensive statistical mechanics", Angra dos Reis, Brazil, 19-21 November 2003 - In honour of the 60th birthday of Constantino Tsallis

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Physica A 344 (2004) 601–607

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### Power law sensitivity to initial conditions for abelian directed self-organized critical models

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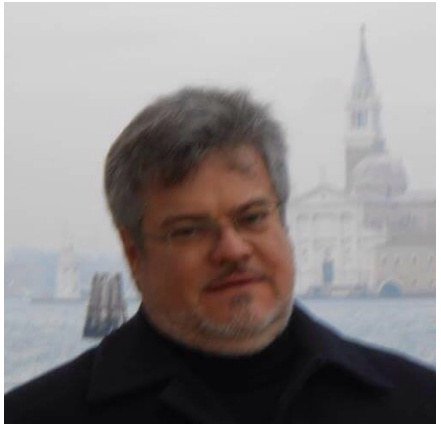
Available online 6 July 2004



http://dx.doi.org/10.1063/1.2982233

JOURNAL OF MATHEMATICAL PHYSICS **49**, 093509 (2008)

# Nondistributive algebraic structures derived from nonextensive statistical mechanics

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(Received 11 June 2008; accepted 21 August 2008; published online 24 September 2008)

*Brazilian Journal of Physics, vol. 39, no. 2A, August, 2009*



## Some properties of deformed $q$-numbers

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(Received on 19 January, 2009)

***"LIKE BEAUTY, COMPLEXITY IS HARD TO DEFINE AND EASY TO IDENTIFY"***

***"LIKE BEAUTY, COMPLEXITY CAN BE SIMPLE AND UNCERTAIN"***

Constantino Tsallis

Vienna, May 2018

# Outline

- Motivation
  - Complex behavior of the transmission dynamics of communicable diseases
- Preliminary
  - The basic ($\mathscr{R}_0$) and time-dependent effective ($\mathscr{R}(t)$) reproduction numbers
- The method
  - Generalization of the next-generation method procedure (previously proposed for estimating $\mathscr{R}_0$)
- Applications
  - Complex scenarios: co-circulation of viruses, transmission of disease between cities, vaccine effect
- Concluding remarks

# A bit of history ....

- The concept of basic reproduction number ($\mathscr{R}_0$) was introduced by MacDonald in the 1950s,
- In 1990, Diekmann and collaborators proposed the next generation method, setting up a clear mathematical definition of $\mathscr{R}_0$ for heterogeneous populations, detailed in 2000.
- In 2002, van der Driessche & Watmough presented a detailed procedure to estimate $\mathscr{R}_0$ for compartmental models.
- In 2004, Fred Brauer highlighted the essential concept of infection age for generalizing reproduction number for any time *t*.
- In 2006, Wallinga and Lipsitch emphasized the role of the generation interval distribution $g(\tau)$ for the effective reproduction number $\mathscr{R}(t)$.
- In 2009, Nishiura and Chowell presented mathematical and statistical properties of $\mathscr{R}(t)$ as well as some applications.

Odo Dieckmann (1948- )

Pauline van den Driessche (1941- )

- We present a generalization of the procedure based on the next generation method with the aim of obtaining $g(\tau)$ and $\mathscr{R}$(t) for heterogeneous models based on incidence data.
- We also apply it to complex models such as stochastical and metapopulation ones to investigate different contexts.

# Our work about the method

(Jorge et al., R. Soc. Open Sci. **9** (2022) 220005)

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Research

**Cite this article:** Jorge DCP, Oliveira JF, Miranda JGV, Andrade RFS, Pinho STR. 2022 Estimating the effective reproduction number for heterogeneous models using incidence data. *R. Soc. Open Sci.* **9**: 220005.
https://doi.org/10.1098/rsos.220005

## Estimating the effective reproduction number for heterogeneous models using incidence data

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Daniel Jorge (Princeton University)

# Preliminary

- Concepts of reproduction numbers
  - Basic reproduction number ($\mathscr{R}_0$) – the number of new cases of an infection caused by an infected individual in a whole susceptible population.
  - Effective reproduction number ($\mathscr{R}$(t)) - time series of reproduction number for which the infection reaches a partial susceptible population which changes on time.
- Next-generation method
  - Consider the infection process in terms of consecutive generations of infected individuals analogously to demographic generations ("epidemiological birth"); regarding the generations: $\phi^{m+1}$=**K**$\phi^{m}$
  - The basic reproduction number may be written in terms of spectrum radius of the matrix **K** looking at multiplications in *m* generations but on per generation when $m \to \infty$:

$$\mathscr{R}_0 = \rho(K) = \lim_{m\to\infty} |K^m|^{1/m}$$

# Basic Reproduction Number ($\mathscr{R}_0$)

- Using method of next generation operator, based on the infective compartments (Diekmann e Heesterbeek, 2000; Van den Driessche & Watmough, 2002), for a general model:

$$\frac{dX_i}{dt} = \mathscr{F}_i(x) - \mathscr{V}_i(x), \quad i = 1, \ldots, n,$$

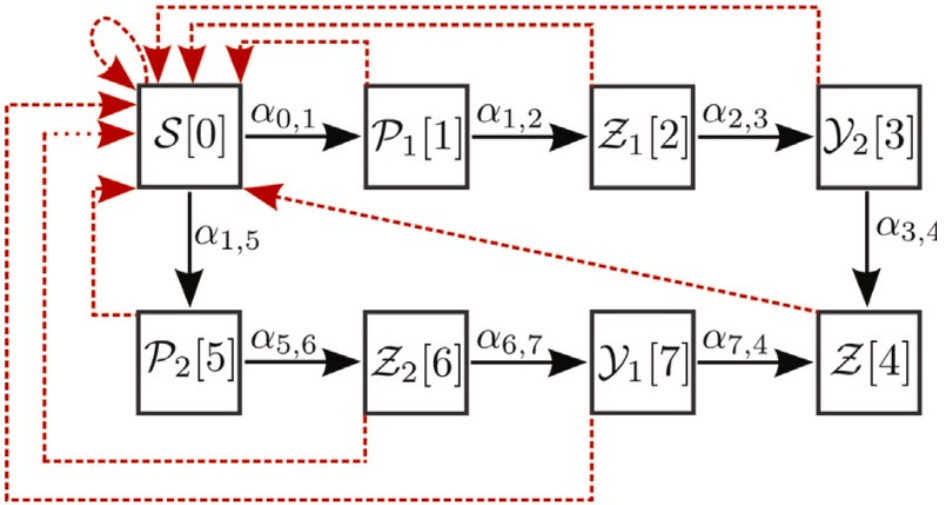
$\mathscr{R}_0$ is estimated in terms of the sub-model of infective compartments:

$$\mathscr{R}_0 = \lambda \implies \det(\boldsymbol{F}\,\boldsymbol{V}^{-1} - \lambda \boldsymbol{I}) = 0$$

with $$F = \left[\frac{\partial \mathscr{F}_i}{\partial x_j}(x_0)\right] \quad \text{and} \quad V = \left[\frac{\partial \mathscr{V}_i}{\partial x_j}(x_0)\right]$$

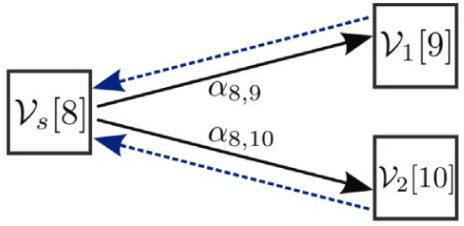
- $F$ corresponds to a matrix whose elements are the rate at which infective individuals in j produce new infections in i, $\boldsymbol{V}$ is a matrix composed by the transition terms of compartments i and j. The eigenvalues are obtained for the free-disease equilibrium and $\mathscr{R}_0$ corresponds to the largest eigenvalue of $\boldsymbol{FV^{-1}}$.

# An stochastic vector-borne model of co-circulation of viruses




## Parameters of the model

| Parameters | Description |
|---|---|
| $\lambda_{1(2)}$ | Rate of human infection by virus 1(2) |
| $\gamma_{1(2)}$ | Rate of human recovery of disease by virus 1(2) |
| $\sigma_{21(12)}$ | Cross-infection parameter from virus 1(2) to virus 2(1) |
| $\delta_{1(2)}$ | Rate of vector infection by virus 1(2) |
| $\mu$ | Human mortality |
| $\mu_v$ | Vector mortality |




Vector-borne diseases

- Zika and dengue – Hirata et al, 2023
- DENV-1, 2, 3, 4 – de Araújo et al. 2023

$$\frac{\mathrm{d}}{\mathrm{d}t}\langle s\rangle = \mu(1-\langle s\rangle) - \lambda_1\langle sv_1\rangle - \lambda_2\langle sv_2\rangle,$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\langle p_{1(2)}\rangle = \lambda_{1(2)}\langle sv_{1(2)}\rangle - (\mu+\gamma_{1(2)})\langle p_{1(2)}\rangle,$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\langle z_{1(2)}\rangle = \gamma_{1(2)}\langle p_{1(2)}\rangle - \sigma_{21(12)}\lambda_{2(1)}\langle z_{1(2)}v_{2(1)}\rangle - \mu\langle z_{1(2)}\rangle,$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\langle y_{2(1)}\rangle = \sigma_{21(12)}\lambda_{2(1)}\langle z_{1(2)}v_{2(1)}\rangle - (\mu+\gamma_{2(1)})\langle y_{2(1)}\rangle,$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\langle v_{1(2)}\rangle = \delta_{1(2)}[\langle(1-v_1-v_2)p_{1(2)}\rangle + \langle(1-v_1-v_2)y_{1(2)}\rangle] - \mu_v\langle v_{1(2)}\rangle.$$

# Basic reproduction number for co-circulation model

For stochastic version of the model:

$$\mathcal{R}_0 = max(\mathcal{R}_1, \mathcal{R}_2),$$

with

$$\mathcal{R}_1 = \sqrt{\frac{\lambda_1 \delta_1}{\mu_v(\mu+\gamma_1)}[\langle s|v_1\rangle\langle v_s|p_1\rangle + \sigma_{12}\langle z_2|v_1\rangle\langle v_s|y_1\rangle]}$$

$$\mathcal{R}_2 = \sqrt{\frac{\lambda_2 \delta_2}{\mu_v(\mu+\gamma_2)}[\langle s|v_2\rangle\langle v_s|p_2\rangle + \sigma_{21}\langle z_1|v_2\rangle\langle v_s|y_2\rangle]}$$

- Assuming

$$\langle w_a w_b\rangle = \langle w_a|w_b\rangle\langle w_b\rangle$$

we recover its deterministic version (Esteva et al. 2003).

- Since

$$P_{1(2)} = P_{1(2)o}e^{\Lambda_{1(2)}t}$$
$$Y_{1(2)} = Y_{1(2)o}e^{\Lambda_{1(2)}t}$$
$$V_{1(2)} = V_{1(2)o}e^{\Lambda_{1(2)}t}.$$

$$\mathcal{R}_{1(2)}{}^2 = \frac{1}{\mu_v(\mu+\gamma_{1(2)})}\frac{(\Lambda_{1(2)}+\mu_v)}{(1-V_{1(2)o}-V_{1(2)o})}\frac{(\Lambda_{1(2)}+\mu+\gamma_{1(2)})}{[1-Z_{1(2)o}-Z_o-Z_{2(1)o}(1-\sigma_{12(21)})]}$$

If there is no imune humans at t=0, then $\mathcal{R}^2_{1(2)} = \frac{(\Lambda_{1(2)}+\mu_v)(\Lambda_{1(2)}+\mu+\gamma_{1(2)})}{V_{so}S_o\mu_v(\mu+\gamma_{1(2)})}.$

# Effective reproduction number ($\mathcal{R}$(t))

- The effective reproduction number, $\mathcal{R}(t)$, may be set up through the concept of *infection-age* (Nishiura & Chowell, 2009), also based on the infective compartments.

