December 13, 2021

Unifying Mathematical Models, Artificial Intelligence and Digital Interactive Tools in the Fight Against COVID-19

CeMEAI
CEPID-FAPESP Centro de Ciências Matemáticas Aplicadas à Indústria

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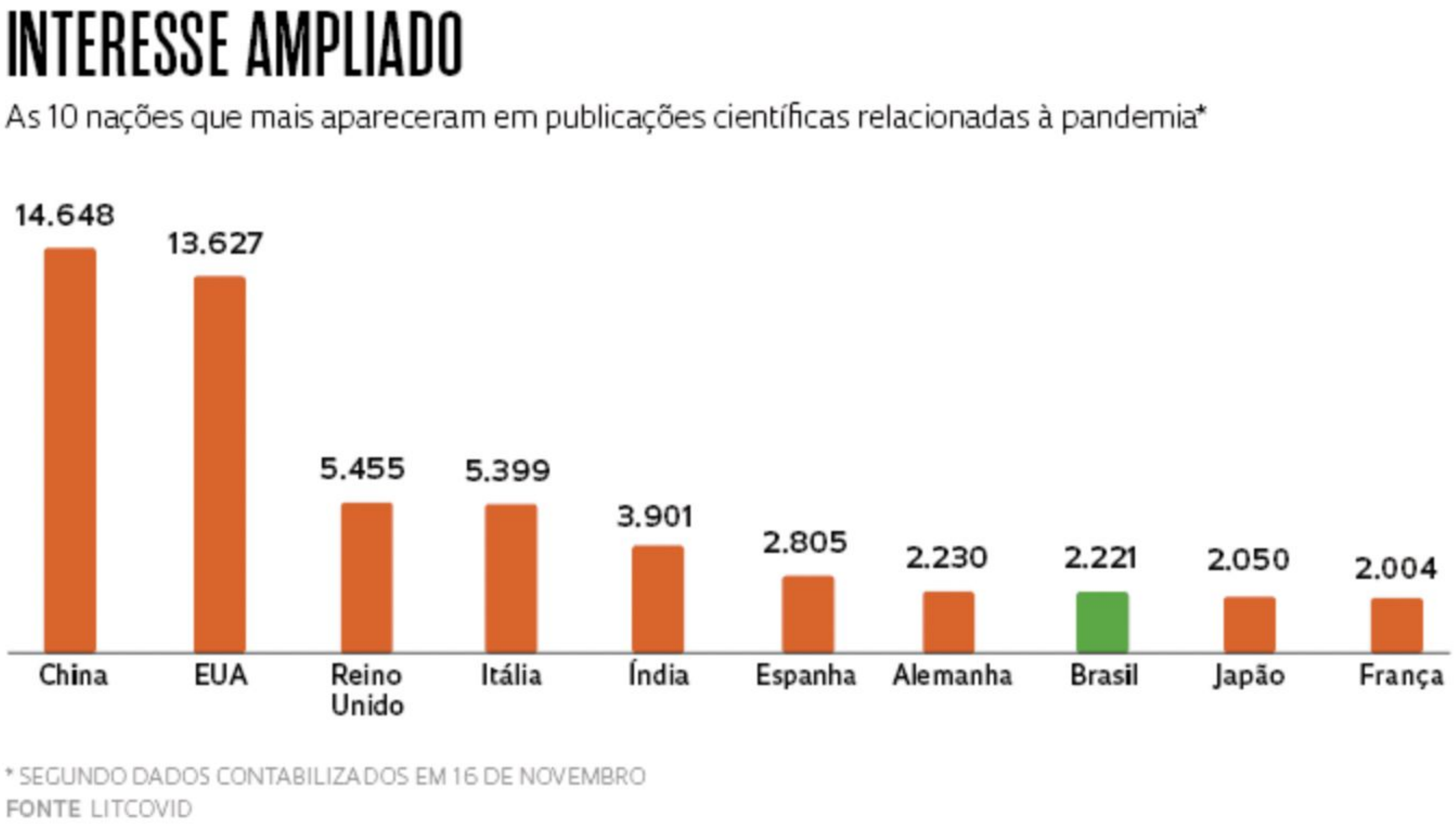
Introduction



SP Covid-19 Info Tracker

- **What is this project about**
  - The availability of a free, interactive tool created to track the Covid-19's progress in São Paulo State and Brazil.

- **What have we been working on?**
  - Daily updates on Info Tracker platform (www.spcovid.net.br).
  - Database that gathers data at municipal and regional levels.
  - Mathematical models and AI-based algorithms for forecasting scenarios of virus spreading.
  - Press collaboration, scientific reports, and research papers.

Info Tracker Team

- Research team members:

Wallace Casaca

Coordenador do Projeto

Professor da UNESP - Campus Rosana

Pesquisador do CeMEAI-USP

Marilaine Colnago

Coordenadora do Projeto

Professora na Univesp e UNESP

Pesquisadora do grupo VISER-UNESP

José Aberto Cuminato

Colaborador do Projeto

Professor da USP - Campus São Carlos

Pesquisador do CeMEAI-USP

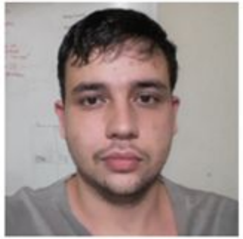
Membro Titular da Academia Brasileira de Ciências

