COVID-19 Vaccination modeling:

Optimal control, noise, and estimation of parameters

June 15, 2022

CONACYT-UNISON-ITSON-UADY Mathematical biology group

To fix ideas:

$$
\begin{aligned}
S'(t) &= -\beta IS \\
I'(t) &= \beta IS - \gamma I \\
R'(t) &= \gamma I \\
&\qquad S(0) = S_0, I(0) = I_0, R(0) = 0 \\
&\qquad S(t) + I(t) + R(t) = 1
\end{aligned}
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"Classic" Vaccination

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With vaccination

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Toy example and classic vaccination OC

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Optimal Controlled:

The Basic Optimization Question

Hypothesis

Cost The **effort** expended in "**preventing-mitigating** an epidemic" by vaccination is **proportional** to the vaccination rate λ_V.

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Jabs Counter If $S(0) \approx 1$, $X(\cdot)$: counts vaccine doses, then

$$X(t) = 1 - \exp(-\lambda_V t),$$

estimates the fraction of vaccinated individuals. Thus, for time horizon T and vaccination coverage

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Given X_{cov}, T

$$\lambda_V = -\frac{1}{T} \ln(1 - X_{cov})$$

estimates the constant vaccination rate s.t., afther time T, we reach X_{cov}.

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X_{COV} : 70%, T: **one** year

$\lambda_V \approx 0.00329$

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If $S(0)N$ corresponds to HMS $(812\,229\,\text{inhabitants})$ $\approx 2668\,\text{jabs}/\text{day}$.

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How to optimize vaccination?

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Common Objectives

Who to vaccine first? (Allocation)

Given X_{cov}, T

$$\lambda_V = -\frac{1}{T}\ln(1 - X_{cov})$$

estimates the constant vaccination rate s.t., after time T, we reach X_{cov}.

X_{COV} : 70%, T: one year

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How to optimize vaccination?

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Common Objectives

Who to vaccine first? (Allocation)

How and when? (Administration)

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Vaccine optimiztion for COVID-19

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Cost

Vaccine optimiztion for COVID-19

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Cost

$$J(u) := \varphi(x(T)) + \int_0^T f(t, x(t), u(t))$$

Vaccine optimiztion for COVID-19

Common Objectives

- ⋆ Who to vaccine first? (Allocation)
- ⋆ How and when? (Administration)

Optimal Control Problem

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\begin{aligned}
\min_{\mathbf{u}\in\mathscr{U}} J(u) &= \varphi(x(T)) + \int_0^T f(t, x(t), u(t)) \\
\dot{x}(t) &= b(t, u(t), x(t)), \qquad \text{a.e. } t \in [0, T], \\
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Vaccine optimiztion for COVID-19

Common Objectives

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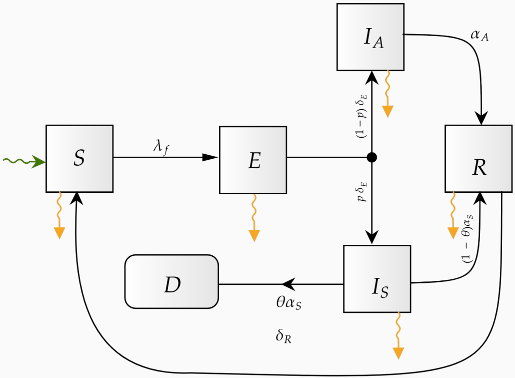
Aim of this part

To illustrate the formulation of optimal vaccination policies based in vaccination rate.

Outline

Model Scheme



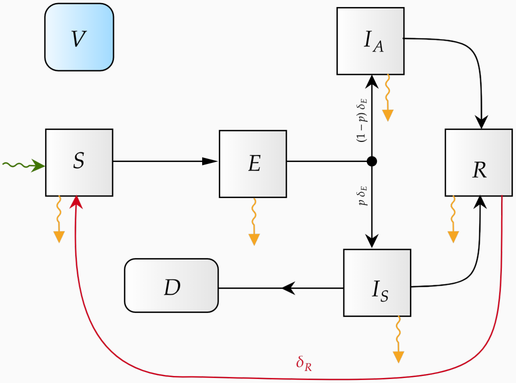
$$\lambda_f := \frac{\beta_A I_A + \beta_S I_S}{N^*}$$

$$N^* := N - D$$

natality

natural death

Model Scheme



Vaccine Hypotheses

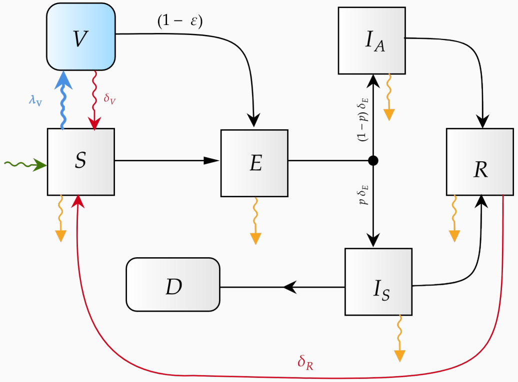
Imperfect preventive

One dose

Symptomatic exception

Action over susceptible

Model Scheme



λ_V : vaccination rate

immunity periods

$\dfrac{1}{\delta_V}$: vaccine-induced

$\dfrac{1}{\delta_R}$: natural

Vaccine Hypotheses

- Imperfect preventive
- One dose
- Symptomatic exception
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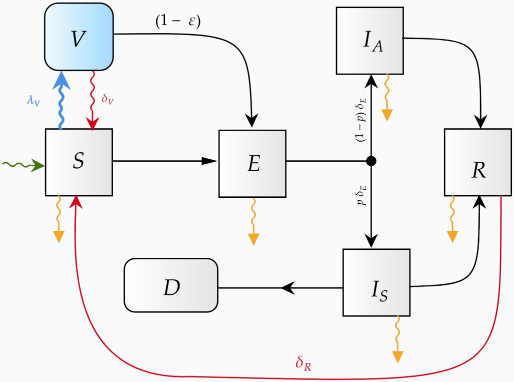

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Notation

ε	vaccine efficacy
p	Generation of symptoms probability

Vaccine Hypotheses

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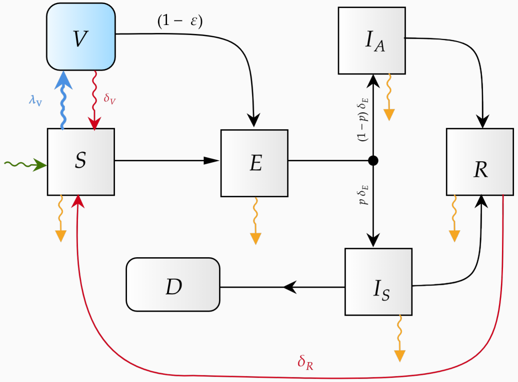
One dose

Symptomatic exception

Action over susceptible



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SAGE objectives

Vaccine profile (Efficacy, immunity)

Coverage

Time Horizon

Notation

ε vaccine efficacy

p Generation of symptoms probability

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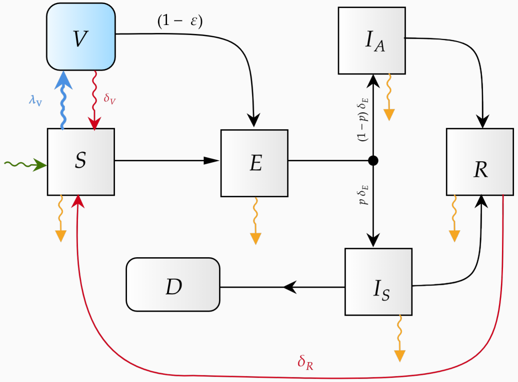