- Let $A(t,\tau)$ be the rate of new infections at time $t$ caused by an infective human at time $\tau \leq t$ ; therefore the number of new infections $\mathcal{F}(t)$ and the reproduction number $\mathcal{R}(t)$ are given by:

$$\mathcal{F}(t) = \int_0^\infty A(t,\tau)\mathcal{F}(t-\tau)d\tau,$$

$$\mathcal{R}(t) \equiv \int_0^\infty A(t,\tau)d\tau.$$

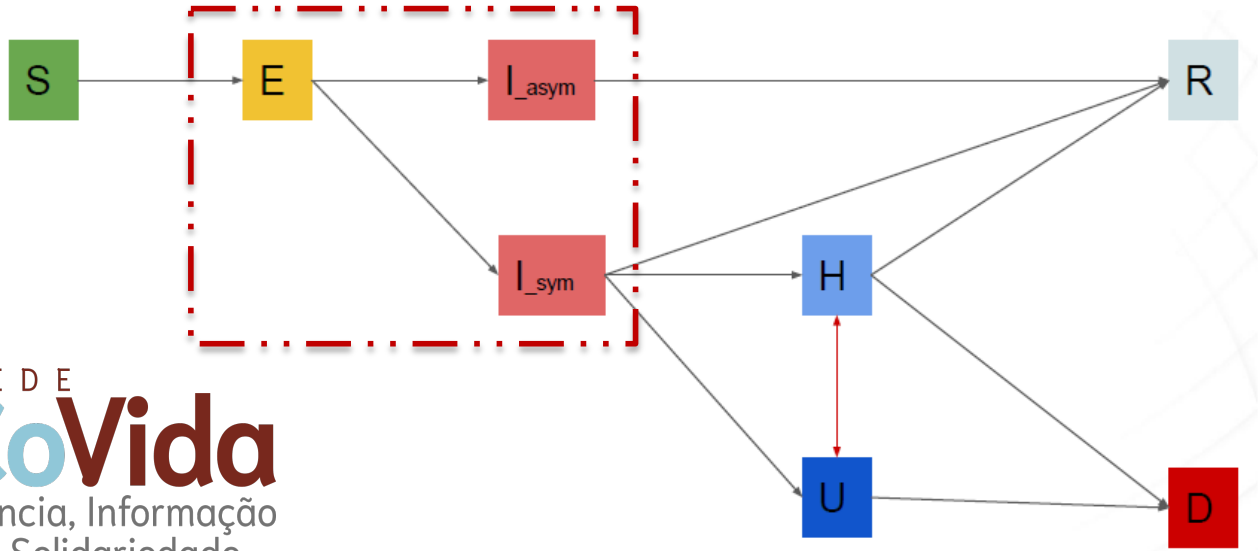
- Consider $g(t,\tau)$ a normalized probability distribution of time interval that an infectious human take to infect secondary cases (generation interval distribution); assuming that g depends only on $\tau$, then:

$$A(t,\tau) = \mathcal{R}(t)g(\tau).$$

and

$$\mathcal{R}(t) = \frac{\mathcal{F}(t)}{\int_0^\infty g(\tau)\mathcal{F}(t-\tau)d\tau}.$$

# SEIIHURD model: COVID-19 dynamics




$$\beta(t) = \beta_0 \mathcal{H}(t_1 - t) + \sum_{i=1}^{n-1} \beta_i \mathcal{H}(t_{i+1} - t)\mathcal{H}(t - t_i) + \beta_0 \mathcal{H}(t - t_n).$$

Heavside distribution

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Oliveira et al., *Nat. Commun.* **12**, 333 (2021)

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https://doi.org/10.1038/s41467-020-19798-3 OPEN

## Mathematical modeling of COVID-19 in 14.8 million individuals in Bahia, Brazil

Juliane F. Oliveira[1,2✉], Daniel C. P. Jorge[3], Rafael V. Veiga[1], Moreno S. Rodrigues[4], Matheus F. Torquato[5], Nivea B. da Silva[6], Rosemeire L. Fiaccone[6], Luciana L. Cardim[1], Felipe A. C. Pereira[7], Caio P. de Castro[3], Aureliano S. S. Paiva[1], Alan A. S. Amad[5], Ernesto A. B. F. Lima[8], Diego S. Souza[1], Suani T. R. Pinho[3,9], Pablo Ivan P. Ramos[1,9] & Roberto F. S. Andrade[1,3,9]

Jorge et al., *Epidemics* **35**, 100465 (2021)

Epidemics 35 (2021) 100465

Contents lists available at ScienceDirect

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## Assessing the nationwide impact of COVID-19 mitigation policies on the transmission rate of SARS-CoV-2 in Brazil

Daniel C.P. Jorge[a,1], Moreno S. Rodrigues[b,1], Mateus S. Silva[a,1], Luciana L. Cardim[c], Nívea B. da Silva[c,d], Ismael H. Silveira[e], Vivian A.F. Silva[c], Felipe A.C. Pereira[f], Arthur R. de Azevedo[d], Alan A.S. Amad[g], Suani T.R. Pinho[a], Roberto F.S. Andrade[a,c], Pablo I.P. Ramos[c], Juliane F. Oliveira[c,h,*]

# A general method for estimation of $\mathscr{R}(t)$ to heterogeneous populations

Density of infective compartments: $\boldsymbol{x}(t,\tau) = (x_1(t,\tau), \ldots, x_n(t,\tau))$

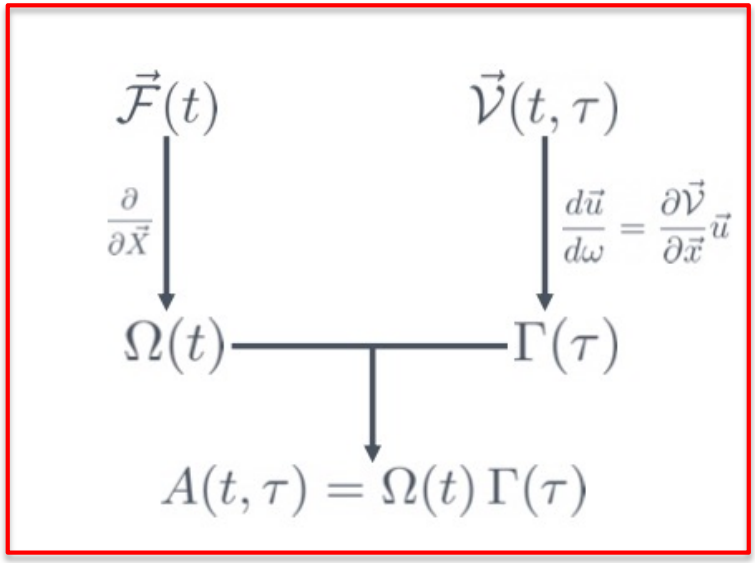
such that $\boldsymbol{X}(t) = \int_0^\infty \boldsymbol{x}(t,\tau)\,\mathrm{d}\tau,$

$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial \tau}\right)\boldsymbol{x}(t,\tau) = -\boldsymbol{\mathcal{V}}(t,\tau)$$

$$\boldsymbol{x}(t,\tau=0) = \boldsymbol{\mathcal{F}}(t).$$

$\longrightarrow$

$$\frac{\mathrm{d}}{\mathrm{d}t}\boldsymbol{X}(t) = \boldsymbol{\mathcal{F}}(t) - \int_0^\infty \boldsymbol{\mathcal{V}}(t,\tau)\,\mathrm{d}\tau.$$




Thus, obtaining the Next-generation Matrix and the Generation Interval Distribution Matrix:

$$\mathcal{R}_{ij}(t) = \int_0^\infty A_{ij}(t,\tau)d\tau$$

$$g_{ij}(t,\tau) = \frac{A_{ij}(t,\tau)}{\int_0^\infty A_{ij}(t,\tau)d\tau}$$

That leads to the renewal equation:

$$\mathcal{F}_i(t) = \sum_i \mathcal{R}_{ij}(t) \int_0^\infty g_{ij}(t,\tau)\,\mathcal{F}_j(t-\tau)d\tau$$

If $\mathcal{F}_i(t) = \alpha_i(t)\mathcal{F}^T(t)$. where $\mathcal{F}^T(t) = \sum_i^n \mathcal{F}_i(t)$ , then $\mathcal{R}^T(t) = \boldsymbol{\alpha}\cdot\overline{\boldsymbol{\mathcal{R}}}$; $\overline{\mathcal{R}}_j(t) = \sum_i^n \mathcal{R}_{ij}(t).$

# Steps of the method

- To calculate $\Omega(t, \tau)$: $\Omega_{ij}(t) = \frac{\partial}{\partial X_j}\mathcal{F}_i(t).$
- To calculate $\Gamma(t, \tau)$ :
  - If $\mathcal{V}(t, \tau)$ depends linearly on $x(t, \tau)$, $\frac{d}{d\omega}\boldsymbol{u}(\omega) = -\frac{\partial \boldsymbol{\mathcal{V}}}{\partial \boldsymbol{x}}\boldsymbol{u}(\omega)$. with $u_i(\omega) = x_i(t_0 + \omega, \tau_0 + \omega)$
  - To obtain the eigenvalues $\lambda$ and the eigenvectores $\vec{v}$ of $-\frac{\partial \boldsymbol{\mathcal{V}}}{\partial \boldsymbol{x}}$
  - To exhibit $\boldsymbol{u}(\omega) = \overline{\Gamma}(\omega)\ \boldsymbol{u}(0)$, with $\overline{\Gamma}(\omega) = \Gamma(t, \tau)$,
- To obtain $\boldsymbol{A}(t, \tau) = \Omega(t, \tau)\Gamma(t, \tau).$ such that $\mathcal{J}_{ij}(t) = \int_0^\infty A_{ij}(t, \tau)\mathcal{F}_j(t - \tau)\,\mathrm{d}\tau,$
- As a consequence: $\mathcal{R}_{ij}(t) = \int_0^\infty A_{ij}(t, \tau)\,\mathrm{d}\tau.$ ; $\overline{\mathcal{R}}_j(t) = \sum_i^n \mathcal{R}_{ij}(t).$

$$g_{ij}(t, \tau) = \frac{A_{ij}(t, \tau)}{\int_0^\infty A_{ij}(t, \tau)\,\mathrm{d}\tau}, \quad ; \quad \overline{g}_j(t, \tau) = \frac{\sum_i^n \mathcal{R}_{ij}(t) g_{ij}(t, \tau)}{\sum_i^n \mathcal{R}_{ij}(t)}$$

$$\overline{\mathcal{J}}_j(t) = \overline{\mathcal{R}}_j(t) \int_0^\infty \overline{g}_j(t, \tau)\ \mathcal{F}_j(t - \tau)\,\mathrm{d}\tau, \quad \text{with} \quad \boxed{\overline{\mathcal{J}}_j(t) = \sum_i^n \mathcal{J}_{ij}(t)}$$

- If $\mathcal{F}_i(t) = \alpha_i(t)\mathcal{F}^T(t).$ with $\mathcal{F}^T(t) = \sum_i^n \mathcal{F}_i(t)$ then $\mathcal{R}^T(t) = \boldsymbol{\alpha} \cdot \overline{\boldsymbol{\mathcal{R}}}$ ; $g^T(t, \tau) = \frac{\sum_i \alpha_i(t)\overline{\mathcal{R}}_i(t)\ \overline{g}_i(\tau)}{\sum_i \alpha_i(t)\overline{\mathcal{R}}_i(t)}.$