Cássio Machiaveli Oishi

Colaborador do Projeto

Professor da UNESP - Campus Presidente Prudente

Pesquisador do CeMEAI-USP

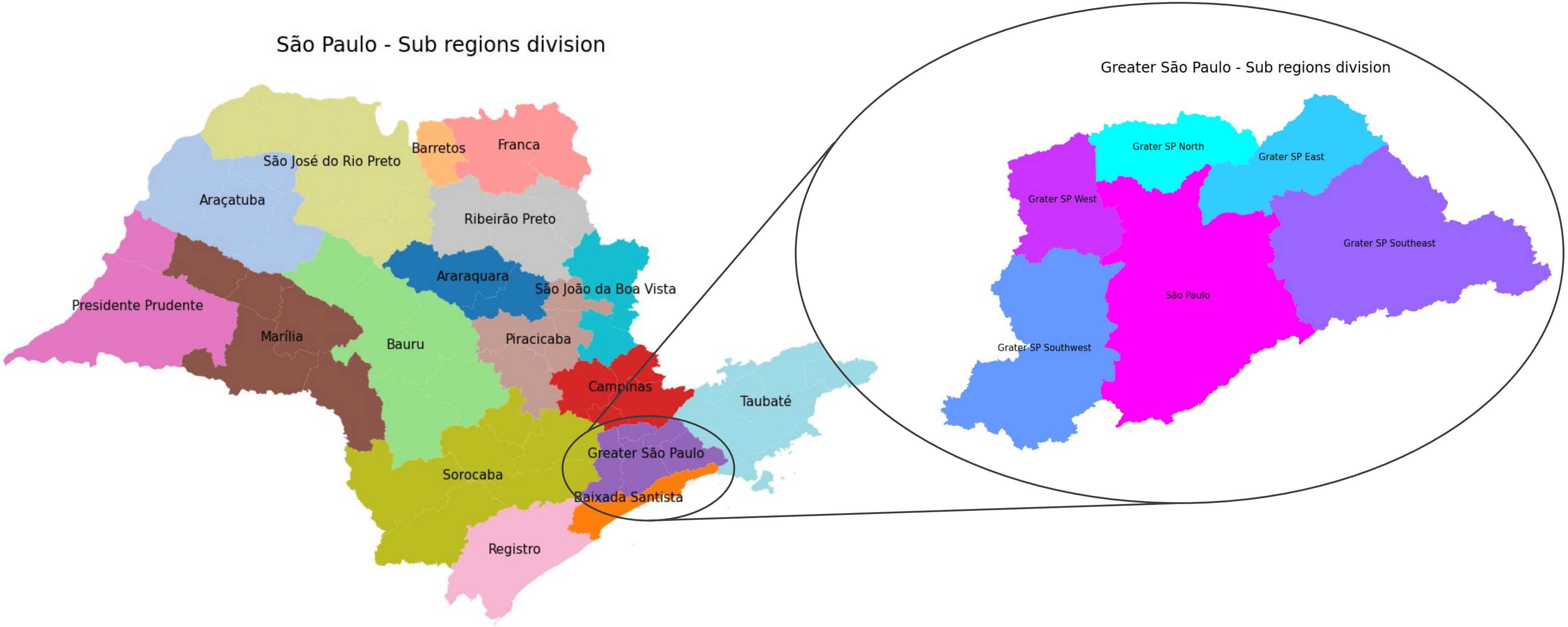


Fábio Vinicius Amaral

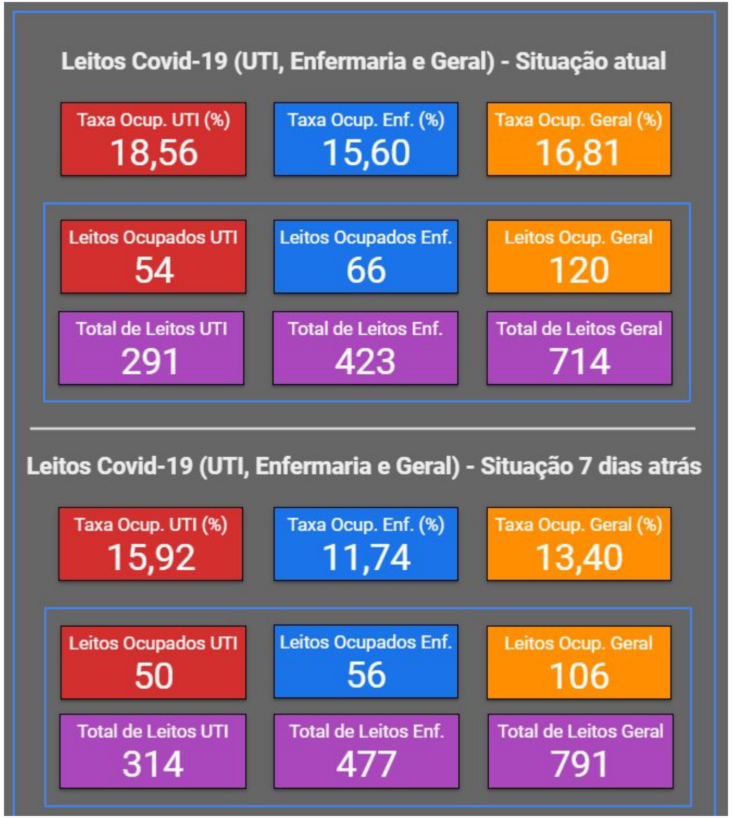
Colaborador do Projeto

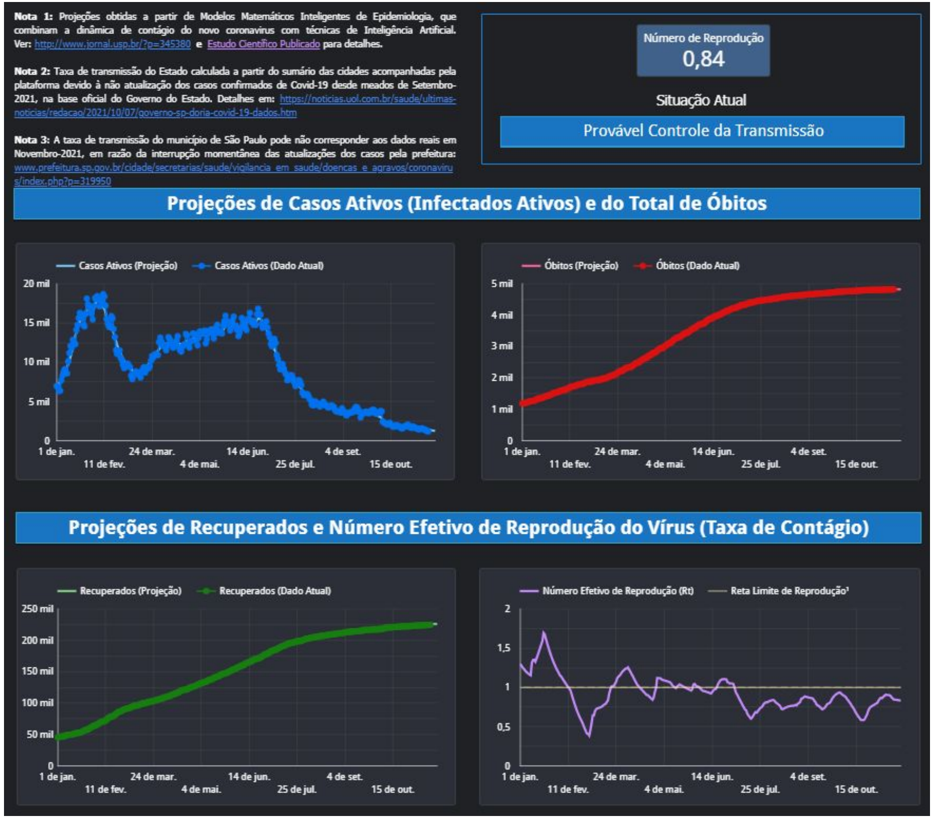
Pesquisador do Programa de Pós-Graduação em Matemática Aplicada e Computacional UNESP

Info Tracker: SP Subregions



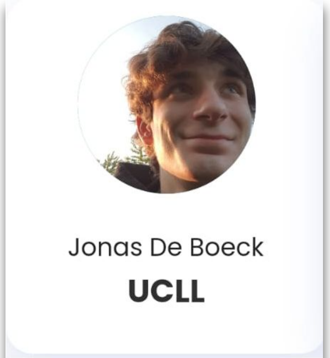
Info Tracker Page

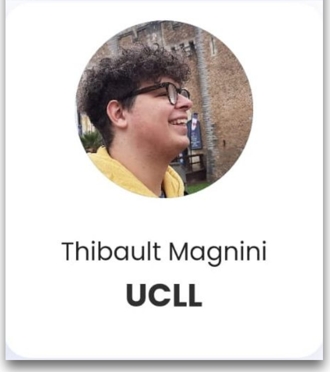


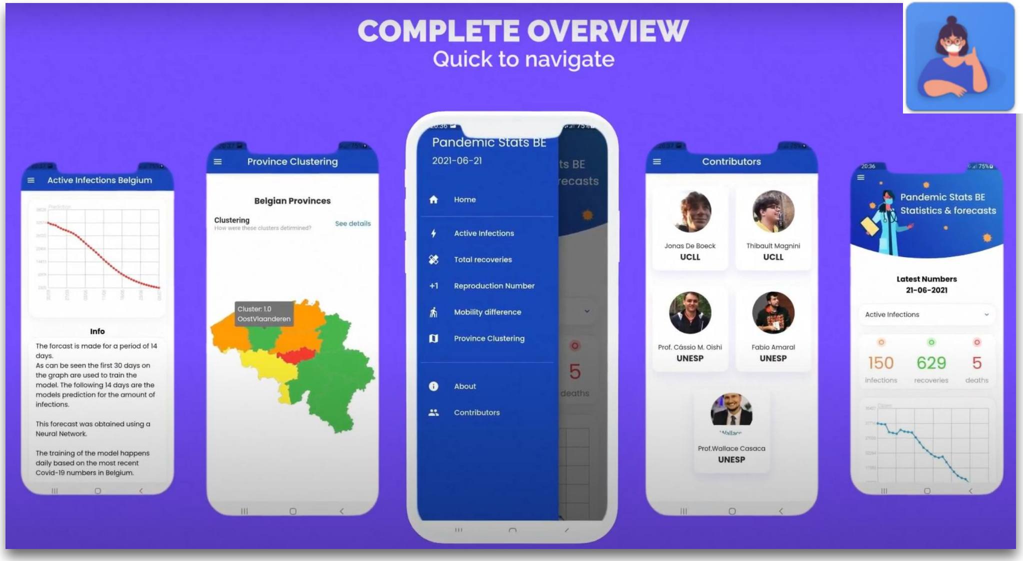


Info Tracker: International Collaboration

- **Team: members abroad (Belgium)**







Pandemic Stats BE

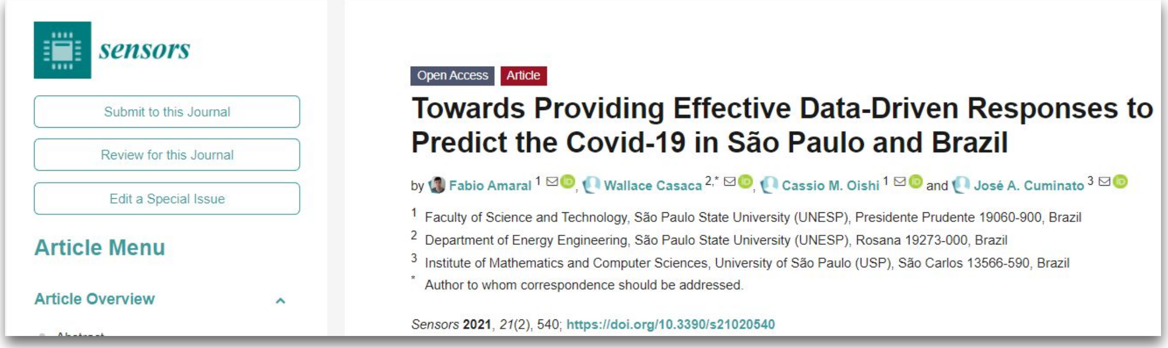
Magnini & De Boeck Development Medical

Google Play

"CEPID-FAPESP CeMEAI: App Pandemic Stats BE é desenvolvido com apoio dos pesquisadores do CEPID-FAPESP CeMEAI" (Jully 23, 2021)