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Vaccine profile (Efficacy, immunity)

Coverage

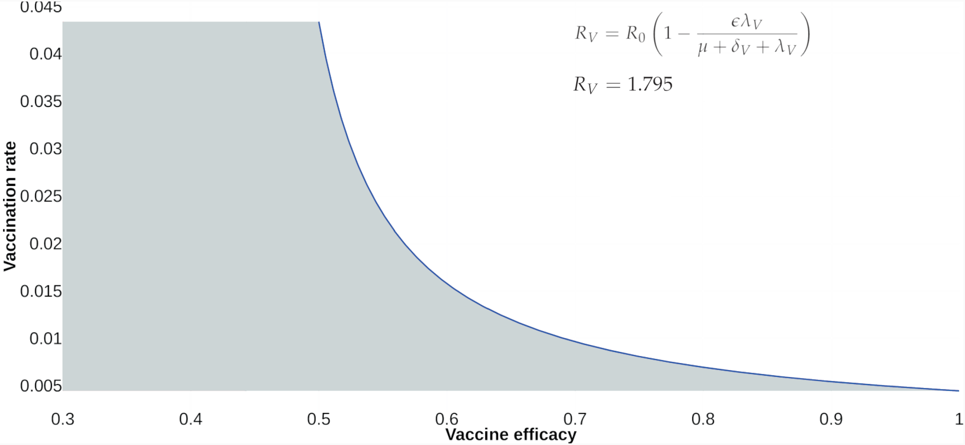
Time Horizon

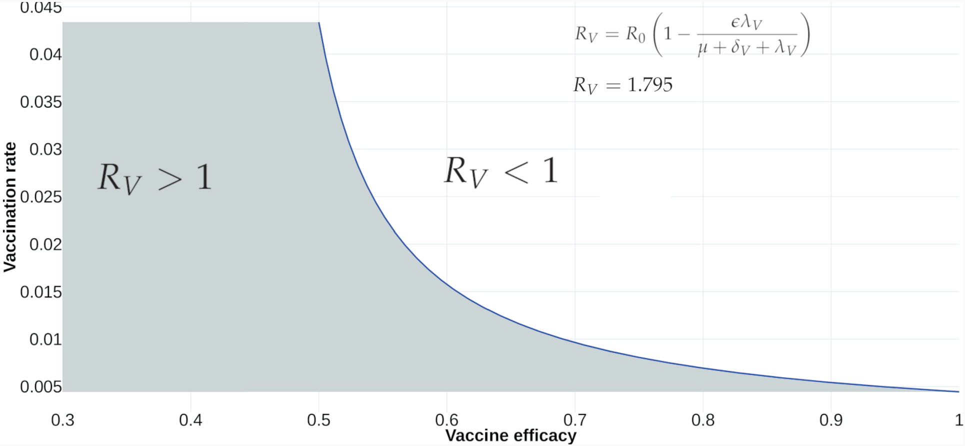
Immunity:

natural (reinfection)

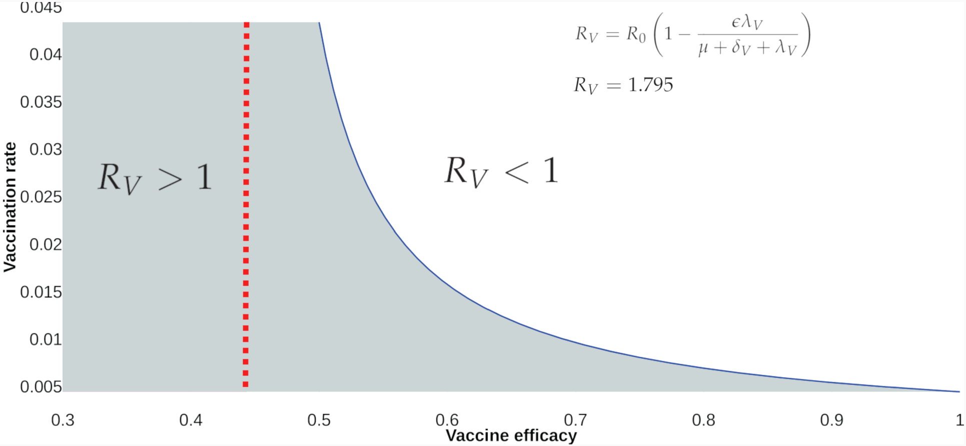
vaccine-induced

Reproductive number




$$R_V = R_0\left(1 - \frac{\epsilon\lambda_V}{\mu + \delta_V + \lambda_V}\right)$$
$R_V = 1.795$
$R_V > 1$
$R_V < 1$
Vaccination rate
0.045
0.04
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Vaccine efficacy

Reproductive number



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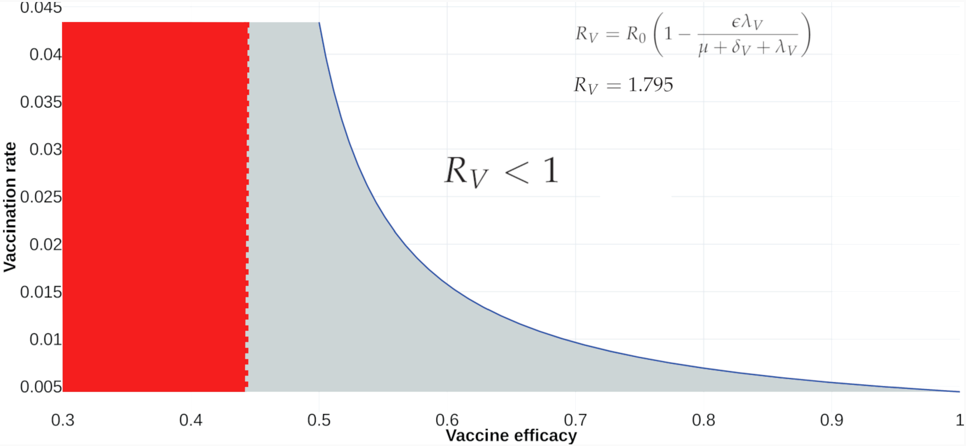

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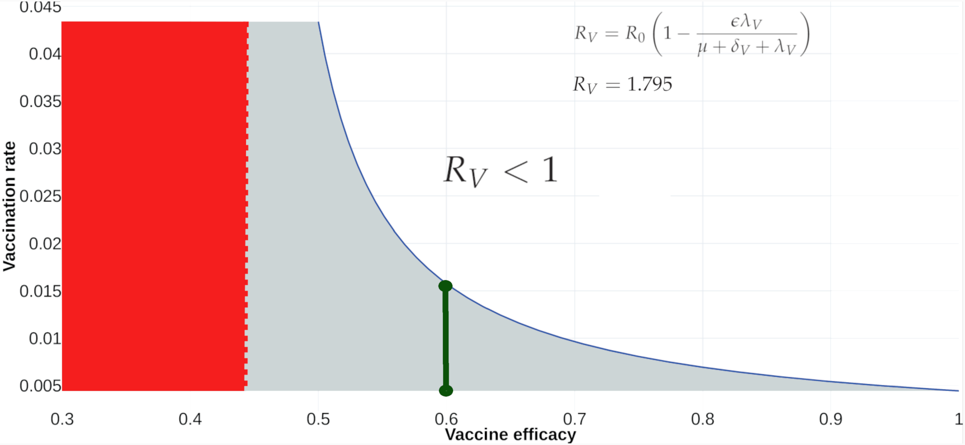