# An example for sequential progression: SEIR model

$$\begin{aligned}
\frac{dS}{dt} &= -\frac{\beta S}{N}\left[I+\epsilon E\right],\\
\frac{dE}{dt} &= \frac{\beta S}{N}\left[I+\epsilon E\right]-\kappa E,\\
\frac{dI}{dt} &= \kappa E-\gamma I,\\
\frac{dR}{dt} &= \gamma I.
\end{aligned}$$

$$\boldsymbol{\mathcal{F}}(t)=\begin{pmatrix}\frac{\beta S}{N}\left[I+\epsilon E\right]\\ 0\end{pmatrix},\quad\rightarrow\quad \boldsymbol{\Omega}(t)=\begin{pmatrix}\epsilon\frac{\beta S}{N} & \frac{\beta S}{N}\\ 0 & 0\end{pmatrix}.$$

$$\boldsymbol{\mathcal{V}}(t,\tau)=\begin{pmatrix}\kappa i_e(t,\tau)\\ \gamma i_i(t,\tau)-\kappa i_e(t,\tau)\end{pmatrix}\rightarrow\quad \boldsymbol{\Gamma}(\tau)=\begin{bmatrix}e^{-\kappa\tau} & 0\\ \frac{\kappa}{\gamma-\kappa}\left[e^{-\kappa\tau}-e^{-\gamma\tau}\right] & e^{-\gamma\tau}\end{bmatrix}.$$

$$\boldsymbol{A}(t,\tau)=\begin{bmatrix}\epsilon\frac{\beta S}{N} & \frac{\beta S}{N}\\ 0 & 0\end{bmatrix}\begin{bmatrix}e^{-\kappa\tau} & 0\\ \frac{\kappa}{\gamma-\kappa}\left[e^{-\kappa\tau}-e^{-\gamma\tau}\right] & e^{-\gamma\tau}\end{bmatrix}.\rightarrow\quad \boldsymbol{\mathcal{R}}(t)=\beta\frac{S}{N}\begin{pmatrix}\frac{\epsilon}{\kappa}+\frac{1}{\gamma} & \frac{1}{\gamma}\\ 0 & 0\end{pmatrix}.\rightarrow\quad \overline{\boldsymbol{\mathcal{R}}}=\beta\frac{S}{N}\begin{pmatrix}\frac{\epsilon}{\kappa}+\frac{1}{\gamma}\\ \frac{1}{\gamma}\end{pmatrix}.$$

Since $\mathcal{F}_1(t)=\mathcal{F}^T(t)$ then $\boldsymbol{\alpha}=(1,0)$

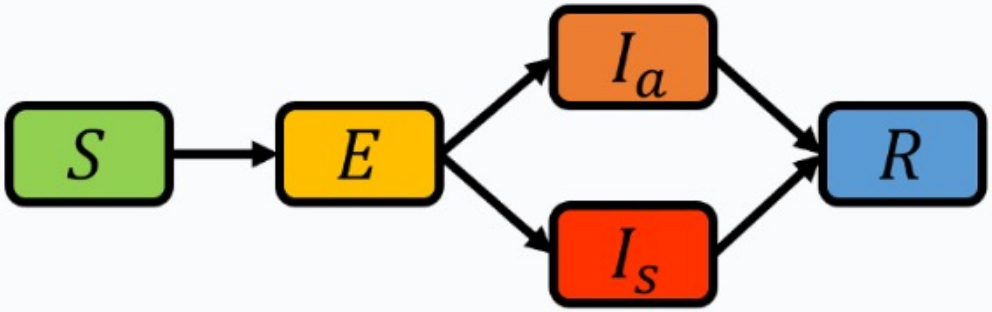
$$\mathcal{R}^T(t)=\boldsymbol{\alpha}\cdot\overline{\boldsymbol{\mathcal{R}}}=\frac{\beta S}{N}\left[\frac{\epsilon}{\kappa}+\frac{1}{\gamma}\right],$$

$$g_{11}(\tau)=\bar{g}_1(\tau)=\frac{\epsilon\, e^{-\kappa\tau}+\frac{\kappa}{\gamma-\kappa}\left[e^{-\kappa\tau}-e^{-\gamma\tau}\right]}{\epsilon/\kappa+1/\gamma}$$

$$g_{12}(\tau)=\bar{g}_2(\tau)=\gamma e^{-\gamma\tau}\ ;\ g_{21}(\tau)=g_{22}\ (\tau)=0$$

$$g^T(\tau)=\frac{\epsilon\, e^{-\kappa\tau}+\frac{\kappa}{\gamma-\kappa}\left[e^{-\kappa\tau}-e^{-\gamma\tau}\right]}{\epsilon/\kappa+1/\gamma}.$$

# SEIIHURD model
# (SEIIR model with $\epsilon = 0$)




$$\begin{aligned}
\frac{dS}{dt} &= -\frac{\beta S}{N}(I_s + \delta I_a), \\
\frac{dE}{dt} &= \frac{\beta S}{N}(I_s + \delta I_a) - \kappa E, \\
\frac{dI_s}{dt} &= p\kappa E - \gamma_s I_s, \\
\frac{dI_a}{dt} &= (1-p)\kappa E - \gamma_a I_a, \\
\frac{dR}{dt} &= \gamma_a I_a + \gamma_s I_s.
\end{aligned}$$

$$\vec{\mathcal{F}}(t) = \frac{\beta S}{N}\begin{pmatrix} I_s + \delta I_a \\ 0 \\ 0 \end{pmatrix}$$

$$\vec{\mathcal{V}}(\tau) = \begin{pmatrix} \kappa i_e \\ \gamma_s i_s - \kappa i_e \\ \gamma_a i_a - \kappa i_e \end{pmatrix}$$

$$\mathcal{R}(t) = \beta\frac{S}{N}\begin{pmatrix} \frac{p}{\gamma_s} + \delta\frac{(1-p)}{\gamma_a} & 1/\gamma_s & 1/\gamma_a \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

$$\mathcal{F}^T(t) = \mathcal{R}^T(t)\int_0^\infty g^T(t,\tau)\mathcal{F}^T(t-\tau)d\tau$$

Whereby $\mathcal{F}^T(t) = \sum \mathcal{F}_i(t)$. For the model, we get:

$$\mathcal{R}^T(t) = \beta\frac{S(t)}{N}\left(\frac{p}{\gamma_s} + \frac{\delta_a(1-p)}{\gamma_a}\right)$$

$$g_{ij}(\tau) \equiv g(\tau) = \frac{\frac{p}{\gamma_s}g^s(\tau) + \frac{\delta(1-p)}{\gamma_a}g^a(\tau)}{\frac{p}{\gamma_s} + \frac{\delta(1-p)}{\gamma_a}},$$

$$g_a(\tau) = \frac{\kappa\gamma_a}{\kappa - \gamma_a}(e^{-\gamma_a\tau} - e^{-\kappa\tau}),$$

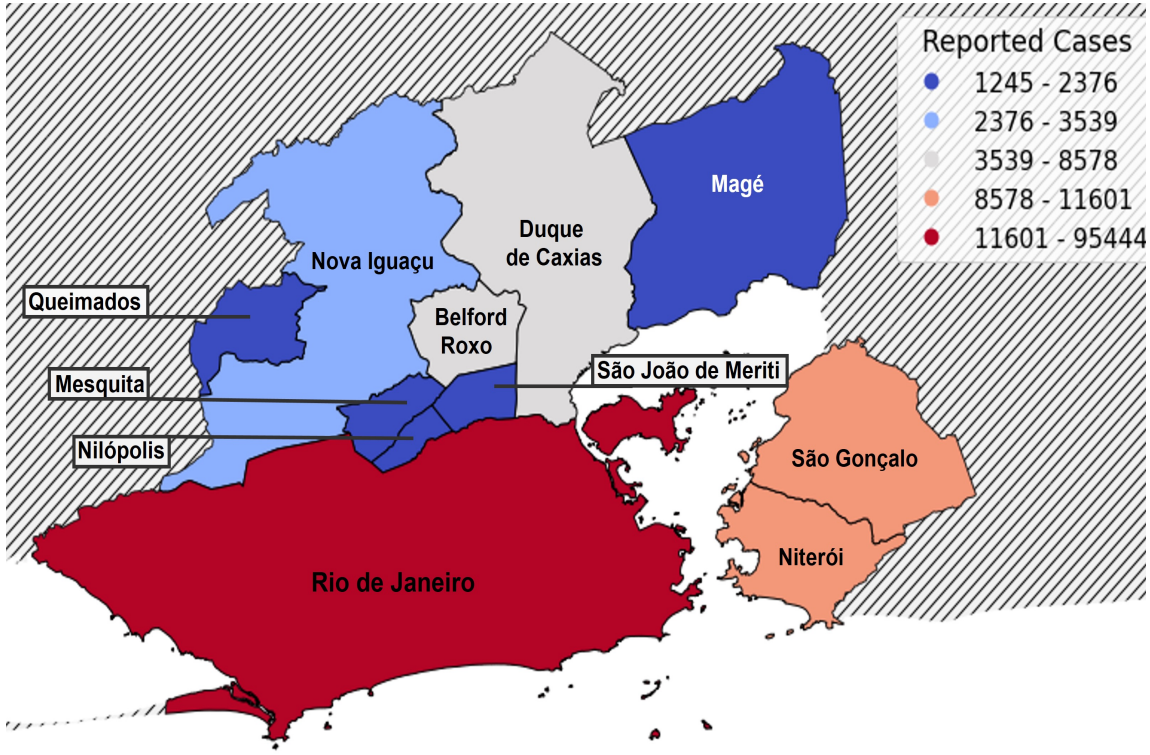
$$g_s(\tau) = \frac{\kappa\gamma_s}{\kappa - \gamma_s}(e^{-\gamma_s\tau} - e^{-\kappa\tau}).$$

Based on real data: $\mathcal{R}^T(t) = \dfrac{\mathcal{B}^T(t)}{\sum_{\tau=0}^{t} g^T(t,\tau)\mathcal{B}^T(t-\tau)\Delta t}$,

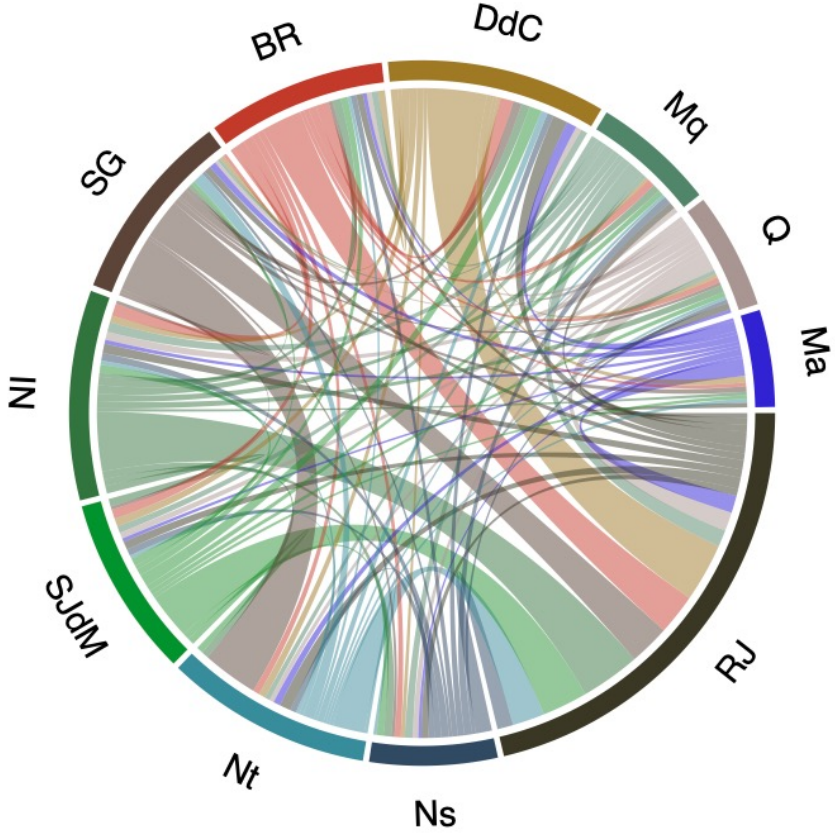
# Application of the method for metapopulation model of COVID-19 epidemics

We chose 11 cities of the metropolitan region of Rio de Janeiro (Brazil) that present the highest number of cases of COVID-19 until september 2020.

