A stochastic epidemic model with random transmission rate and false negative tests: Explaining the dynamics of COVID-19.



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- * The coronavirus (COVID-19) disease is believed to have emerged in Wuhan, China, in late 2019, and spread rapidly to many countries.
- * The WHO declared the COVID-19 epidemic a Public Health Emergency of International Concern (see Organization (2020)).
- * In Colombia, National, and local governments have taken measures to control the spread of infections such as lockdowns, restrictions movements, including closing airports, etc. (see Mayor de Bogotá (2020); Presidencia de la República de Colombia (2021)).
- * Several factors both environmental and demography factors have been introduced to study the role of behaviour.
- * Studying the epidemic development and transmission dynamics of disease play an important role in predicting, assessing and controlling the potential outbreak.

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Figure: The SIR model is one of the simplest epidemiological models, capable of capturing many of the typical characteristics of epidemic outbreaks. The basic assumptions of the model: are a homogeneous population of fixed size.

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Figure: Compartment models to analyze infectious diseases

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SEIR model



$$\begin{cases} \frac{dS}{dt} = I(t)S(t) - \mu S(t) \\ \frac{dE(t)}{dt} = \beta, I(t)S(t) - \upsilon E(t) - \mu E(t) \\ \frac{dI(t)}{dt} = \upsilon E(t) - \gamma I(t) - \mu I(t) \\ \frac{dR(t)}{dt} = \gamma I(t) - \mu R(t) \end{cases}$$
(1)



Figure: Flow chart of the SEIR model with demographics.

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- In Deterministic modeling, the output of the model is fully determined by the parameter values, and Stochastic model parameters are described by random variables
- stochasticity: Demographic vs. Environmental
- Different approach to including stochasticity in the modeling



Professor David Mumford - "The dawning of the age of stochasticity" quotes:

- "... stochastic models and statistical reasoning are more relevant to i) the world, ii) to science and many parts of mathematics and iii) particularly to understanding the computations in our own minds, than exact models and logical reasoning.
- "We argue that stochastic differential equations are more fundamental and relevant to modeling the world than deterministic equations.

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We consider a stochastic epidemic model with parameter perturbation in the population dynamics. The effect of environmental stochasticity, Cai et al. (2018); Gray et al. (2011) has proposed a stochastic version via suitable perturbation of the parameter β , the rate of infection transmission, and is given by

$$\widetilde{\beta} := \beta + \sigma B(t), \qquad (2)$$

where β and σ are positive constants, and $\{B(t)\}_{t\geq 0}$ is the standard Brownian motion on the complete probability space $(\Omega, \Im, \{\Im_t\}_{t\geq 0}, \mathbb{P})$ with filtration $\{\Im_t\}_{t\geq 0}$ satisfying usual conditions.

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The perturbation transforms the deterministic differential equations (1) into the stochastic differential equations.

We now have the following system of equations for the *SEIR model with stochastic perturbations*.

$$\begin{cases} dS(t) = (\Lambda - \beta I(t)S(t) - \mu S(t)) dt - \sigma I(t)S(t) dB(t) \\ dE(t) = (\beta I(t)S(t) - \upsilon E(t) - \mu E(t)) dt + \sigma I(t)S(t) dB(t) \\ dI(t) = (\upsilon E(t) - \gamma I(t) - \mu I(t)) dt \\ dR(t) = (\gamma I(t) - \mu R(t)) dt \end{cases}$$
(3)



Definition

Let be the system of stochastic differential equations

$$dX(t) = f(t, X(t)) dt + g(t, X(t)) dB(t), t \ge 0$$

X(0) = x₀ (4)

where f, g are locally Lipschitz functions from \mathbb{R}^n to \mathbb{R} . We say that $\mathbf{\dot{x}} = X(t_1) \in \mathbb{R}^n$ for some $t_1 \ge 0$, is an equilibrium point of the system, it holds $f(t_1, \mathbf{\dot{x}}) = 0$.

If $\mathbf{\dot{x}} \neq X(0)$ is an equilibrium point, and substituting $\xi(t) = X(t) - \mathbf{\dot{x}}$, we have the system

$$d\xi(t) = f(t,\xi(t) + \mathbf{\dot{x}}) dt + g(t,\xi(t) + \mathbf{\dot{x}}) dB(t),$$

 $\xi(0)$ is an equilibrium point.