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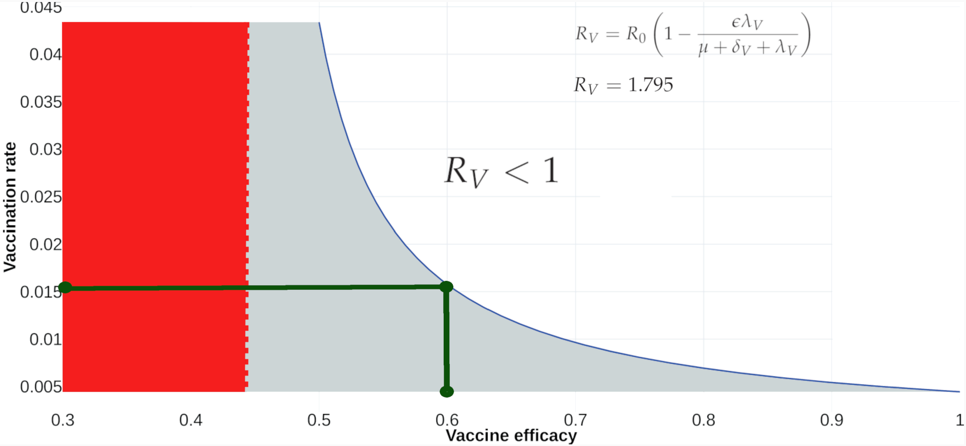
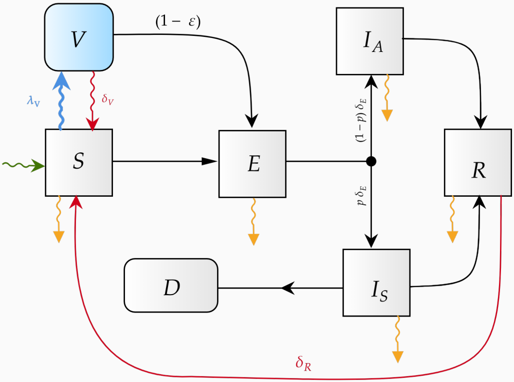


The Optimal Control Problem



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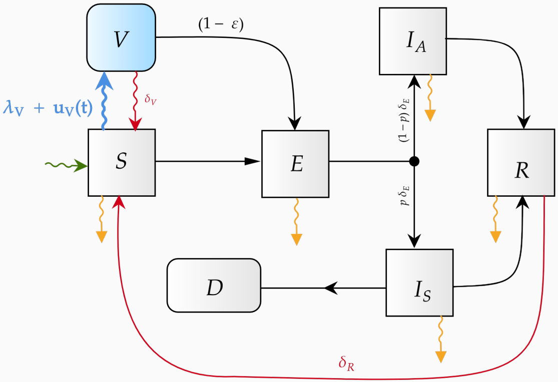
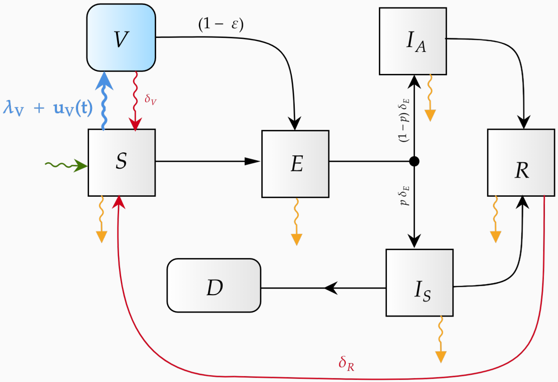


λ_V : vaccination rate

$u_V(t)$: control signal

$\lambda_V + u_V(t)$: modulates the number of administrated vaccine doses per day

The Optimal Control Problem



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$s.\,t.$

$$\dot{x}(t) = b(t, u(t), x(t))$$

$$x(0) = x_0$$

The disability-adjusted life year (DALY)

$DALY(c,s,a,t) = YLL(c,s,a,t) + YLD(c,s,a,t)$

For given cause c, age a, sex s and year t

YLL : Years of life lost due to premature death.

$$YLL(c,s,a,t) = N(c,s,a,t) \times L(s,a)$$

$N(c,s,a,t)$: is the number of deaths due to the cause c
$L(s,a)$: is a standard loss function specifying years of life lost

YLD : Years of life list due to disability

$$YLD(c,s,a,t) = I(c,s,a,t) \times DW(c,s,a) \times L(c,s,a,t)$$

$I(c,s,a,t)$: number of incident cases for cause c
$DW(c,s,a)$: disability weight for cause c
$L(c,s,a,t)$: average duration of the case until remission or death (years)

$$J(u_V) :=$$

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$$\min_{u_V \in \mathscr{U}[0,T]} J(u_V) := \underbrace{a_D(D(T) - D(0))}_{:=YLL} + \underbrace{a_S(Y_{I_S}(T) - Y_{I_S}(0))}_{:=YLD}$$

Optimal Control Problem

$$\min_{u_V \in \mathscr{U}[0,T]} J(u_V) := \underbrace{a_D(D(T) - D(0))}_{:=YLL} + \underbrace{a_S(Y_{I_S}(T) - Y_{I_S}(0))}_{:=YLD}$$

$$u_V(\cdot) \in [u_{\min}, u^{\max}],$$

$$\kappa I_S(t) \leq B, \quad \forall t \in [0, T],$$

$$\min_{u_V \in \mathscr{U}[0,T]} J(u_V) := \underbrace{a_D(D(T) - D(0))}_{:=YLL} + \underbrace{a_S(Y_{I_S}(T) - Y_{I_S}(0))}_{:=YLD}$$

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Optimal Control Problem

$$\min_{u_V \in \mathscr{U}[0,T]} J(u_V) := \underbrace{a_D(D(T) - D(0))}_{:=YLL} + \underbrace{a_S(Y_{I_S}(T) - Y_{I_S}(0))}_{:=YLD}$$

$$u_V(\cdot) \in [u_{\min}, u^{\max}],$$

$$\kappa I_S(t) \leq B, \quad \forall t \in [0, T],$$

Optimal Control Problem

$$\min_{u_V \in \mathscr{U}[0,T]} J(u_V) := a_D(D(T) - D(0)) + a_S(Y_{I_S}(T) - Y_{I_S}(0))$$

s.t.

$$f_\lambda := \frac{\beta_S I_S + \beta_A I_A}{\bar{N}}$$

$$\begin{aligned}
S'(t) &= \mu \bar{N} + \delta_V V + \delta_R R \\
&\quad - (f_\lambda + \mu + \lambda_V + u_V(t))S \\
E'(t) &= f_\lambda (S + (1-\varepsilon)V) - (\mu + \delta_E)E \\
I_S'(t) &= p\delta_E E - (\mu + \alpha_S) I_S \\
I_A'(t) &= (1-p)\delta_E E - (\mu + \alpha_A) I_A \\
R'(t) &= (1-\theta)\alpha_S I_S + \alpha_A I_A - (\mu + \delta_R) R \\
D'(t) &= \theta \alpha_S I_S \\
V'(t) &= (\lambda_V + u_V(t))S - ((1-\varepsilon) f_\lambda V + \mu + \delta_V) V \\
X'(t) &= (\lambda_V + u_V(t))(S + E + I_A + R)
\end{aligned}$$

$$\begin{aligned}
&S(0) = S_0,\ E(0) = E_0,\ I_S(0) = I_{S_0}, \\
&I_A(0) = I_{A_0},\ R(0) = R_0,\ D(0) = D_0, \\
&V(0) = 0,\ X(0) = 0,\ X(T) = x_{coverage}, \\
&u_V(\cdot) \in [u_{\min}, u^{\max}], \\
&\kappa I_S(t) \leq B, \quad \forall t \in [0, T], \\
&\bar{N}(t) = S + E + I_S + I_A + R + V.
\end{aligned}$$