Pendular flow of individuals commuting to work is relevant for COVID-19 tranmission dynamics but it is not the only factor.

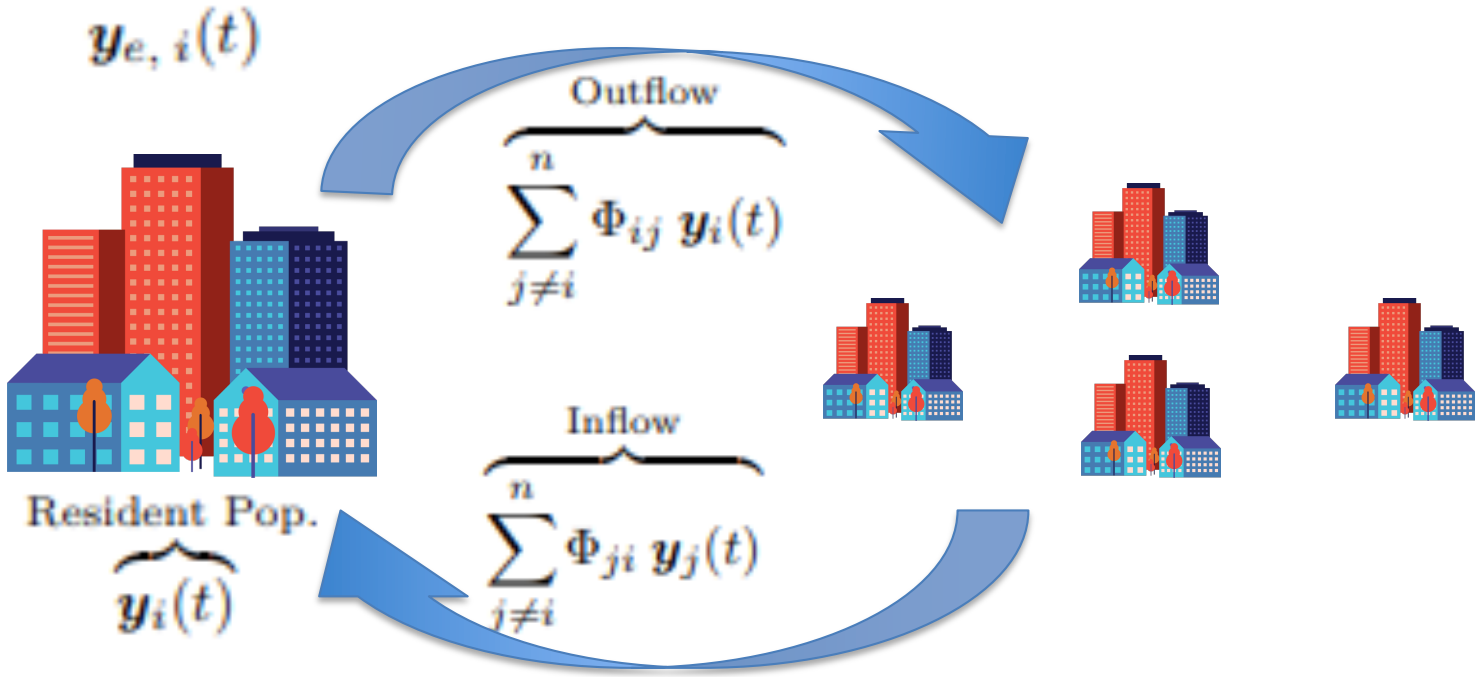



https://covid.saude.gov.br/




https://google.com/covid19/mobility/

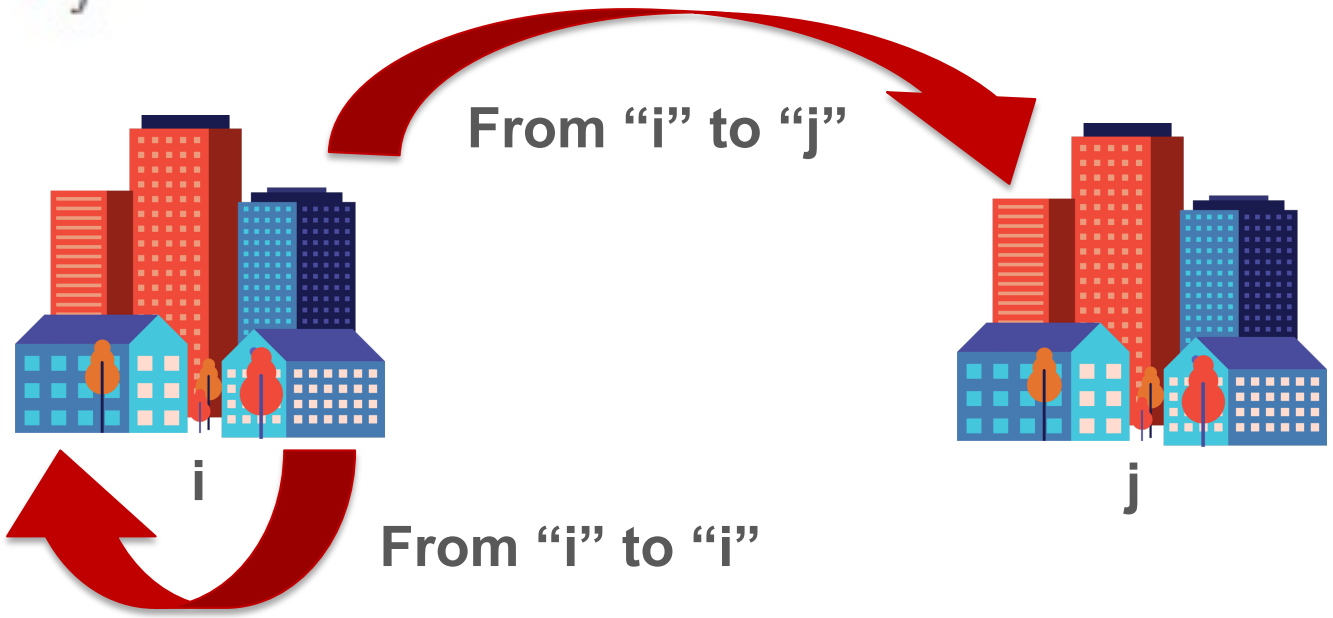
# Constructing a metapopulation transmission model




$$y_{e,\,i}(t) = \overbrace{y_i(t)}^{\text{Resident Pop.}} - \overbrace{\sum_{j\neq i}^{n} \Phi_{ij}\, y_i(t)}^{\text{Outflow}} + \overbrace{\sum_{j\neq i}^{n} \Phi_{ji}\, y_j(t)}^{\text{Inflow}}$$

# The disease transmission

$$\frac{\beta_j}{N_j} \times \overbrace{\Phi_{ij} S_i}^{\text{Susceptible Indv. from “}i\text{” in “}j\text{”}} \times \overbrace{I_{e,j}}^{\text{Infected Indv. in “}j\text{”}} .$$



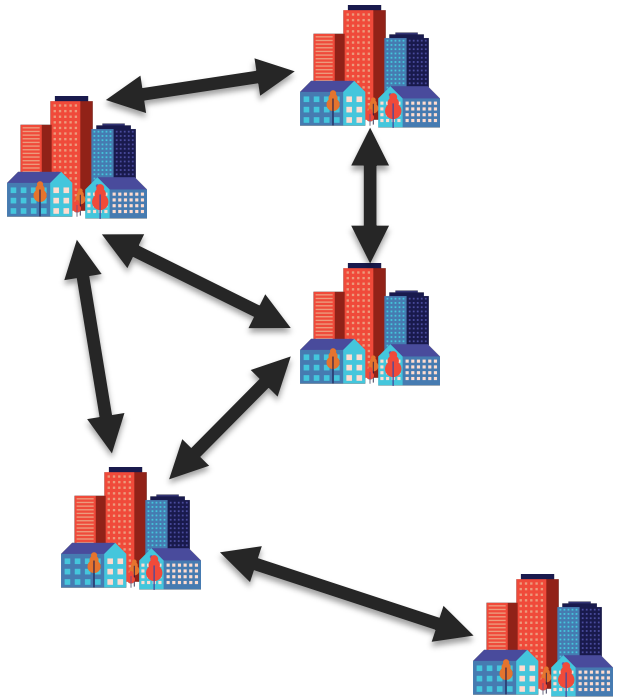

$$\frac{\beta_i}{N_i} \times \overbrace{S_i\left(1-\sum_j^n \Phi_{ij}\right)}^{\text{Susceptible Indv. from “}i\text{” in “}i\text{”}} \times \overbrace{I_{e,i}}^{\text{Infected Indv. in “}i\text{”}} ,$$

# SIR metapopulation model

$$\frac{dS_i}{dt} = -\sum_j^n \lambda_{ij}(t)\, I_j(t)\, S_i(t),$$

$$\frac{dI_i}{dt} = \sum_j^n \lambda_{ij}(t)\, I_j(t)\, S_i(t) - \gamma\, I_i(t),$$

$$\frac{dR_i}{dt} = \gamma I_i(t).$$



$$\lambda_{ii} = \frac{\beta_i}{N_i}\left(1 - \sum_j^n \Phi_{ij}\right)^2 + \sum_j^n \frac{\beta_j}{N_j}\,\Phi_{ij}^2$$

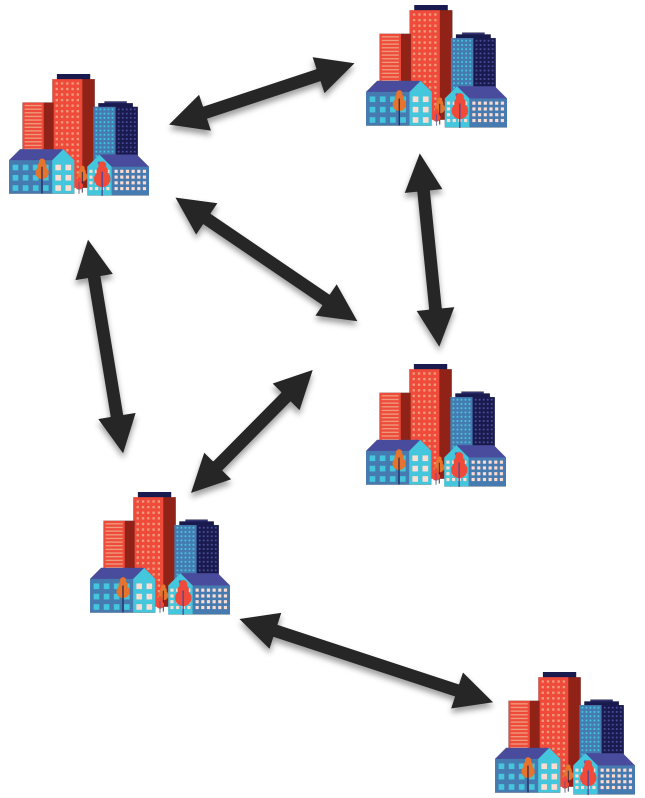
$$\lambda_{ij} = \frac{\beta_i}{N_i}\,\Phi_{ji}\left(1 - \sum_k^n \Phi_{ik}\right) + \frac{\beta_j}{N_j}\,\Phi_{ij}\left(1 - \sum_k^n \Phi_{jk}\right) + \sum_k^n \frac{\beta_k}{N_k}\Phi_{ik}\,\Phi_{jk}$$