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Ríos-Gutiérrez et al. Advances in Difference Equations https://doi.org/10.1186/s13662-021-03445-2 (2021) 2021:288

 Advances in Difference Equations a SpringerOpen Journal

RESEARCH





Studies on the basic reproduction number in stochastic epidemic models with random perturbations

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Abstract

In this paper, we discuss the basic reproduction number of stochastic epidemic models with random perturbations. We define the basic reproduction number in epidemic models by using the integral of a function or survival function. We study the systems of stochastic differential equations for SIR, SIS, and SEIR models and their stability analysis. Some results on deterministic epidemic models are also obtained. We give the numerical conditions for which the disease-free equilibrium point is asymptotically stable.

Keywords: Basic reproduction number; Random perturbations; Brownian motion; Stability analysis



The stability and the asymptotic stability are defined as follows (See, Rios, Arunachalam, and Torres 2021)

Definition

Let be a system defined 4, for which X(0) is an equilibrium point. We say that X(0) is (i) Stable (in probability), if only if, for all $\epsilon > 0$ exist $\delta > 0$ such that if $||X(0)|| < \delta$ then

$$P\left(\sup_{t\geq0}\left\|X\left(t
ight)
ight\|\geq\epsilon
ight)=0$$
 ;

(ii) Asymptotically stable, if it is stable in probability and it exists $\delta > 0$ such that if $||X(0)|| < \delta$ then

$$P\left(\lim_{t\to+\infty}X(t)=0\right)=1.$$

(iii) globally asymptotically stable, if it is stable in probability and for all $X(0) \in \mathbb{R}^n$

$$P\left(\lim_{t\to+\infty}X(t)=0\right)=1.$$



Definition

Let be $\{X(t)\}_{t>0}$ an Itô process and $h(t,x) \in C^2([0,+\infty) \times \mathbb{R})$. We define the differential operator for h as follows

$$\mathcal{L}\left(h\left(X\left(t\right)\right)\right) := \frac{\partial h}{\partial t}\left(t, X\left(t\right)\right) + u(t)\frac{\partial h}{\partial x}\left(t, X\left(t\right)\right) + \frac{1}{2}v^{2}(t)\frac{\partial^{2}h}{\partial x^{2}}\left(t, X\left(t\right)\right).$$
(5)

For observing the stability in SEIR models with random perturbations, using adequate Lyapunov functionsRíos-Gutiérrez et al. (2021), we have

Theorem

Let be V(X(t)) defined on $V : \mathbb{R}^n \longrightarrow \mathbb{R}$ a Lyapunov function (i) If $\mathcal{L}(V(X(t))) \le 0$ for all $t \ge 0$ then X(0) is stable in probability. (ii) If V holds (i) and $\mathcal{L}(V(X(t))) < 0$, then X(t) is asymptotically stable.

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The **basic reproduction number** of a epidemic model R_0 , is given by

$$R_0 := \int_0^{+\infty} b(a) F(a) da, \qquad (6)$$

where b(a) is the average number of new infected individuals, and F(a) is the probability of a new infected individual continuous infecting during the time interval between 0 and a.

Consider the SIR model with random perturbation, the *survival integral* is given by

$$R_{0,v}^{SIR} := \int_{0}^{+\infty} \left(\beta + \sigma B\left(a\right)\right) N e^{-(\mu + \gamma)a} da , \qquad (7)$$

where $R_{0,v}^{SIR}$ is a a normally distributed random variable.



Then, $R_{0,v}^{SIR}$ is the **random basic reproduction variable** on the SIR model with random perturbation and is given by

$$R_{0,\nu}^{SIR} \sim \mathbf{N}\left(\frac{\beta N}{(\mu+\gamma)}, \frac{\sigma^2 N^2}{2(\mu+\gamma)^3}\right),$$
 (8)

Similarly, We assume that **random basic reproduction variables** on the SEIR models with random perturbations are normally distributed and is given by

$$R_{0,\nu}^{SEIR} \sim \mathbf{N} \left(R_0^{SEIR}, \frac{\eta^2 \upsilon^2 \sigma^2 N^2}{2\mu^2 \left(\left(\mu + \upsilon \right) \left(\mu + \gamma \right) \right)^3} \right).$$
(9)

Stochastic Model

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We propose a modified SEIR model for COVID-19, by taking into account, the diagnostic test for the spread of SARS-COVID-19, and incorporating false negative tests in epidemiological models.