Link:
http://www.saocarlos.usp.br/app-pandemic-stats-be-e-desenvolvido-com-apoio-dos-pesquisadores-do-cemeai/

Computing time-series forecasts and assessing the vaccination progress in Brazil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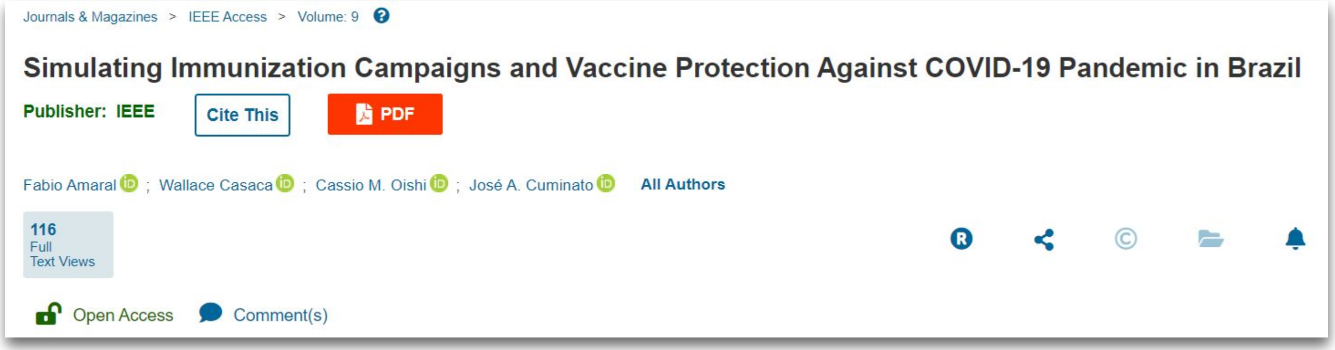
Towards Providing Effective Data-Driven Responses to Predict the Covid-19 in São Paulo and Brazil

by Fabio Amaral [1], Wallace Casaca [2,*], Cassio M. Oishi [1] and José A. Cuminato [3]

1 Faculty of Science and Technology, São Paulo State University (UNESP), Presidente Prudente 19060-900, Brazil
2 Department of Energy Engineering, São Paulo State University (UNESP), Rosana 19273-000, Brazil
3 Institute of Mathematics and Computer Sciences, University of São Paulo (USP), São Carlos 13566-590, Brazil
* Author to whom correspondence should be addressed.

Sensors **2021**, *21*(2), 540; https://doi.org/10.3390/s21020540

Paper available at: https://www.mdpi.com/1424-8220/21/2/540/htm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Simulating Immunization Campaigns and Vaccine Protection Against COVID-19 Pandemic in Brazil

Publisher: IEEE

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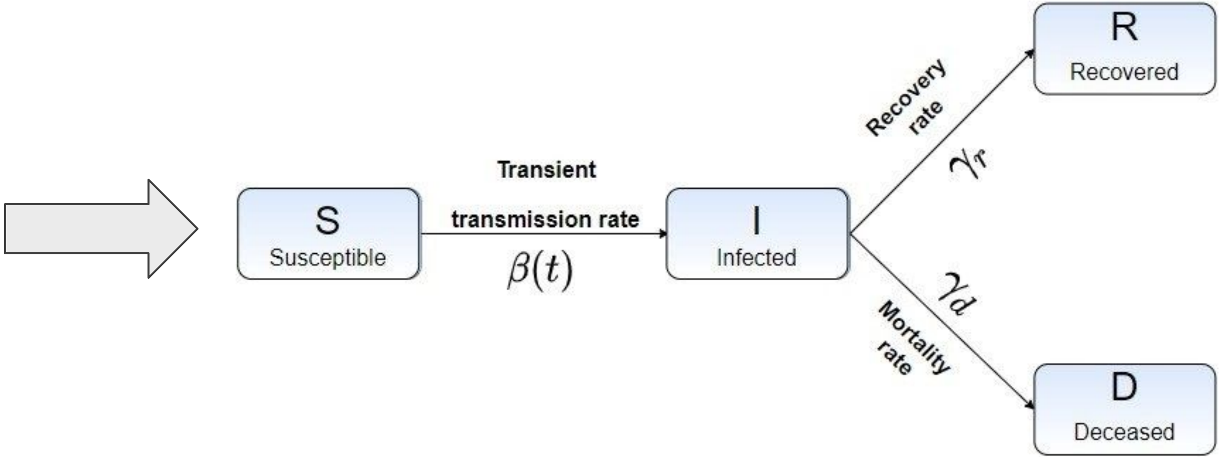
The Proposed Epidemiological Model

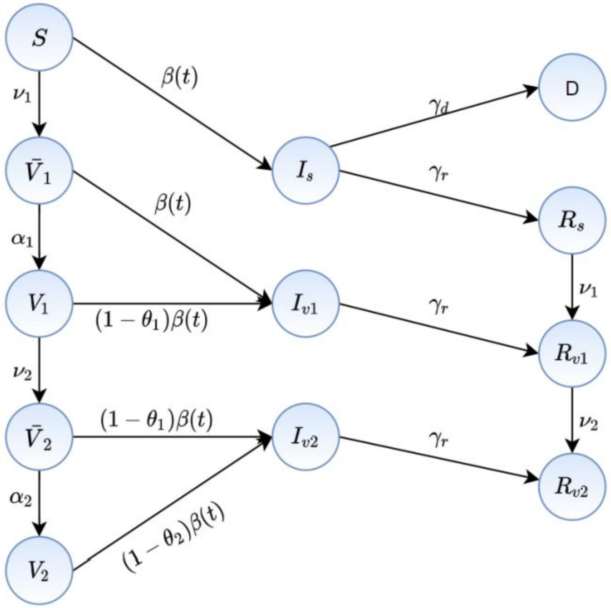
$$\frac{dS}{dt} = -\beta SI,$$
$$\frac{dI}{dt} = \beta SI - (\gamma_r + \gamma_d)I,$$
$$\frac{dR}{dt} = \gamma_r I,$$
$$\frac{dD}{dt} = \gamma_d I.$$



- In our mathematical approach a normalized total population (N = S+I+R+D = 1) is taken in the ODE system

The Proposed Epidemiological Model

Notation	Description
$S(t)$	Number of susceptible at time t
$I_s(t)$	Number of infected from susceptible subgroup at time t
$I_{v,j}(t)$	Number of infected from subgroup V_j, $j = 1, 2$ at time t
$I(t)$	Sum of all subgroups I_j at time t
$R_j(t)$	Number of recovered from subgroup $j = s, v_1, v_2$ at time t
$R(t)$	Sum of all subgroups R_j at time t
$D(t)$	Number of deaths at time t
$\bar{V}_i(t)$	Number of vaccinated but not yet immunized at time t, i = 1,2 doses
$V_i(t)$	Number of immunized at time t, i = 1,2 doses
$\beta(t)$	Transient transmission rate
$\beta_{\text{net}}(t)$	Prediction for the transmission rate at time t
γ_r	Rate of recovered
γ_d	Rate of mortality
ν_1 and ν_2	First and second dose vaccination rates, respectively
θ_1 and θ_2	First and second dose efficacies, respectively
α_i	Time delay for vaccine dose effectiveness, i = 1,2 doses
$R_t(t)$	Time-dependent effective reproduction number



Pipeline overview of the SIR-inspired model (a SIR variant).

The Proposed Epidemiological Model

- The parameters γ_r and γ_d account for the rates of recovered and mortality, respectively.