# Applying the generalized method to SIR metapopulation model

$$\frac{dS_i}{dt} = -\sum_j^n \lambda_{ij}(t)\, I_j(t)\, S_i(t),$$

$$\frac{dI_i}{dt} = \sum_j^n \lambda_{ij}(t)\, I_j(t)\, S_i(t) - \gamma\, I_i(t),$$

$$\frac{dR_i}{dt} = \gamma I_i(t).$$



$$\boldsymbol{\mathcal{F}}(t) = \left[\sum_j^n \lambda_{ij}(t) I_j(t) S_i(t)\right],$$

$$\boldsymbol{\mathcal{V}}(t,\tau) = \left[-\gamma\, i_i(t,\tau)\right]$$

# Applying the generalized method to SIR metapopulation model

$$\boldsymbol{\mathcal{F}}(t) = \left[ \sum_{j}^{n} \lambda_{ij}(t) I_j(t) S_i(t) \right], \qquad \boldsymbol{\mathcal{V}}(t,\tau) = \left[ -\gamma\, i_i(t,\tau) \right]$$

$$\boldsymbol{\Omega}(t) = \begin{pmatrix} \lambda_{11}S_1 & \lambda_{12}S_1 & \dots & \lambda_{1n}S_1 \\ \lambda_{21}S_2 & \lambda_{22}S_2 & \dots & \lambda_{2n}S_2 \\ \vdots & \vdots & \ddots & \vdots \\ \lambda_{n1}S_n & \lambda_{n2}S_n & \dots & \lambda_{nn}S_n \end{pmatrix},$$

$$-\frac{\partial \boldsymbol{\mathcal{V}}}{\partial \boldsymbol{x}} = \begin{pmatrix} \gamma & 0 & \dots & 0 \\ 0 & \gamma & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & \gamma \end{pmatrix}.$$

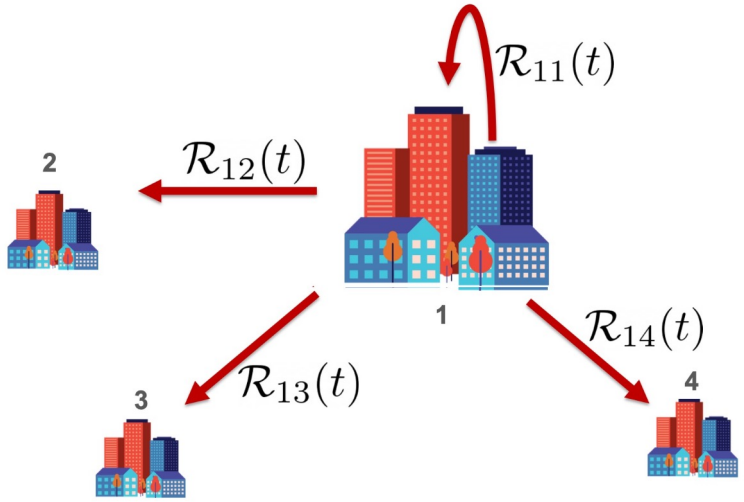
$$\boldsymbol{A}(t,\tau) = \left[ \lambda_{ij} S_i\, e^{-\gamma\tau} \right]$$

# Effective reproduction number matrix for SIR metapopulation model

$$\boldsymbol{A}(t,\tau) = \left[\lambda_{ij} S_i \, e^{-\gamma\tau}\right]$$

$$\boldsymbol{\mathcal{R}}(t) = \left[\frac{\lambda_{ij} S_i}{\gamma}\right].$$

$$g_{ij}(\tau) = g(\tau) = \gamma \, e^{-\gamma\,\tau}.$$




This Reproduction number matrix **cannot** be summed up into a **total reproduction number:** the dynamics of such system cannot be globally determined by a single reproduction number, but by several of them.

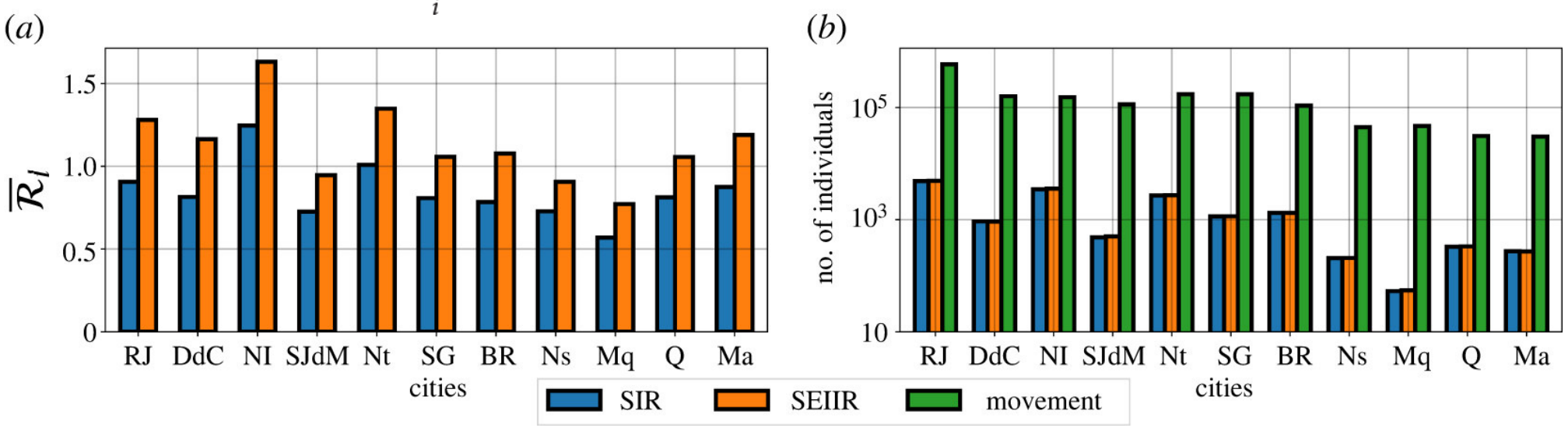
## Number of exported cases

$$\mathcal{T}_{ij}(t) = \mathcal{R}_{ij}(t) \sum_{\tau=0}^{t} g_{ij}(t,\tau)\mathcal{B}_j(t-\tau)\Delta t, \qquad \mathcal{B}_i(t) = \sum_{j\neq i}^{n} \mathcal{T}_{ij}.$$

# Results for SIR and SEIIR metapopulation models

$$\overline{\mathcal{R}}_j(t) = \sum_i^n \mathcal{R}_{ij}(t).$$

Number of exported cases




**SEIIR metapopulation model**

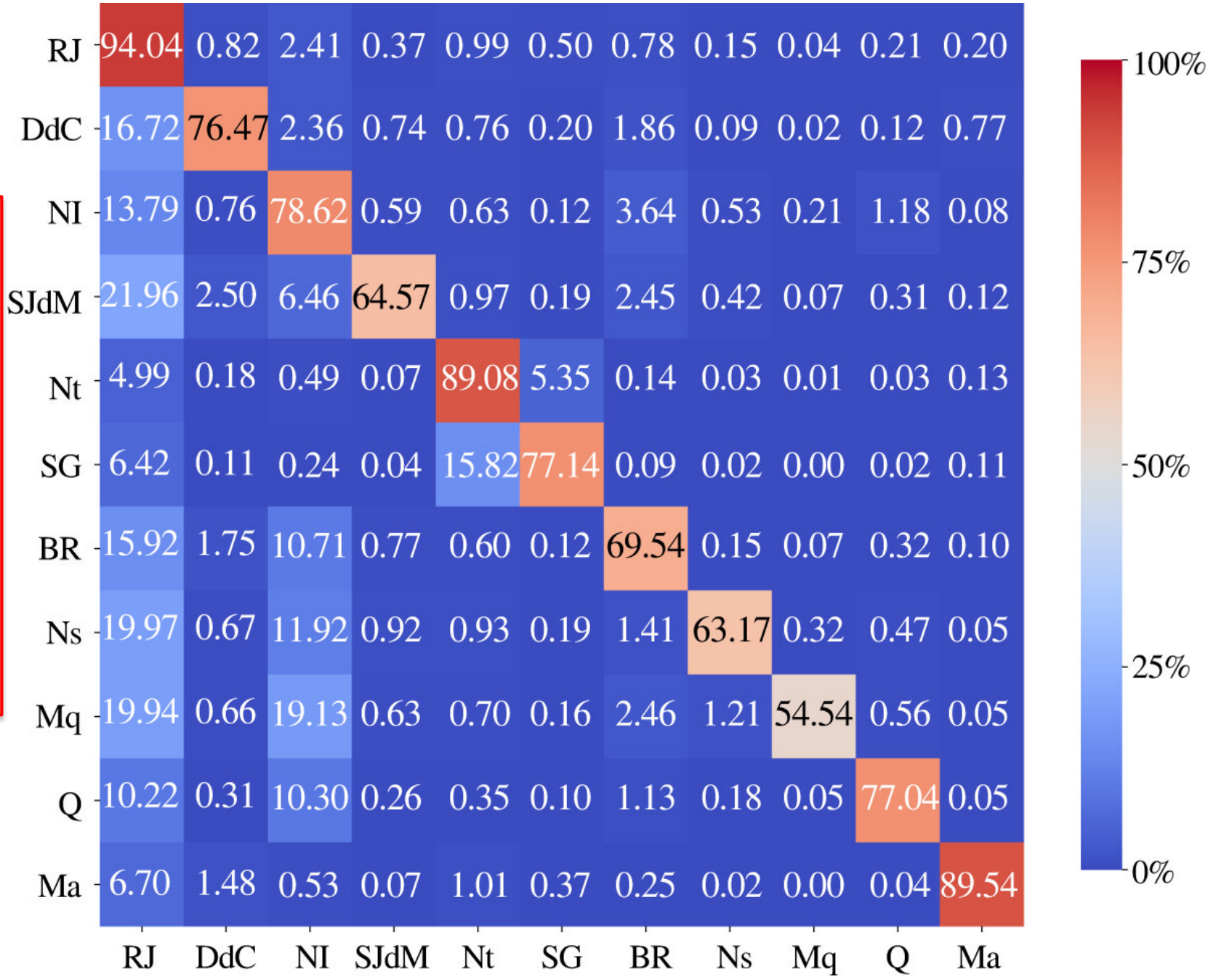
$$\mathcal{R}_{ij}(t) = \left[\lambda_{ij}(t) S_i(t) \left(\frac{p}{\gamma_s} + \delta \frac{(1-p)}{\gamma_a}\right)\right],$$

$$g_{ij}(\tau) \equiv g(\tau) = \frac{\frac{p}{\gamma_s} g^s(\tau) + \frac{\delta(1-p)}{\gamma_a} g^a(\tau)}{\frac{p}{\gamma_s} + \frac{\delta(1-p)}{\gamma_a}},$$