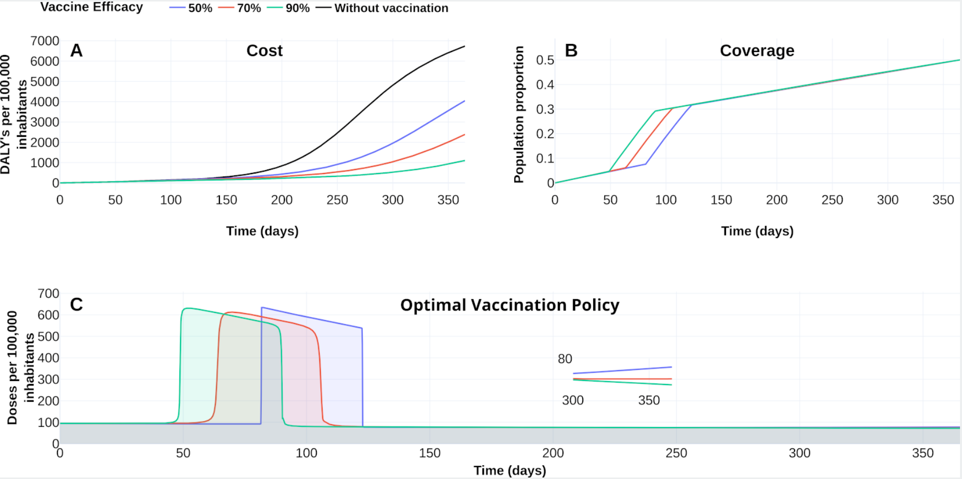
Vaccine efficacy

Developer	Vaccine Name	Efficacy %, (95% CI)	Reference
Pfizer-BioNTech	BNT162b2	95 (90.3–97.6)	[1]
Gamaleya Institute	Sputnik V	91.6 (85.6–95.2)	[4]
Oxford University-AztraZeneca	AZD1222	74.6 (41.6-88.9)	[2]
Johnson & Johnson*	Ad26.COV2.S	57 %, 66 % or 72 %	[3]
Sinovac Biotech*	CoronaVac	50.4 %	[5]

Table: Vaccine efficacy of some of the approved developments for emergency use. (*) No available information about the confidence intervals.

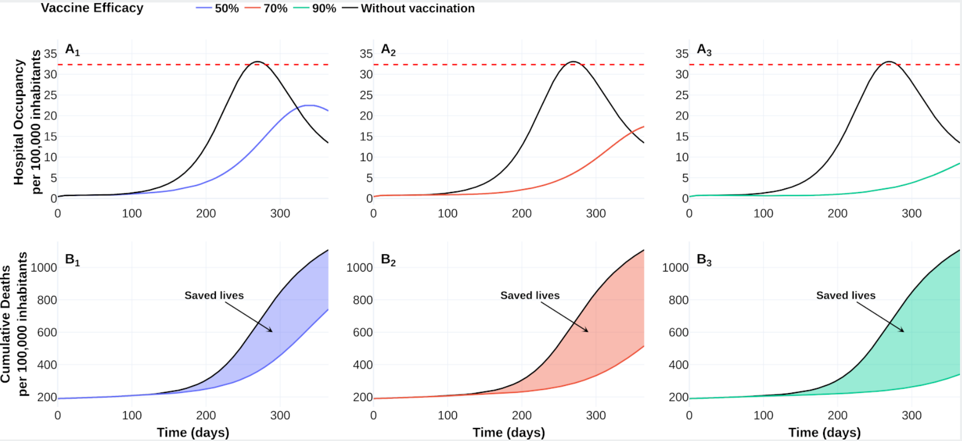
The response of COVID-19 burden due to vaccine efficacy

$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1})$: [50 %, 365 days, $\star$, 730 days, 365 days]



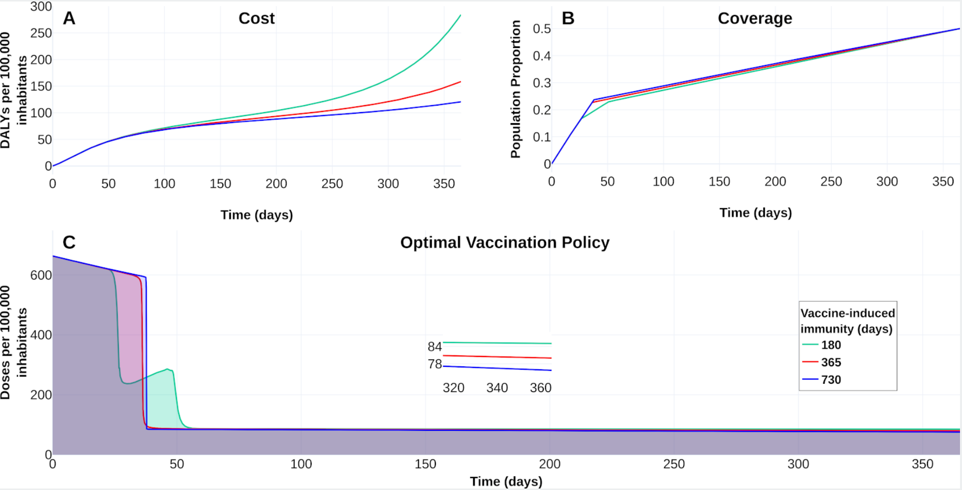
The response of COVID-19 burden due to vaccine efficacy

$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1})$: $[\,50\,\%, 365\ \text{days}, \star, 730\ \text{days}, 365\ \text{days}\,]$



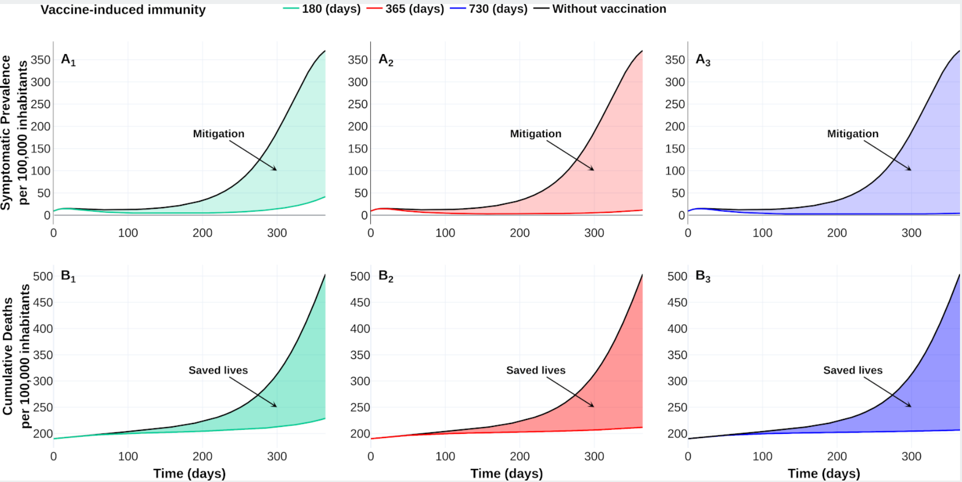
The response of COVID-19 burden due to vaccine-immunity