- Estimate the parameters of the modified SEIR model, considering the vaccinated population, false negatives, positive cases, and untested positive individuals.
- Analyze the effect of vaccination as a measure to control the spread of SARS-CoV-2 in the Pacific of Nariñense using the basic reproductive number before and after vaccination.

We consider the data from the Nariño Departament - Region in the Pacific Coast of Colombia, Source - National Institute of Health (INS), Colombia.

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Infectious Disease Modelling 7 (2022) 199-211



Stochastic modeling, analysis, and simulation of the COVID-19 pandemic with explicit behavioral changes in Bogotá: A case study



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Pacific of Nariñense Region





- Epidemiological modeling of the spread of COVID-19.
- Include: False Negatives, Untested Individuals, and Infected Individuals Tested Positive

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SEIR model with vaccination and the false negative



Figure: Modified SEIR model with vaccination. (S) Susceptible, (V)Vaccinated, (E) Exposed, (U) Infected without performing a diagnostic test (F) False negatives, (P) Infected tested positive, (A) Recovered and not tested, (B) Dead and not tested, (L) Recovered reported as positive, (D) Dead reported as positive



Parameters	Description
D _E	Incubation period (in days).
Dr	Average number of days until recovery of infected people
β	Virus transmission rate.
μ_c	Death rate.
γ_1 , γ_2 , δ_1 , δ_2	Scale factors in the recovery of individuals with false negatives and untested indi-
	viduals and deaths.
r	Probability of being tested for infectious individuals.
f	Probability of a false-negative RT-PCR diagnostic test result.
α_{u}	Scale factor for the rate of spread of infection by people without diagnostic testing
α_p	Scale factor of the rate of spread of infection between patients who tested positive
	to false negatives.
μ	Emigration rate
λ	Rate of influence
α_{v}	Percentage of population vaccinated
ρ	Vaccine effectiveness: $ ho=0$ vaccination is 100% effective, $ ho=1$ vaccination has
	no effect

Table: Description of parameters for the stochastic modified SEIR model

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$$dS = \left(\lambda - \beta(\alpha_u U + F + \alpha_p P)\frac{S}{N} - \mu S - \alpha_v \frac{S}{N} (\alpha_u U + F + \alpha_p P)\right) dt - \sigma S \frac{(\alpha_u U + F + \alpha_p P)}{N} dW$$

$$dV = \left(\alpha_v \frac{S}{N} (\alpha_u U + F + \alpha_p P) - (\rho\beta + \mu)V\right) dt - \sigma_P V \frac{(\alpha_u U + F + \alpha_p P)}{N} dW$$

$$dE = \left(\beta \frac{S}{N} (\alpha_u U + F + \alpha_p P) + V\rho\beta - \frac{E}{D_E} - \mu E\right) dt + \sigma(S + \rho V) \frac{(\alpha_u U + F + \alpha_p P)}{N} dW$$

$$dU = \left(\frac{(1 - r)E}{D_E} - \frac{U}{\gamma_1 D_r} - \delta_1 \mu_c U - \mu U\right) dt$$

$$dF = \left(\frac{rE}{D_E} - \frac{\gamma_2}{D_r}F - \frac{\mu_c}{\delta_2}F - \mu F\right) dt$$

$$dP = \left(\frac{(1 - f)r}{D_E}E - \frac{P}{D_r} - \mu_c P - \mu P\right) dt$$

$$dL = \left(\frac{P}{D_r} - \mu L\right) dt$$

$$dB = \left(\delta_1 \mu_c U + \frac{\mu_c F}{\delta_2}\right) dt$$

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To find the trajectories of the stochastic process by using the Euler-Maruyama method, the following idea is implemented:

$$X_{t_{i+1}} = X_{t_i} + \mu(t_i, X_{t_i}) \Delta t + \sigma(t_i, X_{t_i}) \Delta B_i$$

Algorithm:Define:
$$\mu(t, X_t), \sigma(t, X_t);$$
Input: $t_0, X_{t_0}, \Delta t, k;$ for $i := 0$ to k-1 do $\eta_i \sim N(0, 1)$ $X_{t_{i+1}} = X_{t_i} + \mu(t, X_t) \Delta t + \sigma(t, X_t) \sqrt{\Delta t} \eta_i$ $t_{i+1} = t_i + \Delta t$ print t_{i+1} and $X_{t_{i+1}}$





Using these parameters, by means of a non-linear least squares regression method, r and β are estimated, taking into account that $0 \le r \le 1$, since r is a probability and modeling f.