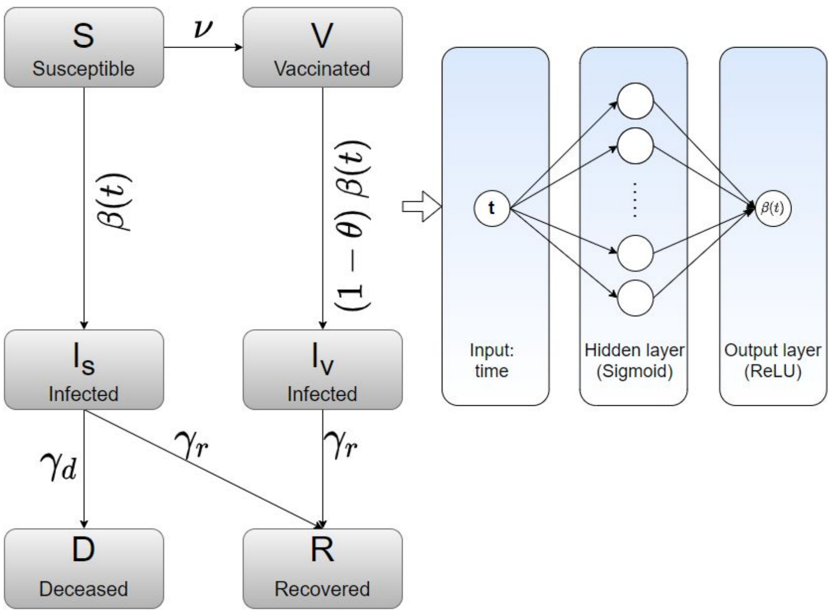
- In our formulation, we assume that the transmission rate has a transient trajectory, i.e., β = β(t). As a consequence, we get a time-dependent reproduction number on the form:

$$R_t(t) = \frac{\beta(t)}{\gamma_r + \gamma_d} S \qquad \text{(SIRD Model)}$$

$$R_t(t) = \frac{\beta(t)}{\gamma_r} \left[\bar{V}_1 + (1-\theta_1)(V_1 + \bar{V}_2) + (1-\theta_2)V_2\right] + \frac{\beta(t)}{\gamma_r + \gamma_d} S \qquad \text{(SVIRD Model)}$$

- The so-called effective reproduction number, $R_t(t)$, is an important epidemiological metric that quantifies the average number of new infections arising from a primary infected individual in the population.

Learning the transmission rate



- Since the actual expression of $\beta(t)$ is unknown, we use a neural network for estimating it
- The training process determines this function by tuning the neural network weights

Learning the transmission rate

- The neural network for estimating $\beta(t)$ is a function

$$\beta_{net}(t) = f_2(\mathbf{W}^{(2)}\mathbf{f}_1(\mathbf{W}^{(1)}t + \mathbf{b}))$$

$$f_1(x) = \frac{1}{1+e^{-x}} \text{ (Sigmoid function)}$$

$$\mathbf{f}_1 : \mathbb{R}^N \to \mathbb{R}^N, [x_i] \mapsto [f_1(x_i)]$$

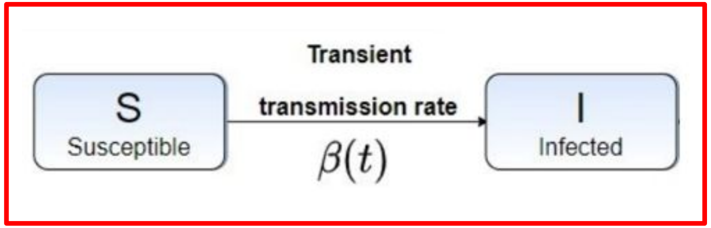
$$f_2(x) = 0.001 + \max\{0, x\} \text{ (adpted ReLU)}$$

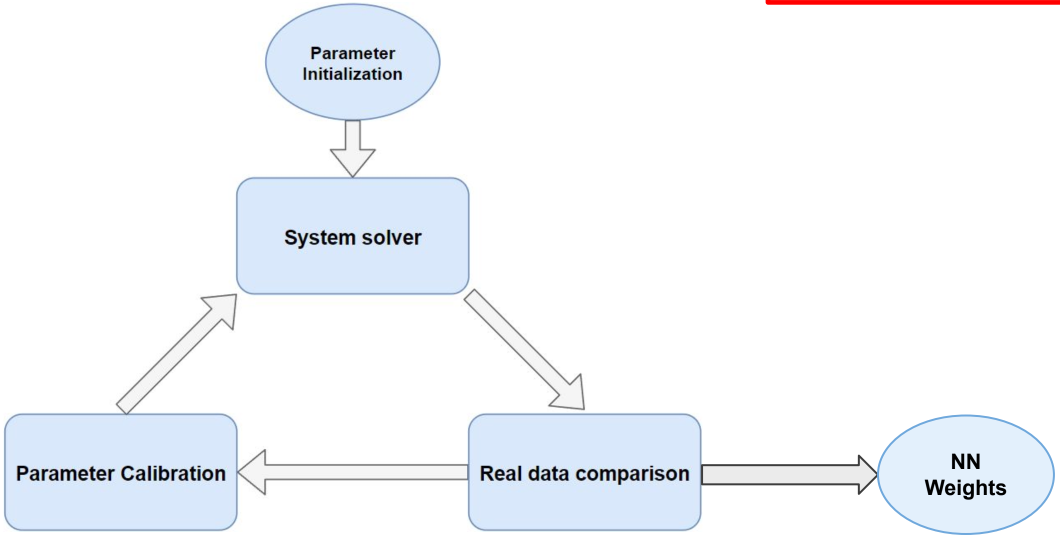
$$\mathbf{W}^{(1)}, \mathbf{b} \in \mathbb{R}^{N\times 1}, \mathbf{W}^{(2)} \in \mathbb{R}^{1\times N}$$

- The NN weights $\{\mathbf{W}^{(1)}, \mathbf{W}^{(2)}, \mathbf{b}\}$ are optimized alongside other equation parameters so the numerical solution fits the real data

Learning the transmission rate

The use of Artificial Neural Network (ANN) to impose a transition behavior for





The proposed scheme to estimate the $\beta(t)$ function.

Learning the transmission rate

- Once the weights are defined, we can use a numerical solver for estimating the variables

$$\boxed{\frac{dS}{dt} = -\beta(t)SI,} \implies \boxed{S(t_{n+1}) = S(t_n) - \Delta t\, \boxed{\beta_{net}(t_n)}\, S(t_n)I(t_n)}$$

$$\frac{dI}{dt} = \beta(t)SI - (\gamma_r + \gamma_d)I,$$

$$\frac{dR}{dt} = \gamma_r I,$$

$$\frac{dD}{dt} = \gamma_d I.$$

$$\Downarrow$$

$$\boxed{\beta_{net}(t) = f_2(\mathbf{W}^{(2)}\mathbf{f}_1(\mathbf{W}^{(1)}t + \mathbf{b}))}$$

- In our implementation we used the LSODA solver implemented in python

Parameter Calibration

$$\underset{W,b,\gamma_r,\gamma_d}{\arg\min}\ \mathcal{L}(\beta_{\text{net}}(t), \gamma_r, \gamma_d),$$

Onde

$$\mathcal{L}(\beta_{net}(t), \gamma_r, \gamma_d, \nu_1, \nu_2) = \sum_{l \in L} l,$$

$$L = \{l_I, l_R, l_D, l_{v1}, l_{v2}, l_{sum}\},$$

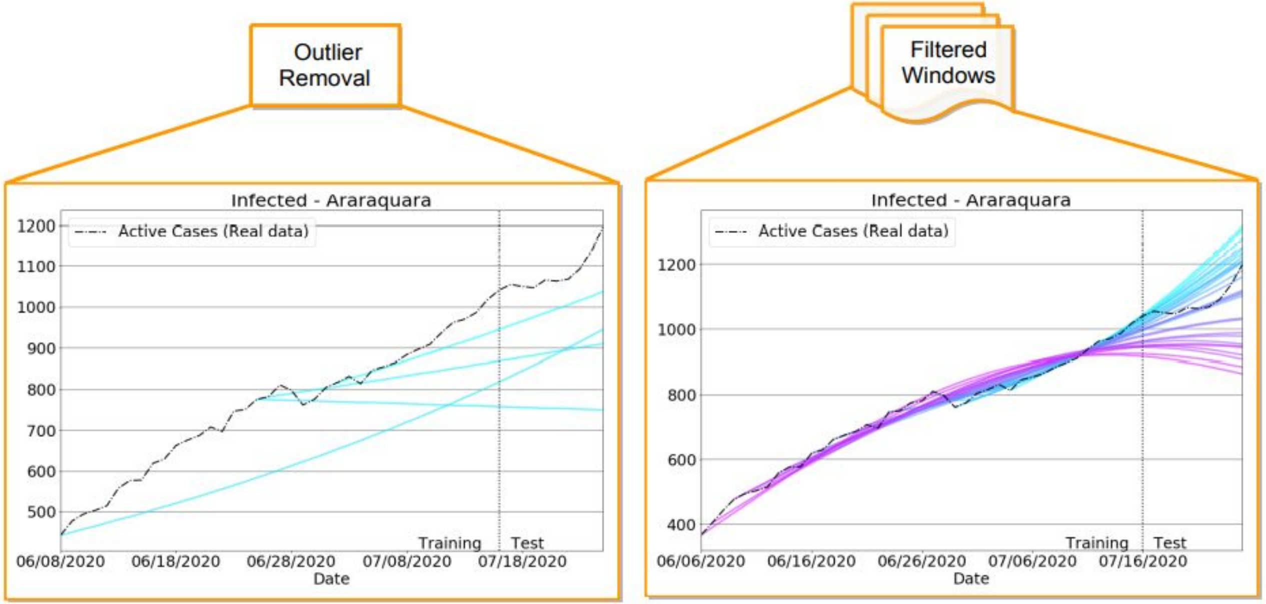
$$l_I = \frac{1}{M}\sum_{i=0}^{M}[\log(I_i) - \log(\tilde{I}_i)]^2, \quad l_R = \frac{1}{M}\sum_{i=0}^{M}[\log(R_i) - \log(\tilde{R}_i)]^2,$$