$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1})$: [50 %, 365 days, 90 %, $\star$, 365 days,]



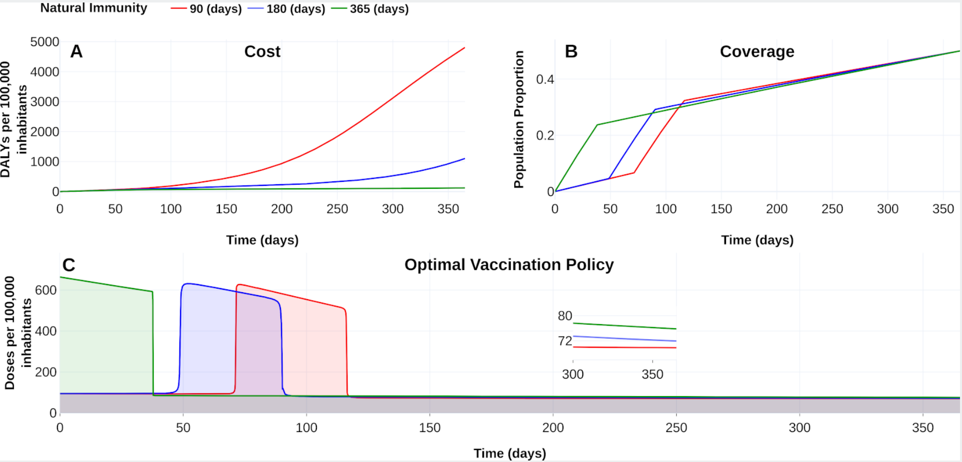
The response of COVID-19 burden due to vaccine-immunity

$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1})$: [50 %, 365 days, 90 %, ⋆, 365 days,]



The response of COVID-19 burden due to natural-immunity

$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1})$: $[50\,\%, 365\,\text{days}, 90\,\%, 730\,\text{days}, \star]$



The response of COVID-19 burden due to natural-immunity

$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1})$: [50 %, 365 days, 90 %, 730 days, $\star$]

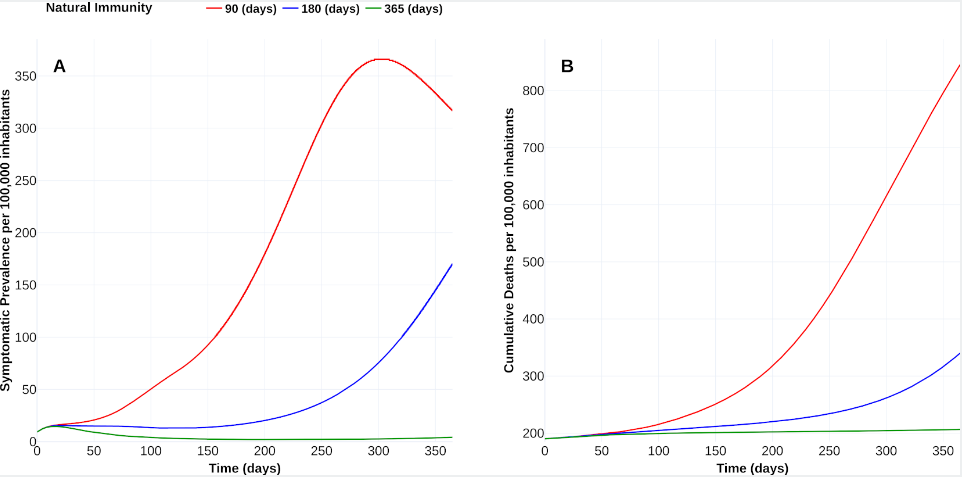


Table of contents

UQ

$ODE + noise = Better\ Model$

To fix ideas

Example

$$dN(t) = aN(t)dt$$

To fix ideas

Example

$$dN(t) = aN(t)dt$$

Perturb in $[t, t + dt)$

To fix ideas

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$$dN(t) = aN(t)dt$$

Perturb in $[t, t + dt)$

$$adt \rightsquigarrow adt + \sigma dB(t)$$

To fix ideas

Example

$$dN(t) = aN(t)dt$$

Perturb in $[t, t + dt)$

$$adt \rightsquigarrow adt + \sigma dB(t)$$

Get a SDE

$$dN(t) = aN(t)dt + \sigma N(t)dB(t)$$

To fix ideas

Example

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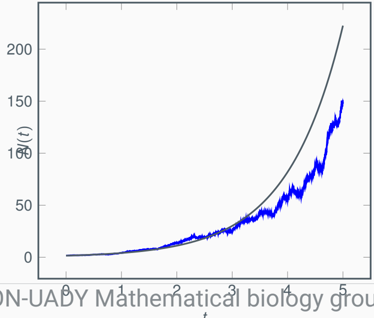
Perturb in $[t, t+dt)$

$$adt \rightsquigarrow adt + \sigma dB(t)$$

Get a SDE

$$dN(t) = aN(t)dt + \sigma N(t)dB(t)$$



Some Important applications

- Finance
- Physics
- Chemistry
- Biology
- Epidemiology

Henston

$$dS_t = \mu S_t dt + \sqrt{V_t} S_t \left(\sqrt{1-\rho^2} dW_t^{(1)} + \rho dW^{(2)} \right)$$

$$dV_t = \kappa(\lambda - V_t) dt + \theta \sqrt{V_t} dW_t^{(2)}$$

Hutzenthaler, M. and Jentzen, A. (2015).
Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.
Memoirs of the American Mathematical Society, 236(1112).

Some Important applications

- Finance
- Physics
- Chemistry
- Biology
- Epidemiology

Langevin

$$dX_t = -(\nabla U)(X_t)dt + \sqrt{2\varepsilon}dW_t$$

Hutzenthaler, M. and Jentzen, A. (2015).
Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.
Memoirs of the American Mathematical Society, 236(1112).

Some Important applications

- Finance
- Physics
- Chemistry
- Biology
- Epidemiology

Brusselator

$$dX_t = \left[\delta - (\alpha+1)X_t + Y_t X_t^2\right] dt + g_1(X_t) dW_t^{(1)}$$
$$dY_t = \left[\alpha X_t + Y_t X_t^2\right] dt + g_2(X_t) dW_t^{(2)}$$

Hutzenthaler, M. and Jentzen, A. (2015).
Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.
Memoirs of the American Mathematical Society, 236(1112).

Some Important applications

- Finance
- Physics
- Chemistry
- Biology
- Epidemiology

Lotka Volterra

$$dX_t = (\lambda X_t - kX_t Y_t)dt + \sigma X_t dW_t$$
$$dY_t = (kX_t Y_t - mY_t)dt$$

Hutzenthaler, M. and Jentzen, A. (2015).
Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.
Memoirs of the American Mathematical Society, 236(1112).

Some Important applications

- Finance
- Physics
- Chemistry
- Biology
- Epidemiology

SIR

$$
\begin{aligned}
dS_t &= (-\alpha S_t I_t - \delta S_t + \delta)dt - \beta S_t I_t dW_t \\
dI_t &= (\alpha S_t I_t - (\gamma + \delta) I_t)dt + \beta S_t I_t dW_t \\
dR_t &= (\gamma I_t - \delta R_t)dt
\end{aligned}
$$

Tornatore, E., Buccellato, S. M., and Vetro, P. (2005).
Stability of a stochastic {SIR} system.
Physica A: Statistical Mechanics and its Applications, 354:111 – 126.