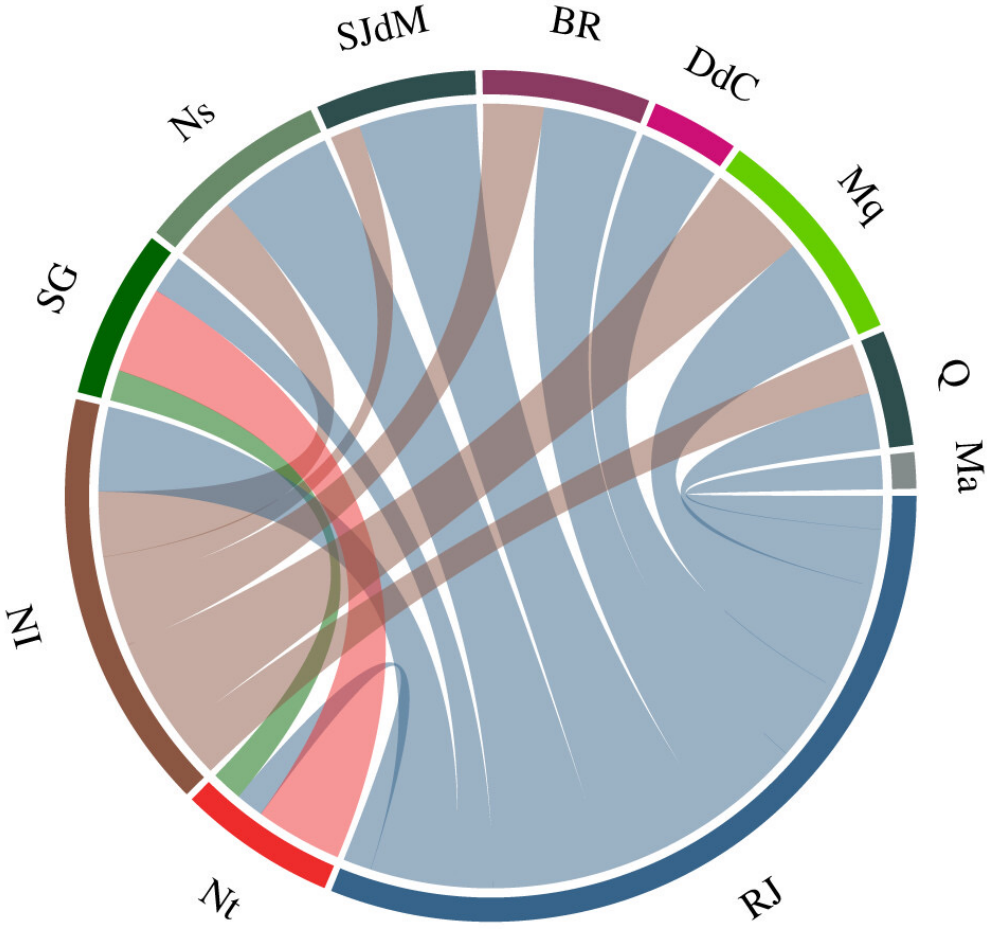
$t$

# Influence on number of infections caused by a count i on a count j

SEIIR metapopu-lation model applied to COVID-19 epidemics in metropolitan regions of RJ-Brazil



# Influence of number of infections caused by a count on another one (SEIIR)




| Municipality | Acronyms |
|---|---|
| Belford Roxo | BR |
| Duque de Caxias | DdC |
| Magé | Ma |
| Mesquita | Mq |
| Nilópolis | Ns |
| Niterói | Nt |
| Nova Iguaçu | NI |
| Queimados | Q |
| **Rio de Janeiro** | RJ |
| São Gonçalo | SG |
| São João de Meriti | SJdM |

The thickness of the lines is proportional to the number of cases that one count generates on the other one

# Ongoing work and concluding remarks

- We are able to generalize the used procedure of estimating the basic reproduction number to the effective reproduction number, also obtaining the generation interval distribution for an arbitrary model using data.
- Since the methodology is very general, we ara applying it to several models of disease transmission:
  - SEIIUHRD model with vaccine against COVID-19 (leaky x all or nothing)
  - Dengue model with vaccine (dengvaxia x qdenga)
  - Dengue model with entomological parameters of aquatic phase of vectors varying with temperature
  - Alert-early system of outbreaks of na unknown transmitted disease
- This method allows us to estimate other key quantities of an epidemic process, such as the number of cases that a count generates on neighbor ones through metapopulation models.
- New features of reproduction numbers as well as derived measures of them were considered when we analyse more complex scenarios.

# The team

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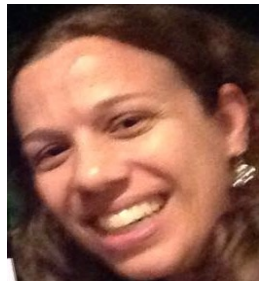
F.M.R. Hirata, D.C.P. Jorge, F.A.C. Pereira, L.M. Skalinski, G. Cruz-Pacheco, M.L.M. Esteva, and S.T.R. Pinho, *Co-circulation of Dengue and Zika viruses: A modelling approach applied to epidemics data*, Chaos Solit. Fractals **173**, 113599 (2023).




*Thank you for your attention!*

*Happy Birthday, Constantino!*γ

χρόνια πολλά!




$\boldsymbol{\Omega}(t)$

# An example for sequential progression: SEIR model

$$\begin{aligned}
\frac{dS}{dt} &= -\frac{\beta S}{N}\left[I+\epsilon E\right],\\
\frac{dE}{dt} &= \frac{\beta S}{N}\left[I+\epsilon E\right]-\kappa E,\\
\frac{dI}{dt} &= \kappa E-\gamma I,\\
\frac{dR}{dt} &= \gamma I.
\end{aligned}$$

$$\boldsymbol{\mathcal{F}}(t)=\begin{pmatrix}\frac{\beta S}{N}\left[I+\epsilon E\right]\\ 0\end{pmatrix}, \quad \rightarrow \quad \boldsymbol{\Omega}(t)=\begin{pmatrix}\epsilon\frac{\beta S}{N} & \frac{\beta S}{N}\\ 0 & 0\end{pmatrix}.$$

$$\boldsymbol{\mathcal{V}}(t,\tau)=\begin{pmatrix}\kappa i_e(t,\tau)\\ \gamma i_i(t,\tau)-\kappa i_e(t,\tau)\end{pmatrix} \quad \rightarrow \quad -\frac{\partial \boldsymbol{\mathcal{V}}}{\partial \boldsymbol{x}}=\begin{bmatrix}-\kappa & 0\\ \kappa & -\gamma\end{bmatrix}$$

$$\boldsymbol{\Gamma}(\tau)=\begin{bmatrix}e^{-\kappa\omega} & 0\\ \frac{\kappa}{\gamma-\kappa}[e^{-\kappa\tau}-e^{-\gamma\tau}] & e^{-\gamma\tau}\end{bmatrix}$$

$$A_{11}(t,\tau)=\epsilon\frac{\beta S}{N}e^{-\kappa\tau}+\frac{\beta S}{N}\frac{\kappa}{\gamma-\kappa}[e^{-\kappa\tau}-e^{-\gamma\tau}],$$

$$A_{12}(t,\tau)=\frac{\beta S}{N}e^{-\gamma\tau}. \qquad A_{21}(t,\tau)=A_{22}(t,\tau)=0$$

$$\rightarrow \quad \boldsymbol{\mathcal{R}}(t)=\beta\frac{S}{N}\begin{pmatrix}\frac{\epsilon}{\kappa}+\frac{1}{\gamma} & \frac{1}{\gamma}\\ 0 & 0\end{pmatrix} \quad \rightarrow \quad \overline{\boldsymbol{\mathcal{R}}}=\beta\frac{S}{N}\begin{pmatrix}\frac{\epsilon}{\kappa}+\frac{1}{\gamma}\\ \frac{1}{\gamma}\end{pmatrix}.$$

Since $\mathcal{F}_1(t)=\mathcal{F}^T(t)$ then $\boldsymbol{\alpha}=(1,0)$ and

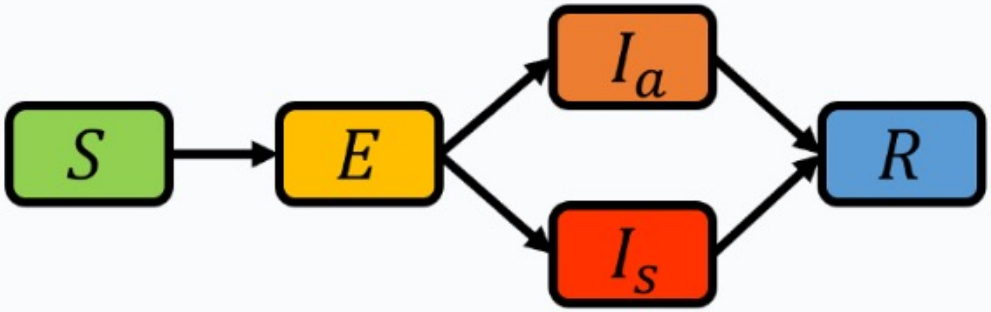
$$\mathcal{R}^T(t)=\boldsymbol{\alpha}\cdot\overline{\boldsymbol{\mathcal{R}}}=\frac{\beta S}{N}\left[\frac{\epsilon}{\kappa}+\frac{1}{\gamma}\right],$$

$$g_{11}(\tau)=\bar{g}_1(\tau)=\frac{\epsilon\, e^{-\kappa\tau}+\frac{\kappa}{\gamma-\kappa}[e^{-\kappa\tau}-e^{-\gamma\tau}]}{\epsilon/\kappa+1/\gamma}$$

$$g_{12}(\tau)=\bar{g}_2(\tau)=\gamma e^{-\gamma\tau};\ g_{21}(\tau)=g_{22}(\tau)=0$$

$$\rightarrow \quad g^T(\tau)=\frac{\epsilon\, e^{-\kappa\tau}+\frac{\kappa}{\gamma-\kappa}[e^{-\kappa\tau}-e^{-\gamma\tau}]}{\epsilon/\kappa+1/\gamma}.$$

# SEIIHURD model
# (SEIIR model with $\epsilon = 0$)




$$\mathcal{R}(t) = \beta \frac{S}{N} \begin{pmatrix} \frac{p}{\gamma_s} + \delta \frac{(1-p)}{\gamma_a} & 1/\gamma_s & 1/\gamma_a \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

$$\mathcal{F}^T(t) = \mathcal{R}^T(t) \int_0^\infty g^T(t,\tau)\mathcal{F}^T(t-\tau)d\tau$$

Whereby $\mathcal{F}^T(t) = \sum \mathcal{F}_i(t)$. For the model, we get:

$$\mathcal{R}^T(t) = \beta \frac{S(t)}{N}\left(\frac{p}{\gamma_s} + \frac{\delta_a(1-p)}{\gamma_a}\right)$$

$$\begin{aligned}
\frac{dS}{dt} &= -\frac{\beta S}{N}(I_s + \delta I_a), \\
\frac{dE}{dt} &= \frac{\beta S}{N}(I_s + \delta I_a) - \kappa E, \\
\frac{dI_s}{dt} &= p\kappa E - \gamma_s I_s, \\
\frac{dI_a}{dt} &= (1-p)\kappa E - \gamma_a I_a, \\
\frac{dR}{dt} &= \gamma_a I_a + \gamma_s I_s.
\end{aligned}$$

$$\vec{\mathcal{F}}(t) = \frac{\beta S}{N}\begin{pmatrix} I_s + \delta I_a \\ 0 \\ 0 \end{pmatrix} \qquad \vec{\mathcal{V}}(\tau) = \begin{pmatrix} \kappa i_e \\ \gamma_s i_s - \kappa i_e \\ \gamma_a i_a - \kappa i_e \end{pmatrix}$$

$$g_{ij}(\tau) \equiv g(\tau) = \frac{\frac{p}{\gamma_s} g^s(\tau) + \frac{\delta(1-p)}{\gamma_a} g^a(\tau)}{\frac{p}{\gamma_s} + \frac{\delta(1-p)}{\gamma_a}},$$