$$l_D = \frac{1}{M}\sum_{i=0}^{M}[\log(D_i) - \log(\tilde{D}_i)]^2, \quad l_{v1} = \frac{1}{M}\sum_{i=0}^{M}[\log(V_{1,i}) - \log(\tilde{V}_{1,i})]^2,$$

$$l_{v2} = \frac{1}{M}\sum_{i=0}^{M}[\log(V_{2,i}) - \log(\tilde{V}_{2,i})]^2, l_{sum} = \frac{1}{M}\sum_{i=0}^{M}[\log(\tilde{T}_i)]^2$$

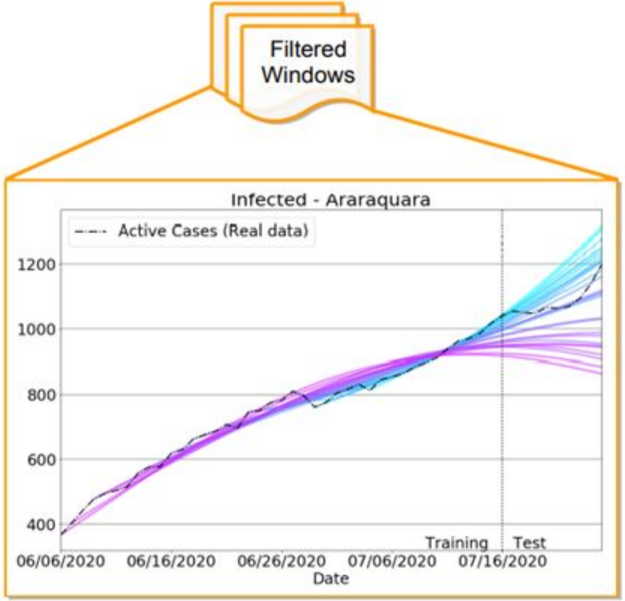
Dealing with ill-behaved data portions

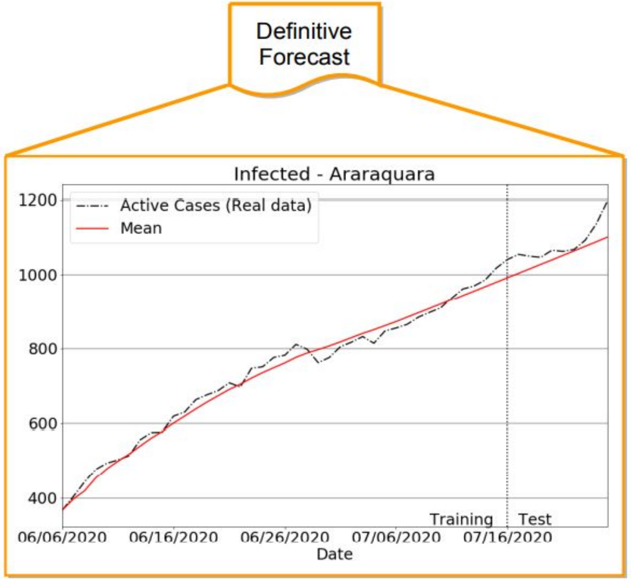
- Improving the data fitting capability x ill-behaved data portions



(Left) The selected ill-behaved training periods (discarded trainings) and (Right) training results that have passed the error criteria for good training.

Dealing with ill-behaved data portions

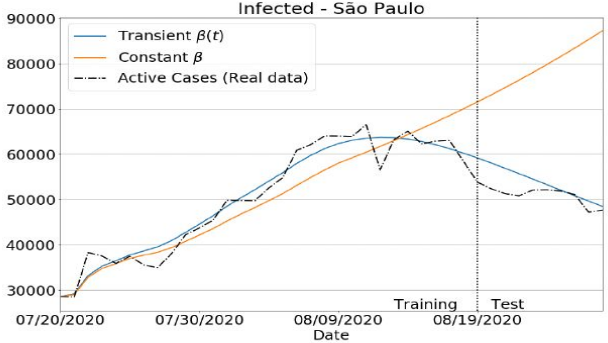




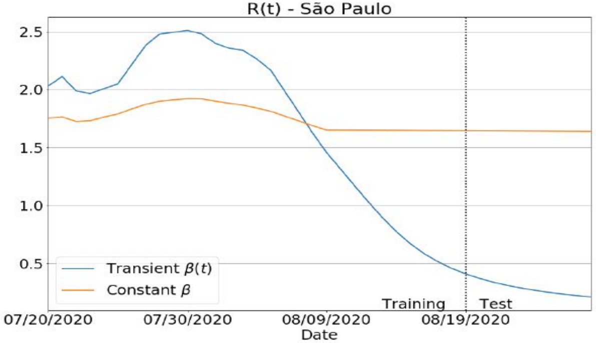
Computing geometric mean w.r.t. well-behaved predictions (left) as the definitive prediction (right plot).