Why noise?

Environmental effects

- Extinction
- Outbreaks

Why noise?

Environmental effects

- Extinction
- Outbreaks

Environmental Brownian noise suppresses explosions.

Mao, X., Marion, G., and Renshaw, E. (2002).
Environmental brownian noise suppresses explosions in population dynamics.
Stochastic Processes and their Applications, 97(1):95–110.

Why noise?

Environmental effects

Extinction

Outbreaks

Noise color induces extinction

Ripa, J. and Lundberg, P. (1996).
Noise Colour and the Risk of Population Extinctions.
Proceedings of the Royal Society B: Biological Sciences, 263(1377):1751–1753.

Why noise?

Environmental effects

- Extinction
- Outbreaks

$\mathscr{R}_0$: Endemic g.a.e. $\rightarrow$ periodic oscillations

Allen, L. and van den Driessche, P. (2013).
Relations between deterministic and stochastic thresholds for disease extinction in continuous- and discrete-time infectious disease models.
Mathematical Biosciences, 243(1):99–108.

Alternativas

In Biology

- **DTMC, CTMC**
- Stochastic perturbation of parameters
- Mean reverting processes

Environmental effects

- Extinction
- Outbreaks

DTMC + CTMC + ME → *SDE*

Allen, L. J. (2017).
A primer on stochastic epidemic models: Formulation, numerical simulation, and analysis.
Infectious Disease Modelling, 2(2):128–142.

Alternativas

In Biology

- DTMC, CTMC
- **Stochastic perturbation of parameters**
- Mean reverting processes

Environmental effects

- Extinction
- Outbreaks

$$\varphi dt \rightsquigarrow \varphi dt + \sigma dB_t$$

Gray, A., Greenhalgh, D., Hu, L., Mao, X., and Pan, J. (2011).
A Stochastic Differential Equation SIS Epidemic Model.
SIAM Journal on Applied Mathematics, 71(3):876–902.

Alternativas

In Biology

- DTMC, CTMC
- **Stochastic perturbation of parameters**
- Mean reverting processes

Environmental effects

- Extinction
- Outbreaks

$$\varphi dt \rightsquigarrow \varphi dt + F(x) dB_t$$

Schurz, H. and Tosun, K. (2015). **Stochastic Asymptotic Stability of SIR Model with Variable Diffusion Rates.** *Journal of Dynamics and Differential Equations*, 27(1):69–82.

In Biology

- DTMC, CTMC
- Stochastic perturbation of parameters
- Mean reverting processes

Environmental effects

- Extinction
- Outbreaks

$$d\varphi_t = (\varphi_e - \varphi_t)dt + \sigma_\varphi dBt$$

Allen, E. (2016).
Environmental variability and mean-reverting processes.
Discrete and Continuous Dynamical Systems - Series B, 21(7):2073–2089.

CDMX Covid-19 data

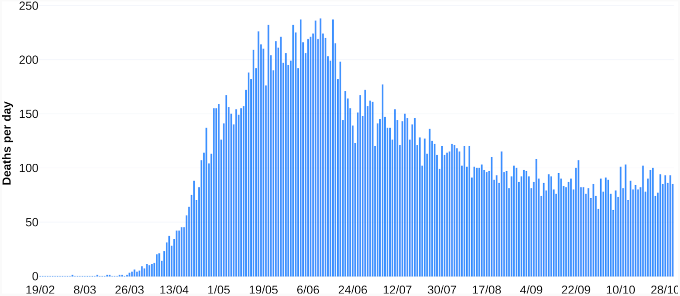


Figure: CDMX data

Example: Estimation of the infection rates β_s, β_a, and ratio of asymptomatic cases p.

Argument: Noise could improve the uncertainty quantification.

[1]

[1] Work in progress. Collaboration with Fernado Baltazar (UNAM-CU) and Francisco Delgado (UNAM-OAXACA)

MCMC with a deterministic SEIRS structure

$$
\begin{aligned}
f_\beta &:= \beta_s I_S + \beta_a I_a \\
S' &= \mu + \gamma R - (\mu + f_\beta)\, S \\
E' &= f_\beta S - (\kappa E + \mu E) \\
{I_a}' &= p\kappa E - (\alpha_a + \mu)\, I_a \\
{I_s}' &= (1-p)\kappa E - (\alpha_s + \mu) I_s \\
R' &= \alpha_a I_a + \alpha_s (1-\theta) I_s - (\mu + \gamma) R \\
D' &= \theta \alpha_s I_s.
\end{aligned}
\tag{1}
$$

$$
\begin{aligned}
Y_t &\sim \mathrm{Poisson}(\lambda_t) \\
\lambda_t &= \int_0^t (1-p)\delta_E E \\
p &\sim \mathrm{Uniform}(0.3, 08) \\
\kappa &\sim \mathrm{Gamma}(10, 50) \\
\beta_a, \beta_s &\sim \mathcal{N}(0.5, 0.1)
\end{aligned}
$$

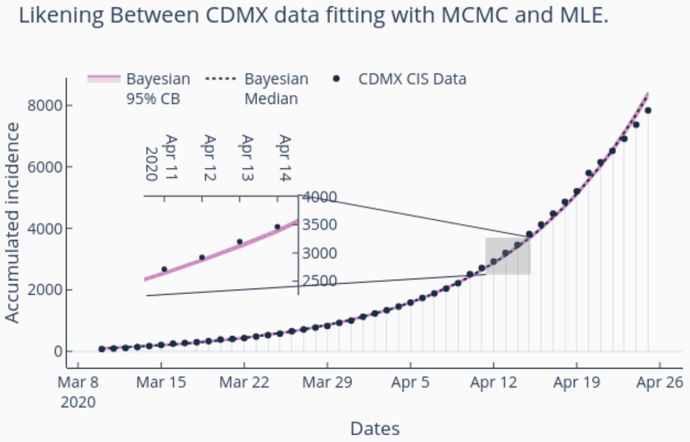


Figure: MCMC Fit of diary new cases of Mexico city during exponential growth. See `https://plotly.com/~sauld/53/` for an electronic version.

Stochastic perturbation

Perturbing the above deterministic base by Brownian Motion

$\mu dt \rightsquigarrow \mu dt + \sigma dW(t)$ gives our SDE SEIR-Covid-19

$$
\begin{aligned}
dS(t) &= \left[\mu - \mu S(t) - f_\beta S(t) + \gamma R(t)\right] dt + \sigma \left(1 - S(t)\right) dW(t) \\
dE(t) &= \left[f_\beta S(t) - \kappa E(t) - \mu E(t)\right] dt - \sigma E(t) dW(t) \\
dI_a(t) &= \left[p\kappa E(t) - (\alpha_a + \mu) I_a(t)\right] dt - \sigma I_a(t) dW(t) \\
dI_s(t) &= \left[(1-p)\kappa E(t) - (\alpha_s + \mu) I_s(t)\right] dt - \sigma I_s(t) dW(t) \\
dR(t) &= \left[\alpha_a I_a(t) + \alpha_s I_s(t) - (\mu + \gamma) R(t)\right] dt - \sigma R(t) dW(t), \\
& \qquad t \in [0, T].
\end{aligned}
$$