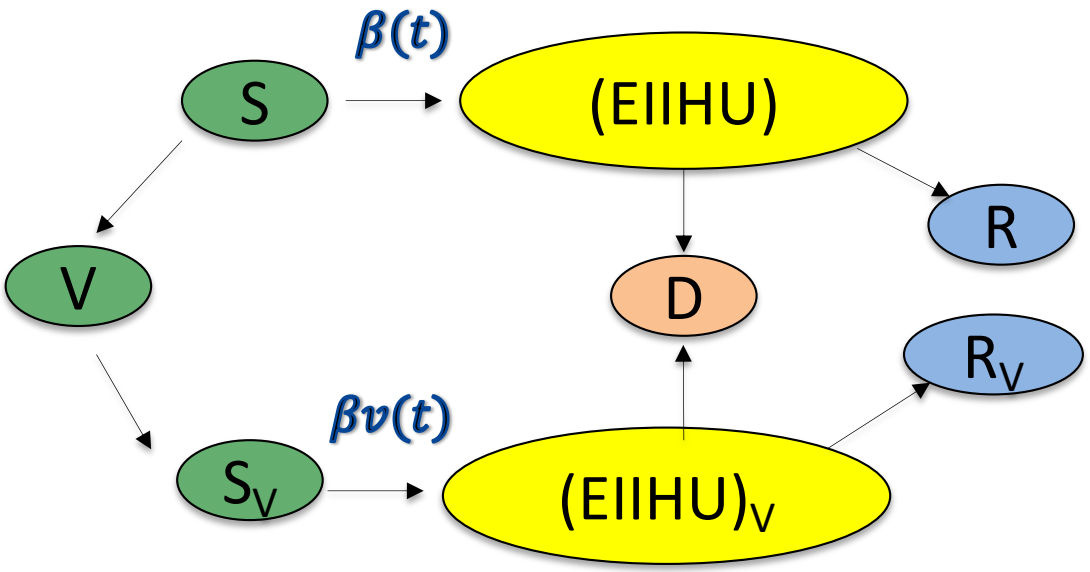
$$g_a(\tau) = \frac{\kappa\gamma_a}{\kappa - \gamma_a}(e^{-\gamma_a\tau} - e^{-\kappa\tau}),$$

$$g_s(\tau) = \frac{\kappa\gamma_s}{\kappa - \gamma_s}(e^{-\gamma_s\tau} - e^{-\kappa\tau}).$$

Based on real data: $\mathcal{R}^T(t) = \dfrac{\mathcal{B}^T(t)}{\sum_{\tau=0}^{t} g^T(t,\tau)\mathcal{B}^T(t-\tau)\Delta t}$,

# Reproduction numbers of SEIIHURD model with vaccine

## LEAKY VACCINE(SEVIIHURD)




PS: For an "all or none" vaccine, there would be an arrow from V to $R_V$ and $\beta_{v(t)} = \beta(t)$, leading to $\mathcal{R}(t)$ that do NOT depend on vaccine efficacy.

Particular case (SEIIHURD) :

$$\mathcal{R}(t) = \beta(t)S(t)\mathcal{P}$$

$$J(t) = \frac{I(t+1/k)}{b}$$

$$g(\tau) = \frac{\mathcal{Q}(\tau)}{\mathcal{P}}$$

$$\mathcal{R}^T(t) = \beta(S(t)+V(t))[\mathcal{P}+c(t)\mathcal{P}_v]$$

$$c(t) = \frac{\beta_v S_v(t)}{\beta(S(t)+V(t))}$$

$$\mathcal{P} = \frac{p}{\gamma_s} + \frac{\delta(1-p)}{\gamma_a}$$

$$\mathcal{P}_v = \frac{p_v}{\gamma_{vs}} + \frac{\delta_v(1-p_v)}{\gamma_{va}}$$

$$\beta_v(t) = (1-\varepsilon)\,\beta(t)$$

$$\mathcal{R}(t) = \frac{J(t)}{\int_0^\infty J(t-\tau)g(t,\tau)d\tau}$$

$$J(t) = \frac{I(t+1/k)}{p} + \frac{I_v(t+1/k_v)}{p_v}$$

$$g(t,\tau) = \frac{\mathcal{Q}(\tau)+c(t)\mathcal{Q}_v(\tau)}{\mathcal{P}+c(t)\mathcal{P}_v}$$

# Vaccine effect in a dengue model with one serotype

## Basic reproduction number

Denguevaxia x Qdenga

$$
\begin{aligned}
S' &= -\lambda MS \\
I' &= \lambda MS - \gamma I \\
Z' &= \gamma I - \phi pZ \\
Z_v' &= \phi pZ \\
M' &= \delta I(1 - M) - \nu M
\end{aligned}
$$

$$R_0 = \frac{\sqrt{S_0}\sqrt{\delta}\sqrt{\lambda}}{\sqrt{\gamma}\sqrt{\nu}}$$

$$
\begin{aligned}
S' &= -\lambda MS - \phi pS \\
S_v' &= -\lambda MS_v(1 - \epsilon) + \phi pS \\
I' &= \lambda MS - \gamma I \\
I_v' &= \lambda M(1 - \epsilon)S_v - \gamma I_v \\
Z' &= \gamma I \\
Z_v' &= \gamma I_v \\
M' &= [\delta I + \delta(1 - \epsilon)I_v](1 - M) - \nu M
\end{aligned}
$$

For **two serotypes**, both values of $R_0$ depend on their vaccine efficacies. Comparing those values, we obtain in which scenarios Qdenga is more beneficit for population transmission and vice-versa.

$$R_0 = \frac{\sqrt{\delta}\sqrt{S_0 + S_{v0}(-1+\epsilon)^2}\sqrt{\lambda}}{\sqrt{\gamma}\sqrt{\nu}}$$

# Vaccine effect in a dengue model with one serotype

## Effective reproduction number

Denguevaxia X Qdenga

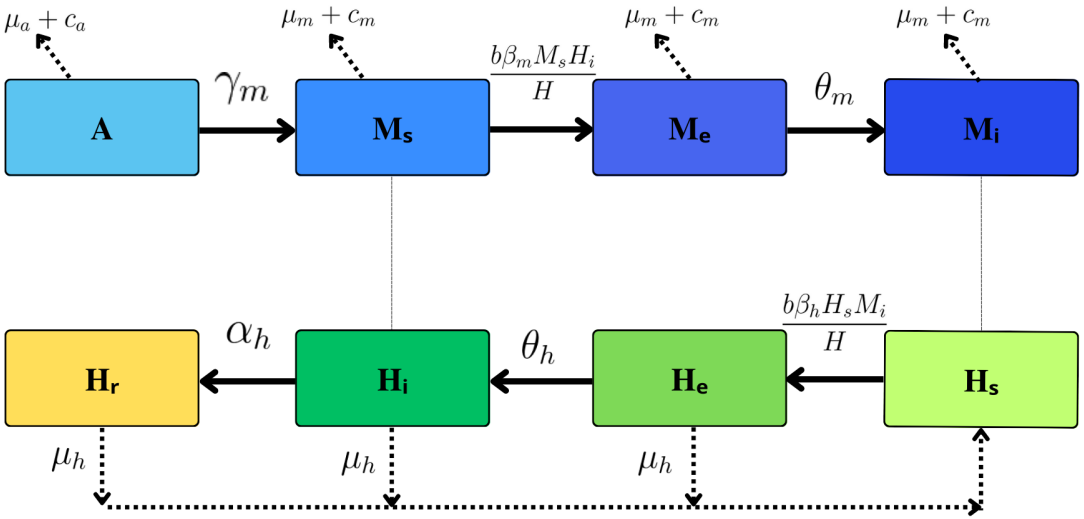
$$\mathcal{R}(t) = \begin{pmatrix} 0 & \frac{s\lambda}{\nu} \\ \frac{\delta M_s}{\gamma} & 0 \end{pmatrix} \qquad \mathcal{R}(t) = \begin{pmatrix} 0 & 0 & \frac{S\lambda}{\nu} \\ 0 & 0 & \frac{S_v(1-\epsilon)\lambda}{\nu} \\ \frac{M_s\delta}{\gamma} & \frac{M_s(1-\epsilon)\delta}{\gamma} & 0 \end{pmatrix}$$

$$R^T(t) = \sqrt{\mathcal{R}_h\mathcal{R}_m} = \sqrt{\mathcal{R}_{12}\mathcal{R}_{21}} \qquad R^T(t) = \sqrt{\mathcal{R}_{13}\mathcal{R}_{31} + \mathcal{R}_{23}\mathcal{R}_{32}}$$

$$G(\tau) = \int_0^\tau g_m(a)g_h(\tau - a)da \quad \text{leads to} \quad G(\tau) = \frac{(e^{-\tau\nu} - e^{-\tau\gamma})\gamma\nu}{\nu-\gamma}$$

$$R^T(t) = \frac{B(t)}{\int_0^\infty G(\tau)B(t-\tau)d\tau}$$

# Reproduction number for vector-borne diseases



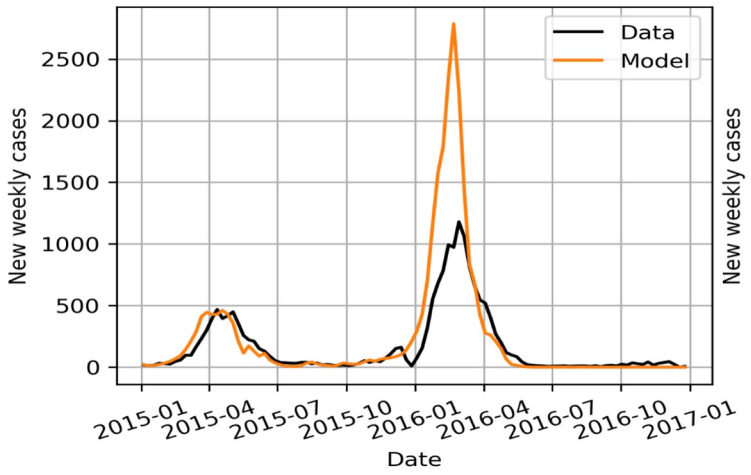

(P. et al, 2010)

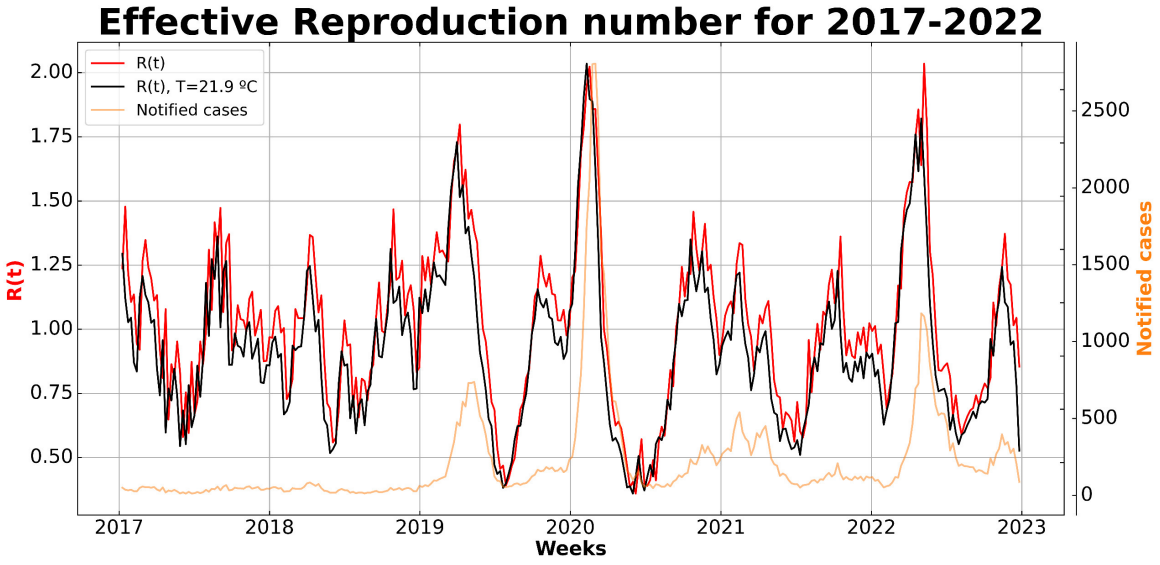
$$\mathcal{R}(t) = \frac{\mathcal{F}(t)}{\int_0^\infty g(\tau)\mathcal{F}(t-\tau)d\tau}.$$

$$g(t) = \sum_{i=1}^{4} \frac{s_1(t)s_2(t)s_3 s_4 e^{-s_i(t)t}}{\prod_{j=1, j\neq i}^{4}(s_j(t) - s_i(t))}$$