Results and Simulations

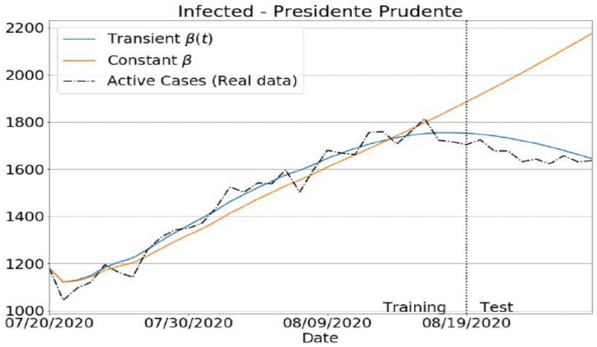
Predicting COVID-19 in São Paulo



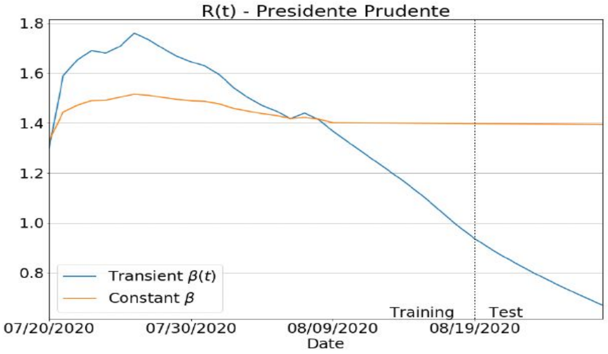
(a) Active cases



(b) $R_0(t)$



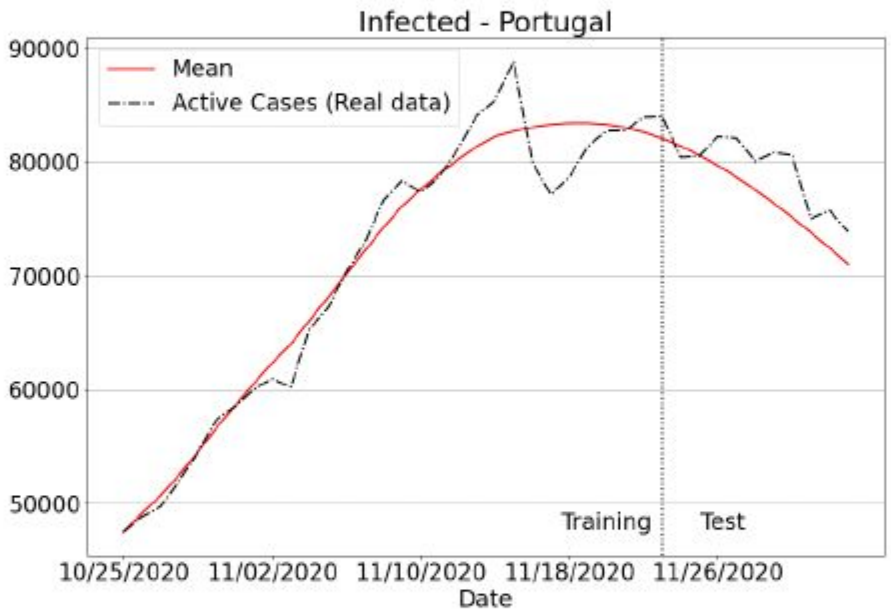
(c) Active cases

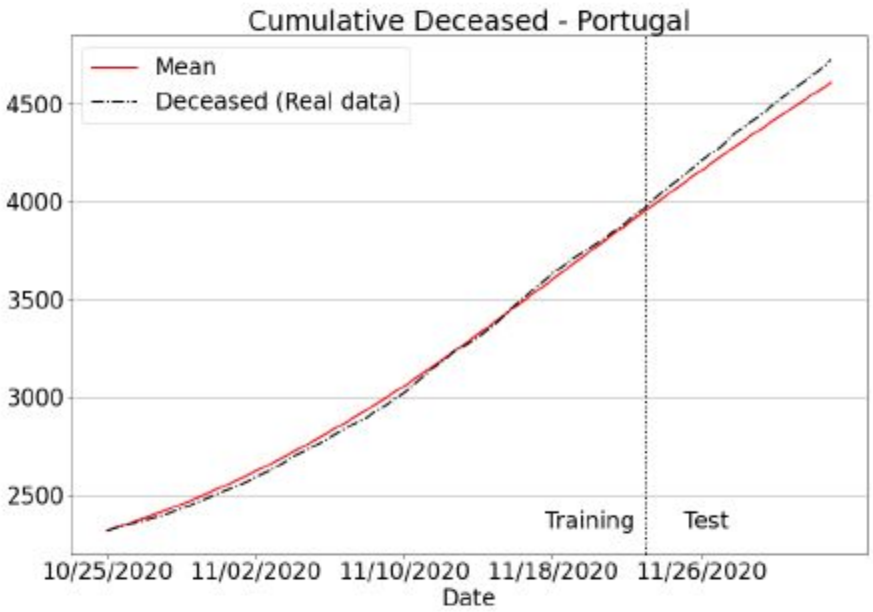


(d) $R_0(t)$

The Transient Behavior of Transmission Rate

The spread for different data set



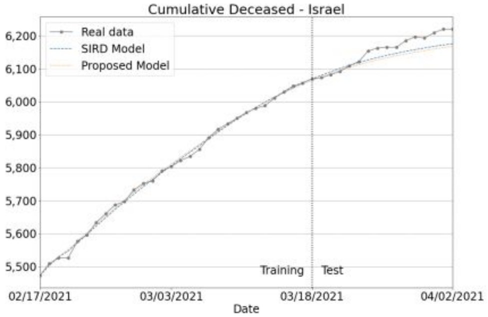


Simulating vaccination campaigns

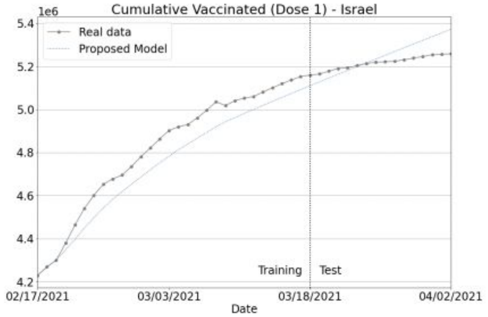
1. **General goal:** Measuring the impact of the vaccination roll-out, focusing on different vaccines and immunization speed rates.
2. **Regions/countries studied**:
    1. Israel,
    2. Serrana (São Paulo State's town)
    3. São Paulo State
    4. Brazil

Validation with real vaccination data

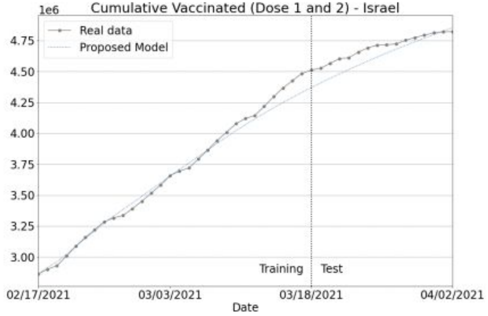
(a) Cases



(b) Deaths

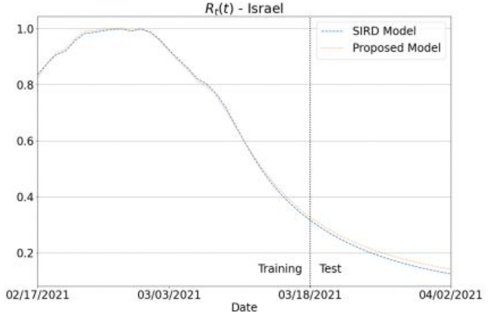


(c) Vaccinated people (dose 1).



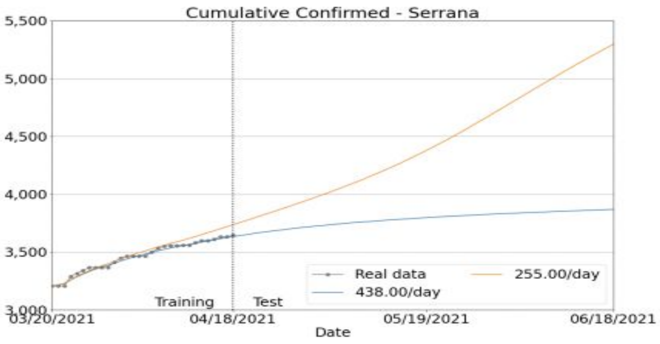
(d) Vaccinated people (doses 1 and 2).

(e) Active cases

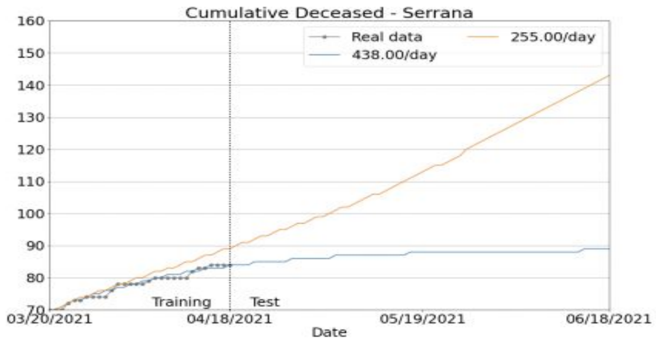


(f) $R_t(t)$

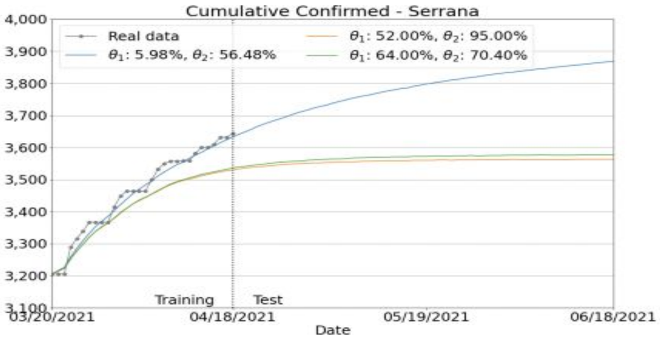
Serrana's town scenarios results



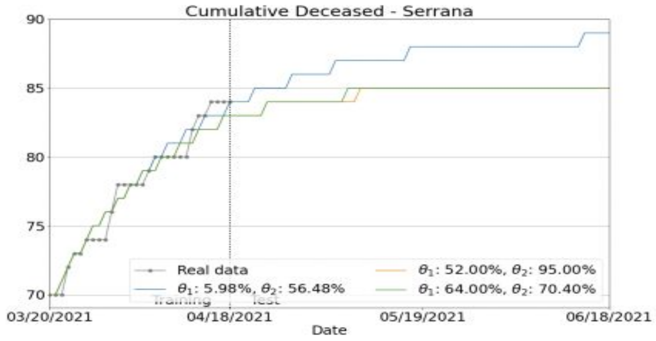
(a) Cases



(b) Deaths



(d) Cases



(e) Deaths

Parameters adopted to run the simulations

Vaccine	Efficacy Dose 1	Efficacy Dose 2	Efficacy Delay
Coronavac (Sinovac)	$\theta_1 = 5.98\%$	$\theta_2 = 66.48\%$	$\alpha = \frac{1}{14}$
Pfizer (BioNTech)	$\theta_1 = 52.00\%$	$\theta_2 = 95.00\%$	$\alpha = \frac{1}{21}$
AstraZeneca (Oxford)	$\theta_1 = 64.00\%$	$\theta_2 = 70.40\%$	$\alpha = \frac{1}{14}$

Efficacy adopted for specific vaccine types

(For details about the selected vaccine efficacies, see the full paper).