Using Itô and Lamperti transformations

$$
\begin{aligned}
dS(t) &= \left[\mu - \mu S(t) - f_\beta S(t) + \gamma R(t)\right] dt + \sigma \left(1 - S(t)\right) dW(t)\\
dE(t) &= \left[f_\beta S(t) - \kappa E(t) - \mu E(t)\right] dt - \sigma E(t) dW(t)\\
dI_a(t) &= \left[p\kappa E(t) - (\alpha_a + \mu) I_a(t)\right] dt - \sigma I_a(t) dW(t)\\
dI_s(t) &= \left[(1-p)\kappa E(t) - (\alpha_s + \mu) I_s(t)\right] dt - \sigma I_s(t) dW(t)\\
dR(t) &= \left[\alpha_a I_a(t) + \alpha_s I_s(t) - (\mu + \gamma) R(t)\right] dt - \sigma R(t) dW(t),\\
&\quad t \in [0, T].
\end{aligned}
$$

$$
-\frac{1}{\sigma} d\mathbf{X}_{\beta,p}(t) = F\left(\mathbf{X}_{\beta,p}(t)\right) dt + d\mathbf{W}(t),
$$

$$
\mathbf{X}_{\beta,p}(t) := \begin{pmatrix} \log\left(1 - S(t)\right) \\ \log\left(E(t)\right) \\ \log\left(I_a(t)\right) \\ \log\left(I_s(t)\right) \\ \log\left(R(t)\right) \end{pmatrix}, \quad F(\mathbf{X}_{\beta,p}(t)) := \begin{pmatrix} \frac{\mu}{\sigma} - \frac{f_\beta S(t)}{\sigma(1 - S(t))} + \frac{\gamma R(t)}{\sigma(1 - S(t))} + \frac{1}{2}\sigma \\ -\frac{f_\beta S(t)}{\sigma E(t)} + \frac{\kappa}{\sigma} + \frac{\mu}{\sigma} + \frac{1}{2}\sigma \\ -\frac{\kappa p E(t)}{\sigma I_a(t)} + \frac{(\alpha_a + \mu)}{\sigma} + \frac{1}{2}\sigma \\ -\frac{\kappa(1-p)E(t)}{\sigma I_s(t)} + \frac{(\alpha_s + \mu)}{\sigma} + \frac{1}{2}\sigma \\ -\frac{\alpha_a I_a(t) + \alpha_s I_s(t)}{\sigma R(t)} + \frac{\mu + \gamma}{\sigma} + \frac{1}{2}\sigma \end{pmatrix}, \quad d\mathbf{W}(t) := \begin{pmatrix} dW(t) \\ dW(t) \\ dW(t) \\ dW(t) \\ dW(t) \end{pmatrix}.
$$

Define $f_\beta := (\beta_s I_s(t) + \beta_a I_a(t))$, thus

$$f_\beta - f_{\beta_0} = (\beta_s - \beta_{s,0}) I_s(t) + (\beta_a - \beta_{a,0}) I_a(t).$$

With this notation we write

$$[F(\mathbf{X}_{\beta,p}(t)) - F(\mathbf{X}_{\beta_0,p_0}(t))] = \begin{pmatrix} -(f_\beta - f_{\beta_0})\dfrac{S(t)}{\sigma(1-S(t))} \\ -(f_\beta - f_{\beta_0})\dfrac{S(t)}{\sigma E(t)} \\ -(p-p_0)\dfrac{\kappa E(t)}{\sigma I_a(t)} \\ (p-p_0)\dfrac{\kappa E(t)}{\sigma I_s(t)} \\ 0 \end{pmatrix},$$

Let $\mathbb{P}_{\beta,p}$ the law of solution to SDE. We use the following result [2].

Theorem (Likelihood ratio of Itô processes Särkkä and Solin (2019, Thm. 7.4))

Consider the Itô processes

$$\begin{aligned} dx &= f(x,t) + dB_t, \qquad x(0) = x_0, \\ dy &= g(y,t) + dB_t, \qquad y(0) = x_0. \end{aligned}$$

Then the ratio of probability laws of $\mathscr{X}_t$ and $\mathscr{Y}_t$ is given as

$$\begin{aligned} \frac{p(\mathscr{X}_t)}{p(\mathscr{Y}_t)} &= Z(t), \\ Z(t) = \exp\Big(-\frac{1}{2} \int_0^t & [f(y,\tau) - g(y,\tau)]^\top \mathbb{Q}^{-1} [f(y,\tau) - g(y,\tau)] d\tau \\ &+ \int_0^t [f(y,\tau) - g(y,\tau)]^\top \mathbb{Q}^{-1} dB_\tau \Big) \end{aligned}$$

in the sense that for an arbitrary functional $h(\cdot)$ of the path from 0 to t,

$$\mathbb{E}[h(\mathscr{X}_t)] = \mathbb{E}[Z(t)h(\mathscr{Y}_t)]$$

[2] Särkkä, Simo; Solin, Arno, Applied stochastic differential equations. Institute of Mathematical Statistics Textbooks, 10. Cambridge University Press, Cambridge, 2019. ix+316 pp. ISBN: 978-1-316-64946-6

Then we obtainb the likelihood (Radon-Nikodyn derivative)

$$\frac{d\mathbb{P}_\beta}{d\mathbb{P}_{\beta_0}} = \exp\left[\int_0^T [F(\mathbf{X}_{\beta,p}(t)) - F(\mathbf{X}_{\beta_0,p_0}(t))]^T Q^{-1} d\mathbf{W}(t) \right.$$
$$\left. - \frac{1}{2}\int_0^T [F(\mathbf{X}_{\beta,p}(t)) - F(\mathbf{X}_{\beta_0,p_0}(t))]^T Q^{-1} [F(\mathbf{X}_{\beta,p}(t)) - F(\mathbf{X}_{\beta_0,p_0}(t))] \right]$$

$$f_\beta = (\beta_s I_s(t) + \beta_a I_a(t))$$

$$[F(\mathbf{X}_{\beta,p}(t)) - F(\mathbf{X}_{\beta_0,p_0}(t))] = \begin{pmatrix} -(f_\beta - f_{\beta_0})\dfrac{S(t)}{\sigma(1-S(t))} \\ -(f_\beta - f_{\beta_0})\dfrac{S(t)}{\sigma E(t)} \\ -(p-p_0)\dfrac{\kappa E(t)}{\sigma I_a(t)} \\ (p-p_0)\dfrac{\kappa E(t)}{\sigma I_s(t)} \\ 0 \end{pmatrix}, \qquad \mathbb{Q} = \mathbb{I}_5 \text{ (identity)}$$

Therefore we can estimate $\widehat{\varphi} = (\beta_s, \beta_a, p)$ by maximizing $-\log(\text{likelihood})$.