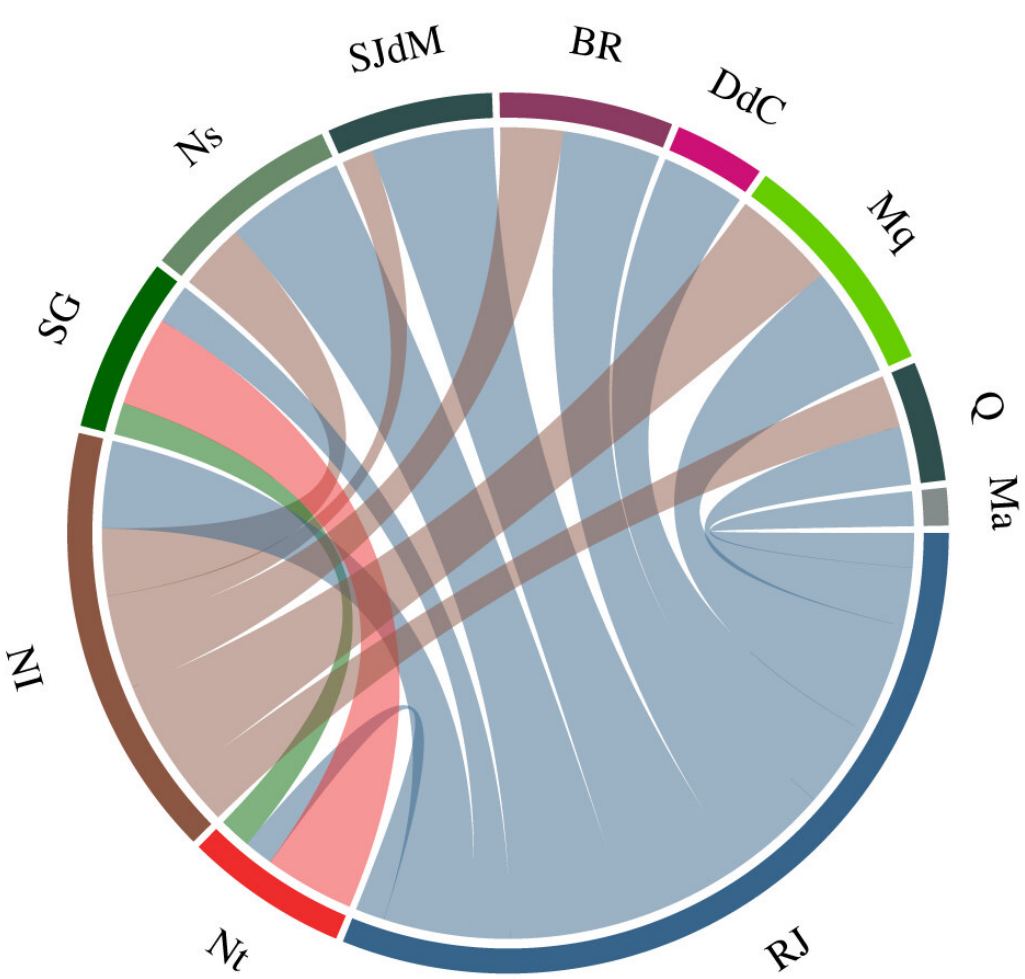
for which $s_i(t)$ varies depends on the entomological parameters that varies with temperature.

Foz do Iguaçu - Brazil

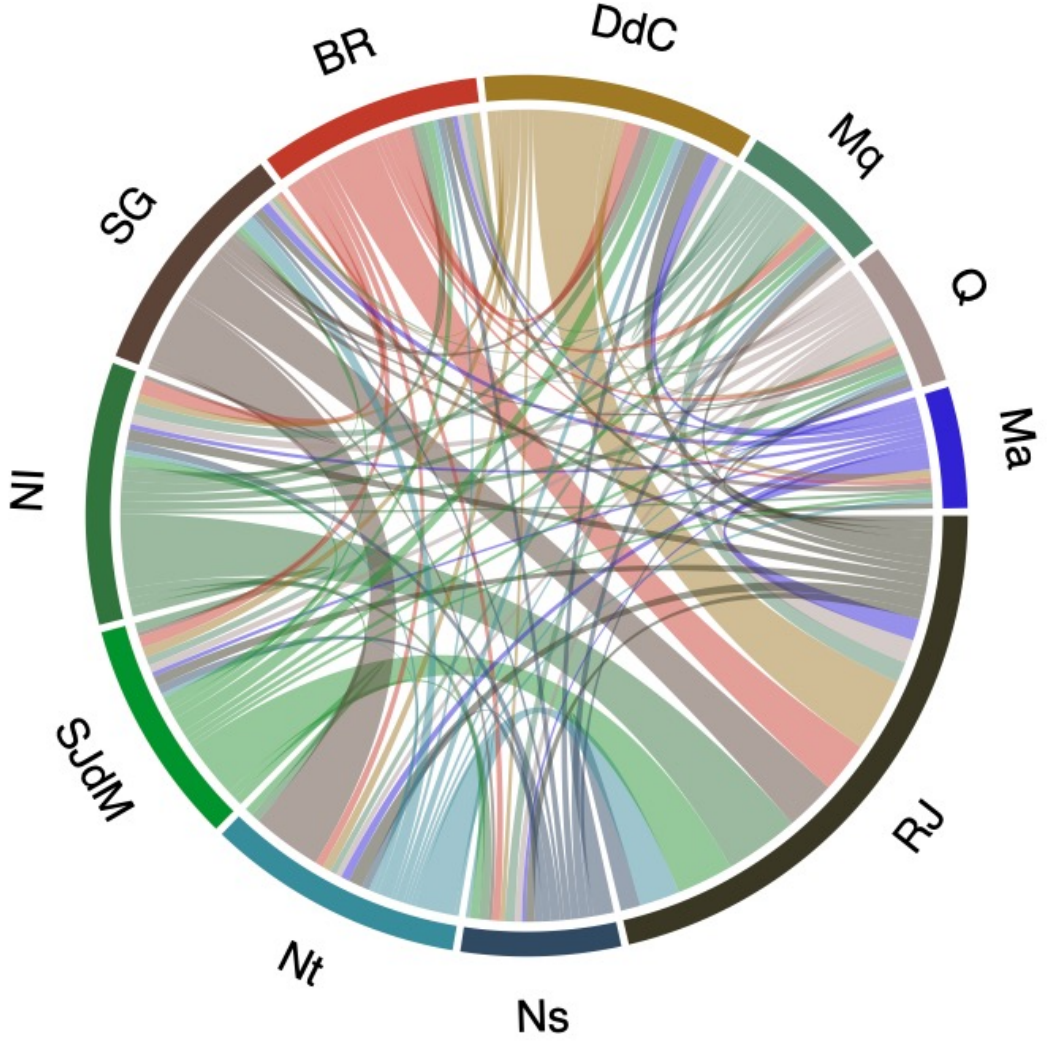


# Exported cases X Movement




Exported Cases




Total Movement

# An example for parallel progression: SIIR model

$$
\begin{aligned}
\frac{dS}{dt} &= -\frac{(\beta_1 I_1 + \beta_2 I_2)S}{N}, \\
\frac{dI_1}{dt} &= p\frac{(\beta_1 I_1 + \beta_2 I_2)S}{N} - \gamma_1 I_1, \\
\frac{dI_2}{dt} &= q\frac{(\beta_1 I_1 + \beta_2 I_2)S}{N} - \gamma_2 I_2, \\
\frac{dR}{dt} &= \gamma_1 I_1 + \gamma_2 I_2.
\end{aligned}
$$

$$
\boldsymbol{\mathcal{F}}(t) = \frac{S}{N}\begin{pmatrix} p(\beta_1 I_1 + \beta_2 I_2) \\ q(\beta_1 I_1 + \beta_2 I_2) \end{pmatrix} \longrightarrow \boldsymbol{\Omega}(t) = \frac{S}{N}\begin{pmatrix} p\beta_1 & p\beta_2 \\ q\beta_1 & q\beta_2 \end{pmatrix}
$$

$$
\boldsymbol{\mathcal{V}}(t,\tau) = \begin{pmatrix} \gamma_1 i_1(t,\tau) \\ \gamma_2 i_2(t,\tau) \end{pmatrix} \longrightarrow -\frac{\partial \boldsymbol{\mathcal{V}}}{\partial \boldsymbol{x}} = \begin{pmatrix} -\gamma_1 & 0 \\ 0 & -\gamma_2 \end{pmatrix}
$$

$$
\boldsymbol{\Gamma}(\tau) = \begin{pmatrix} e^{-\gamma_1 \tau} & 0 \\ 0 & e^{-\gamma_2 \tau} \end{pmatrix},
$$

$$
\boldsymbol{A}(t,\tau) = \frac{S}{N}\begin{pmatrix} p\beta_1\, e^{-\gamma_1\tau} & p\beta_2\, e^{-\gamma_2\tau} \\ q\beta_1\, e^{-\gamma_1\tau} & q\beta_2\, e^{-\gamma_2\tau} \end{pmatrix} \longrightarrow \boldsymbol{A} = \boldsymbol{\alpha} \otimes \overline{\boldsymbol{A}} = \begin{pmatrix} p \\ q \end{pmatrix} \bigotimes \begin{pmatrix} \frac{\beta_1 S}{N}\, e^{-\gamma_1\tau} \\ \frac{\beta_2 S}{N}\, e^{-\gamma_2\tau} \end{pmatrix}.
$$

$$
\overline{\boldsymbol{\mathcal{R}}}(t) = \int_0^\infty \overline{\boldsymbol{A}}(t,\tau)d\tau = \frac{S}{N}\begin{pmatrix} \beta_1/\gamma_1 \\ \beta_2/\gamma_2 \end{pmatrix} \longrightarrow \mathcal{R}^T(t) = \boldsymbol{\alpha}\cdot\overline{\boldsymbol{\mathcal{R}}} = \frac{S(t)}{N}\left[p\frac{\beta_1}{\gamma_1} + q\frac{\beta_2}{\gamma_2}\right].
$$

$$
\overline{g}_i(t,\tau) = \frac{\overline{A}_i(t,\tau)}{\overline{\mathcal{R}}_i(t)} \longrightarrow \begin{aligned} \overline{g}_1(\tau) &= \gamma_1 e^{-\gamma_1\tau} \\ \overline{g}_2(\tau) &= \gamma_2 e^{-\gamma_2\tau} \end{aligned} \longrightarrow g^T(t,\tau) = \frac{\sum_i \alpha_i(t)\overline{\mathcal{R}}_i(t)\ \overline{g}_i(\tau)}{\sum_i \alpha_i(t)\overline{\mathcal{R}}_i(t)} = \frac{p\beta_1\, e^{-\gamma_1\tau} + q\beta_2\, e^{-\gamma_2\tau}}{p\beta_1/\gamma_1 + q\beta_2/\gamma_2}.
$$

# Application of the method for multi-group models

Let us consider a metapopulation model for estimating the exported cases of COVID-19 between counts.

## Metropolitan region of Rio de Janeiro, Brazil