Vaccination scenarios by varying the vaccine efficacy

Coronavac	AstraZeneca	Pfizer	Resultant Efficacy	Color
80%	20%	0%	$\theta_1 = 18\%$ $\theta_2 = 59\%$	blue (baseline)
40%	30%	30%	$\theta_1 = 37\%$ $\theta_2 = 72\%$	orange
100%	0%	0%	$\theta_1 = 6\%$ $\theta_2 = 56\%$	purple
0%	100%	0%	$\theta_1 = 64\%$ $\theta_2 = 70\%$	red
0%	0%	100%	$\theta_1 = 52\%$ $\theta_2 = 95\%$	green

Mixed vaccine proportions and their resultant effectiveness used to run the experiments.

Vaccination scenarios by varying the vaccine efficacy

Coronavac	AstraZeneca	Pfizer	Resultant Efficacy	Color
80%	20%	0%	$\theta_1 = 18\%$ $\theta_2 = 59\%$	blue (baseline)
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0%	100%	0%	$\theta_1 = 64\%$ $\theta_2 = 70\%$	red
0%	0%	100%	$\theta_1 = 52\%$ $\theta_2 = 95\%$	green

Mixed vaccine proportions and their resultant effectiveness used to run the experiments.

Comparing vaccine efficacies by assuming the baseline scenario observed in Brazil during March 2021

Forecast Period:

- Abril – June 2021

PFIZER

ASTRAZENECA

CORONAVAC

Efficacy	Cases		Deaths	
	São Paulo	**Brazil**	**São Paulo**	**Brazil**
Baseline	1,395,106	4,217,642	66,339	191,676
$\theta_1 = 37\%$ $\theta_2 = 72\%$ (Orange)	1,241,105 (-11.0%)	3,955,485 (-6.2%)	62,326 (-6.0%)	186,396 (-2.8%)
$\theta_1 = 52\%$ $\theta_2 = 95\%$ (Green)	1,137,064 (-18.5%)	3,783,811 (-10.3%)	59,605 (-10.2%)	182,920 (-4.6%)
$\theta_1 = 64\%$ $\theta_2 = 70\%$ (Red)	1,113,243 (-20.2%)	3,713,921 (-11.9%)	58,743 (-11.5%)	181,273 (-5.4%)
$\theta_1 = 6\%$ $\theta_2 = 56\%$ (Purple)	1,474,225 (+5.7%)	4,353,357 (+3.2%)	68,407 (+3.1%)	194,424 (+1.4%)

Qualitative results: cumulative cases and deaths in Brazil

PFIZER

CORONAVAC

ASTRAZENECA

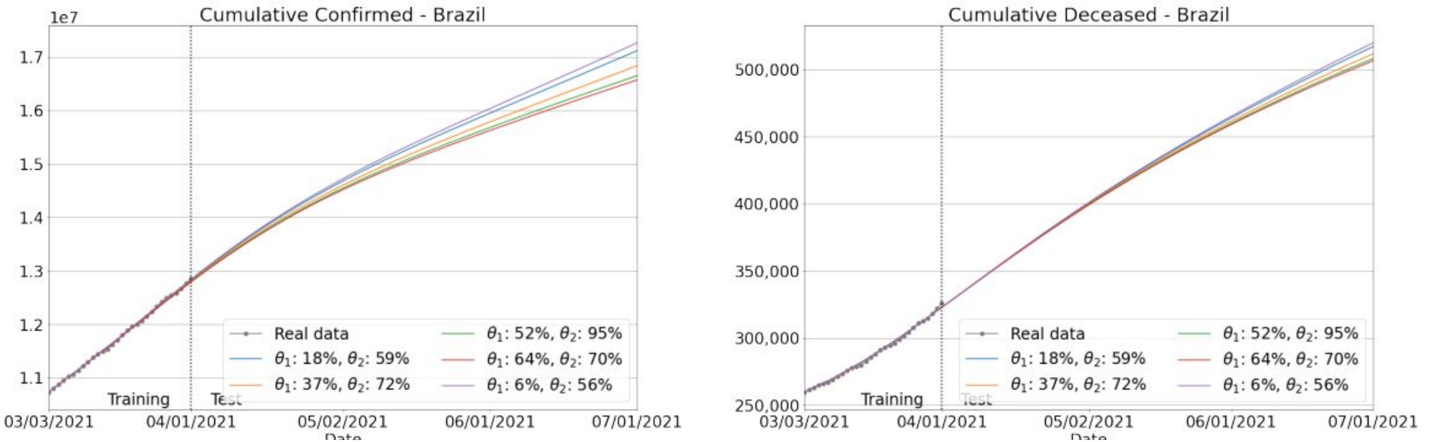


Figure: Assessing different vaccine efficacies concerning Covid-19 cases (left) and deaths (right) in Brazil (period: April to June 2021)

The impact of increasing the immunization rate

- **Simulations with different vaccination rates vs. the real immunization roll-out as observed in March 2021 in the State of SP and Brazil**:
  - Significant reductions were found in the number of new cases and deaths during

Campanhas de Vacinação	Casos Confirmados Covid-19		Óbitos por Covid-19	
	Estado de SP	Brasil	Estado de SP	Brasil
Referências para as comparações (campanhas atuais, de SP e Brasil, com dados de vacinação compilados de janeiro – março de 2021)	1,395,106	4,217,642	66,339 Real: 56.793 MAPE: 16,81%	191,676 Real: 189,505 MAPE: 1,15%
Campanhas com projeções (velocidade de vacinação aumentadas em relação à campanha descrita acima, isto é, aplicando-se em torno de 2.2 milhões de doses diárias por dia – Brasil –, e 296 mil doses diárias no Estado de SP)	925,808 (-33,6%) (casos evitados no período: 469,298)	3,303,194 (-21,7%) (casos evitados no período: 914,448)	36,511 (-45%) (óbitos evitados no período: 29,828)	135,479 (-29,3%) (óbitos evitados no período: 56,197)

Table: Comparison of vaccination campaigns (simulations) in Brazil and State of SP considering a three-month projection period (April – June 2021).

Increasing the immunization rate vs vaccine types

Eficácia resultante (ver Tabela 5)	Casos Confirmados Covid-19		Óbitos por Covid-19	
	Estado de SP	Brasil	Estado de SP	Brasil
Referência p/ comparações (campanha atual, SEM aumentar a velocidade de vacinação	1,395,106	4,217,642	66,339	191,676
$\theta_1 = 18\%$ $\theta_2 = 59\%$ (campanha atual, mas com veloc. de vac. aumentada)	925,808 (-33,6%)	3,303,194 (-21,7%)	36,511 (-45%)	135,479 (-29,3%) (vidas salvas: 56,197)
$\theta_1 = 52\%$ $\theta_2 = 95\%$ (somente Pfizer, com veloc. de vac. aumentada)	538,536 (-61,4%)	2,404,922 (-43%)	30,648 (-53,8%)	124,115 (-35,2%) vidas salvas: 67,561)
$\theta_1 = 64\%$ $\theta_2 = 70\%$ (somente AstraZeneca, com veloc. de vac. aumentada)	610,734 (-56,2%)	2,549,897 (-39,5%)	31,348 (-52,7%)	125,126 (-34,7%) vidas salvas: 66,550)
$\theta_1 = 6\%$ $\theta_2 = 56\%$ (somente Coronavac, com veloc. de vac. aumentada)	1,026,201 (-26,4%)	3,524,649 (-16,4%)	38,043 (-42,7%)	138,380 (-27,8%) vidas salvas: 53,296)

Table: Comparisons of different vaccines in Brazil and São Paulo State considering a fast vaccination roll-out (period: April-June 2021).