For exmple, to estimte p, we derive the $-\log(\text{likelihood})$ with respect to p and deduce an expresion to find a extrema.

$$(p-p_0)\underbrace{\left(\int_0^T \Big[\frac{\kappa^2 E^2(t)}{I_s^2(t)}+\frac{\kappa^2 E^2(t)}{I_a^2(t)}\Big]dt\right)}_{:=J_2(T)}-\sigma\int_0^T \Big[-\frac{\kappa E(t)}{I_a(t)}+\frac{\kappa E(t)}{I_s(t)}\Big]dW(t)=0$$

$$\hat{p}_{ML}-p_0=\frac{\sigma}{J_2(T)}\int_0^T \Big[-\frac{\kappa E(t)}{I_a(t)}+\frac{\kappa E(t)}{I_s(t)}\Big]dW(t),$$

Estimator consistency

Let $X_0^+ := \{(S(t_0), E(t_0), I_a(t_0), I_s(t_0))\}$ initial state where all populations classes are strictly positive. Denote by $\varphi := \{\mu, \beta_s, \beta_a, \kappa, p, \theta, \alpha_s, \alpha_a, \gamma\}$, a model parameter configuration. The reproductive number for the deterministic version $(\sigma = 0)$

$$\mathscr{R}_0^D := \frac{p\kappa\beta_s}{(\mu+\kappa)(\mu+\alpha_s)} + \frac{(1-p)\kappa\beta_a}{(\mu+\kappa)(\mu+\alpha_a)}.$$

Define

$$\begin{aligned}\Omega^* := \{(S, E, I_a, I_s, R) \times [t_0, T] : S(T) \leq S(t) < S(t_0),\\ E(t) > E(t_0),\ I_a(t) > I_a(t_0),\ I_s(t) > I_s(t_0)\}.\end{aligned}$$

Theorem

Let $T_0 > 0$ such that for all $t \in [0, T_0]$

i. The deterministic threshold $\mathscr{R}_0^D > 1$

ii. The initial condition X_0^+ and parameters configuration φ are such that $\Omega^* \neq \emptyset$

Then, the estimators $(\hat{\beta}_{s,ML}, \hat{\beta}_{a,ML}, \hat{p}_{ML})$ are strongly consistent, that is,

$$\lim_{T \to T_0} \begin{pmatrix} \hat{\beta}_{s,ML} \\ \hat{\beta}_{a,ML} \\ \hat{p}_{ML} \end{pmatrix} = \begin{pmatrix} \beta_{s,0} \\ \beta_{a,0} \\ p_0 \end{pmatrix}, \qquad \text{w.p.1.}$$

To estimate the parameter of diffusion σ, we use the quadratic variation over $[0, T]$, $<*,*>_T$, of the solution processes

$$\hat{\sigma}^2 := \sum_{i=1}^{5} \frac{\hat{\sigma}_i^2}{5},$$

where

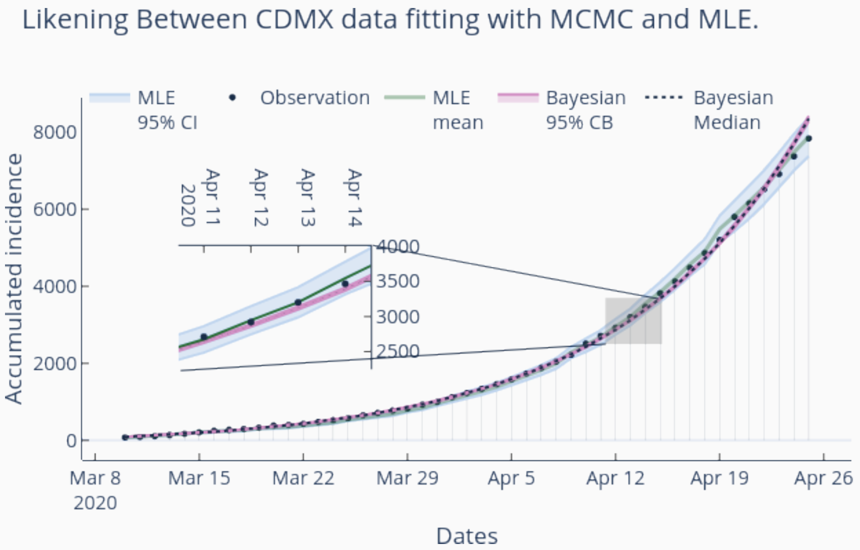
$$\hat{\sigma}_1^2 = \frac{<S,S>_T}{\int_0^T (1-S(t))^2 dt}, \qquad \hat{\sigma}_2^2 = \frac{<E,E>_T}{\int_0^T E(t)^2 dt}, \qquad \hat{\sigma}_3^2 = \frac{<I_a,I_a>_T}{\int_0^T I_a(t)^2 dt},$$

$$\hat{\sigma}_4^2 = \frac{<I_s,I_s>_T}{\int_0^T I_s(t)^2 dt}, \qquad \hat{\sigma}_5^2 = \frac{<R,R>_T}{\int_0^T R(t)^2 dt}.$$

Algorithm 1 Approximation by Euler-Mayurama. $I_s^{mx}(t_n)$ observation data.

1: Fix $E(0), I_a(0)$ and $R(0)$, $S(0) = 1 - E(0) - I_a(0) - R(0) - I_s^{mx}$, and make $n = 0$.
2: Generate $\Delta W \sim N(0, \Delta)$.
3:

$$\begin{aligned}
S(t_{n+1}) =& S(t_n) + [\mu + \gamma R(t_n) - (\mu + \beta_a I_a(t_n) + \beta_s I_s^{mx}(t_n)) S(t_n)]\Delta \\
&+ \sigma(1 - S(t_n))\Delta W \\
E(t_{n+1}) =& E(t_n) + [(\beta_a I_a(t_n) + \beta_s I_s^{mx}(t_n)) S(t_n) - (\kappa + \mu) E(t_n)]\Delta \\
&- \sigma(E(t_n))\Delta W \\
I_a(t_{n+1}) &= I_a(t_n) + (p\kappa E(t_n) - \alpha_a + \mu) I_a(t_n)\Delta - \sigma I_a(t_n)\Delta w \\
R(t_{n+1}) &= 1 - S(t_{n+1} - E(t_{n+1}) - I_a(t_{n+1}) - I_s^{mx}(t_{n+1})
\end{aligned}$$


Likening Between CDMX data fitting with MCMC and MLE.
MLE 95% CI
Observation
MLE mean
Bayesian 95% CB
Bayesian Median
Accumulated incidence
8000
6000
4000
2000
0
Apr 11 2020
Apr 12
Apr 13
Apr 14
4000
3500
3000
2500
Mar 8 2020
Mar 15
Mar 22
Mar 29
Apr 5
Apr 12
Apr 19
Apr 26
Dates

Discrete time

Closed Loop Policies

Games

Git-Hub

Dagan, N., Barda, N., Kepten, E., Miron, O., Perchik, S., Katz, M. A., Hernán, M. A., Lipsitch, M., Reis, B., and Balicer, R. D.
BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting.
New England Journal of Medicine (feb 2021), NEJMoa2101765.

Emary, K. R. W., Golubchick, T., Aley, P. K., Ariani, C. V., Angus, B. J., Bibi, S., Blane, B., Bonsall, D., Cicconi, P., Charlton, S., Clutterbuck, E., Collins, A., Cox, T., Darton, T., and et. al.
Efficacy of ChAdOx1 nCoV-19 (AZD1222) Vaccine Against SARS-CoV-2 VOC 202012/01 (B.1.1.7).
SSRN (2021).

Johnson & Johnson.
Johnson & Johnson Announces Single-Shot Janssen COVID-19 Vaccine Candidate Met Primary Endpoints in Interim Analysis of its Phase 3 ENSEMBLE Trial, January 2021.
Accessed February 15, 2021.

Lugonov, D. Y., Dolzhikova, I. V., Shcheblyakov, D. V., Tukhvatulim, A. I., Zubkuva, O. V., Dzharullaeva, A. S., Kovyrshina, A. V., Lubenets, N. L., Grousova, D. M., Erohova, A. S., Botikov, A. G., Izhaeva, F. M. Popova, O., Ozharovskaya, T. A., Esmagambetov, I. B., Favorskaya, I. A., Zrelkin, D. I., and Voronina, D. V.
Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia.
The Lancet (2021).

New York Times.
Coronavirus Vaccine Tracker, January 2020.
Accessed January 20, 2021.