Let $\theta = (\theta_1, ..., \theta_m)$ be a multidimensional parameter with a neighborhood defined by $B_{\Delta k}(p) = \{\theta_k \in \mathbb{R} : ||p|| \le \Delta k\}$ and $1 \le k \le m$, where Δk is the radius of the trust region. Consider $f : \mathbb{R}^n \to \mathbb{R}$ a function that depends on the parameter θ . Given some points $(x_1, y_1) \cdots (x_n, y_n)$, the residual sum of squares is defined as:

$$g(\theta) = ||y - f(x; \theta)||_2^2 = ||R(\theta)||_2^2$$

For each parameter, its respective standard deviation is estimated using the formula:

$$SE(\theta) = \sqrt{Var(\theta_k)}$$

Data Analysis



Infected =Cumulative frequency of infected - Cumulative frequency of recoveries - Cumulative Frequency of Deaths



Figure: Infected

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The following steps are followed:

- Calculate the probability that a person dies given that they have the virus: $P_m = \frac{\text{total deceased}}{\text{total deceased} + \text{total recovered}}$
- Calculate D_r by finding the average number of days it takes a person to recover from the disease and dividing by $1 P_m$

$$D_r = rac{ ext{average days it takes a person to recover}}{1 - P_m}$$

• Calculate μ_c as:



Other parameters are taken from the previous study: Incorporating false negative tests in epidemiological models for SARS-CoV-2 transmission and reconciling with seroprevalence estimates ? carried out in India that are described in the table

Parameter	Value
D _E	5.2
λ	0
μ	0
f	0.1, 0.3, 0.048, 0
δ_1	0.3
δ_2	0.7
γ_1	0.6
γ_2	0.7

Table: Parameters for the study: Incorporating false negative tests in epidemiological models for SARS-CoV-2 transmission and reconciling with seroprevalence estimates ?

Table of parameters for different values of f without vaccination f



f	Parameter	Value	Standard deviation	R_0
0	β	0.40902	0.00139	3.118
	r	0.35976	0.00322	
0.048	β	0.40472	0.00147	3.186
	r	0.32700	0.00301	
0.1	β	0.40059	0.00155	3.259
	r	0.35213	0.00331	
0.3	β	0.38969	0.00189	3.546
	r	0.33761	0.00354	

Table: Table of estimated parameters for different values o f = 0, f = 0.048, f = 0.1 y f = 0.3 without vaccination

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f	Parameter	Value	Standard deviation	R ₀
0	β	0.194894	0.01434	1.891
	r	0.29102	0.01943	
0.048	β	0.18442376	0.02137664	2.042
	r	0.30011677	0.03052771	
0.1	β	0.18046702	0.02099582	2.078
	r	0.28313102	0.002419797	
0.3	β	0.17154699	0.01491504	2.108
	r	0.26872638	0.01647014	

Table: Table of estimated parameters f = 0, f = 0.048, f = 0.1 and f = 0.3 with vaccination

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Stochastic simulations taking different values of f





Figure: Stochastic simulations taking different values of the probability of having a false negative result (f)

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Conclusions



- In this work, a stochastic epidemiological model is proposed that accounts for randomness in the dynamics of COVID-19.
- Primary results of the model seem to capture the data from the Colombian city of Bogotá reasonably well and are potentially limited due to the lack of prevalence data.
- The proposed stochastic epidemiological model is also limited because there is no data on false negatives and untested individuals, which also vary over time.
- With the modified SEIR model with vaccination, a lower basic reproductive number is obtained, which indicates that an infected individual under this model infects fewer individuals than if it were in the model without vaccination.
- This work also opens a way to explore new compartment models one can take into account other factors such as migrations, demographics, and the effects of Waning immunity to vaccines.

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