Qualitative results: cumulative cases and deaths in Brazil

PFIZER

CORONAVAC

ASTRAZENECA

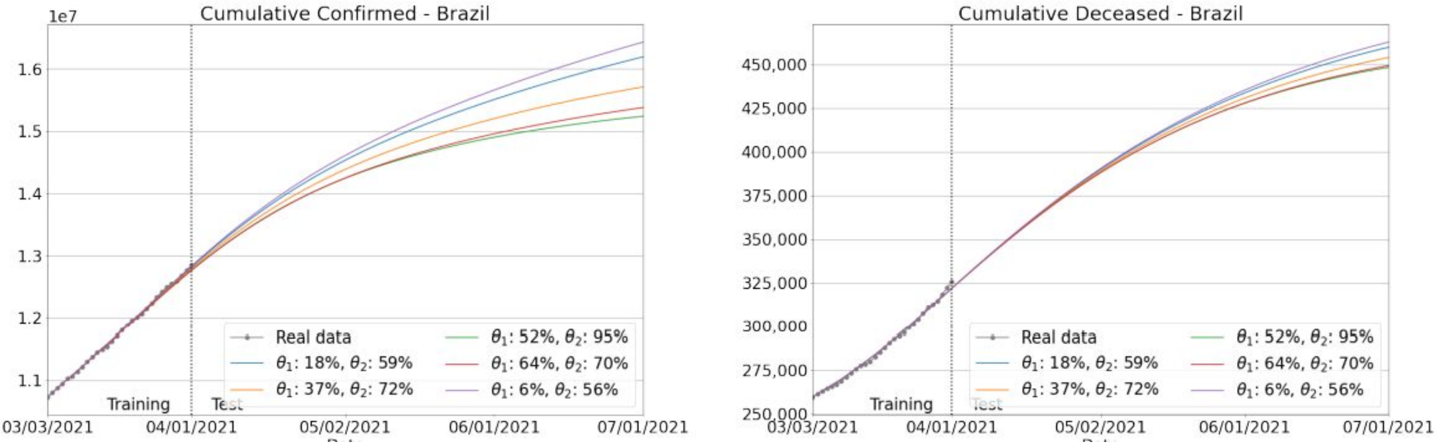


Figure: Assessing different immunization speed rates: (left) cases and (right) deaths in Brazil (period: April to June 2021).

Concluding Remarks

1. If more people had been vaccinated more quickly, 60,000 deaths could have been avoided (period: April – June 2021).

2. There are no significant differences between vaccines (in terms of efficacy) since more people are getting vaccinated in a shorter time span (**vaccinating faster matters more than vaccine efficacy**!).

3. Our methodology can be successfully used to perform numerical investigation concerning the recent strategy of mix-and-match vaccination.

Next steps

Omicron: Three vaccine doses key for protection against variant

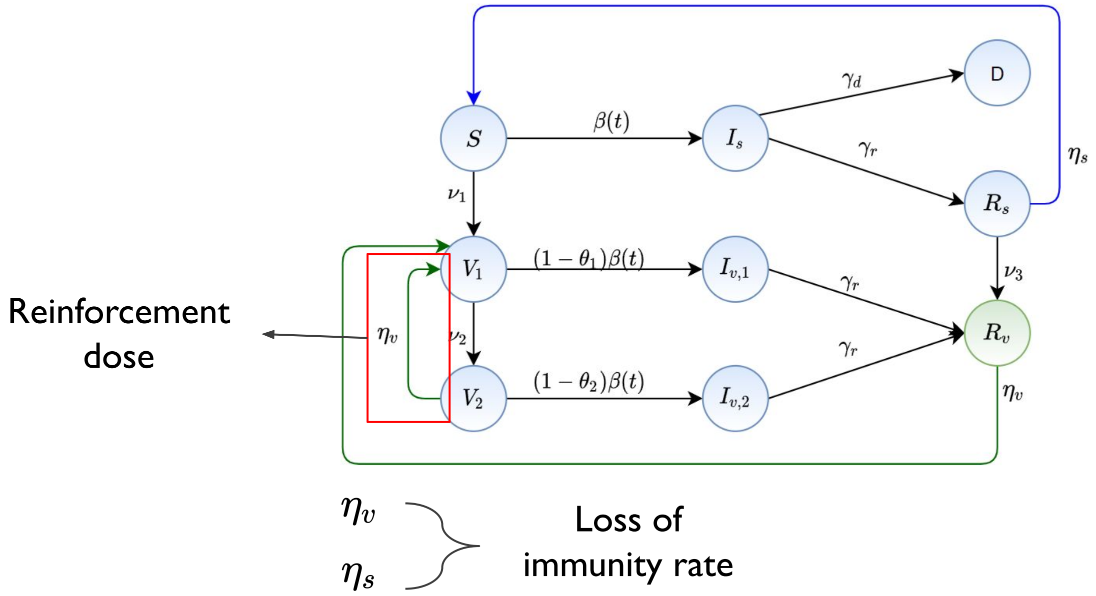
By James Gallagher
Health and science correspondent

2 days ago | Comments

Coronavirus pandemic

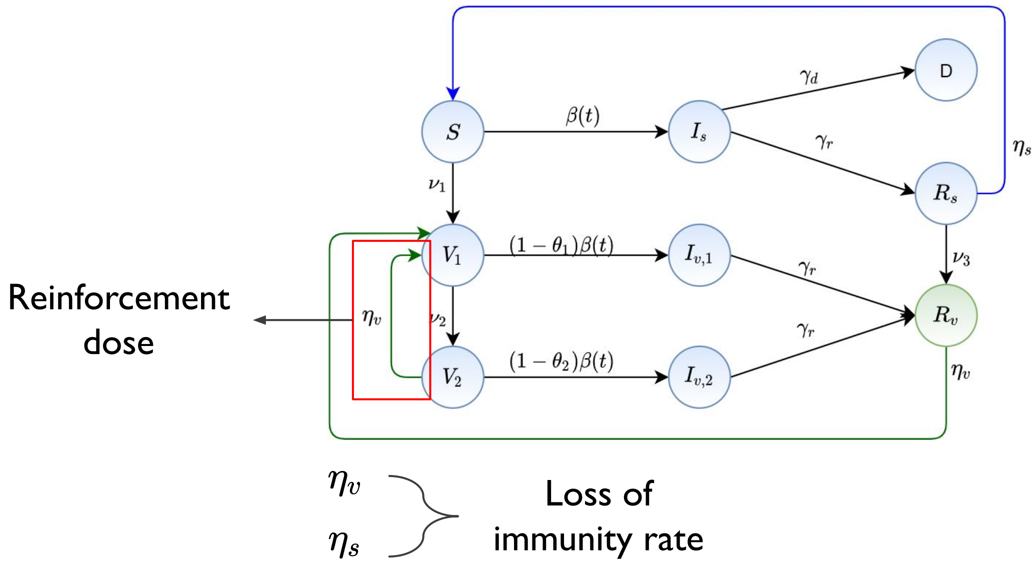
Model Adaptation: Reinfection and loss of Immunity

- With the new variants and the growing reinfection cases, we suggest an adaptation of the proposed model
- Simplified variables
- More connections
- Reinforcement dose are modeled by the loss of immunity rate. Given a period after the immunization, the individual backs to a group that need take another vaccine shot



Model Adaptation: Reinfection and loss of Immunity

- Some parameters has to be estimated by the literature
- This model captures some keys dynamics of the infection
- Historical analysis can be done to compare variants impact on their detection period



Model Adaptation: Loss metric

- For dealing with zero valued variables, we changed the MSLE for the RMSE function

$$L = \{l_I, l_R, l_D, l_{v1}, l_{v2}, l_{sum}\},$$

$$l_I = \sqrt{\frac{1}{M}\sum_{i=0}^{M}(I_i - \tilde{I}_i)^2}, \quad l_R = \sqrt{\frac{1}{M}\sum_{i=0}^{M}(R_i - \tilde{R}_i)^2},$$

$$l_D = \sqrt{\frac{1}{M}\sum_{i=0}^{M}(D_i - \tilde{D}_i)^2}, \quad l_{v1} = \sqrt{\frac{1}{M}\sum_{i=0}^{M}(V_{1,i} - \tilde{V}_{1,i})^2},$$

$$l_{v2} = \sqrt{\frac{1}{M}\sum_{i=0}^{M}(V_{2,i} - \tilde{V}_{2,i})^2}, l_{sum} = \sqrt{\frac{1}{M}\sum_{i=0}^{M}(1 - \tilde{T}_i)^2}$$

- SP Covid-19 Info Tracker:
  - www.spcovid.com.br
  - www.spcovid.net.br