Stochastic SEIPHAR model for epidemic of the SARS-CoV-2 virus

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Stochastic SEIPHAR model

The population is divided into seven mutually exclusive compartments

- S - susceptible individuals
- E - individuals exposed to the virus SARS-CoV-2
- I - symptomatic infectious individuals
- P - infectious superspreaders
- H - hospitalized infected individuals
- A - asymptomatic infected individuals
- R - recovered individuals

The total population size at time $t \geq 0$:

$$N(t) = S(t) + E(t) + I(t) + P(t) + A(t) + H(t) + R(t)$$

System of SDEs

$$\begin{aligned}
dS(t) &= \left(\Lambda - \left(\tfrac{\beta}{N(t)}\left(I(t) + lH(t)\right) + \tfrac{\beta'}{N(t)}P(t) + \mu\right) S(t)\right) dt \\
&\quad -\tfrac{\sigma_1}{N(t)}\left(I(t) + lH(t)\right) S(t) dB_1(t) - \tfrac{\sigma_2}{N(t)} P(t) S(t) dB_2(t)
\end{aligned}$$

$$\begin{aligned}
dE(t) &= \left(\tfrac{\beta}{N(t)}\left(I(t) + lH(t)\right) S(t) + \tfrac{\beta'}{N(t)}P(t)S(t) - (\kappa + \mu)E(t)\right) dt \\
&\quad +\tfrac{\sigma_1}{N(t)}\left(I(t) + lH(t)\right) S(t) dB_1(t) + \tfrac{\sigma_2}{N(t)} P(t) S(t)\, dB_2(t)
\end{aligned}$$

$$\begin{aligned}
dI(t) &= \left(\kappa\rho_1 E(t) - (\gamma_a + k_1\gamma_i + \delta_i)I(t)\right) dt \\
dP(t) &= \left(\kappa\rho_2 E(t) - (\gamma_a + k_2\gamma_i + \delta_p)P(t)\right) dt \\
dH(t) &= \left(\gamma_a(I(t) + P(t)) - (\gamma_r + \delta_h)H(t)\right) dt \\
dA(t) &= \left(\kappa(1 - \rho_1 - \rho_2)E(t) - (\gamma_i + \mu)A(t)\right) dt \\
dR(t) &= \left(\gamma_i(A(t) + k_1 I(t) + k_2 P(t)) + \gamma_r H(t) - \mu R(t)\right) dt
\end{aligned}$$

Noise is introduced via independent standard Brownian motions

$$B_1 = \{B_1(t),\, t \geq 0\} \text{ and } B_2 = \{B_2(t),\, t \geq 0\}$$

with intensities $\sigma_1 > 0$ and $\sigma_2 > 0$ in the transmission coefficients β and β' of the corresponding deterministic ODE model:

$$\beta\, dt \to \beta\, dt + \sigma_1 dB_1(t)$$

$$\beta'\, dt \to \beta'\, dt + \sigma_2 dB_2(t)$$

Parameters of the model

Symbol	Description	Value
Λ	Estimated daily number of newborns in Wuhan in 2019	310 [7]
β	Transmission coefficient due to infected individuals	2.55 [5]
l	Relative transmissibility from hospitalized individuals	1.56 [5]
β'	Transmission coefficient due to superspreaders	7.65 [5]
κ	Rate at which exposed individuals become infectious	0.25 [5]
ρ_1	Proportion of transitions from exposed do symptomatic infected class	0.58 [5]
ρ_2	Proportion of transitions from exposed to superspreaders	0.001 [5]
γ_a	Hospitalization rate	0.94 [5]
γ_r	Recovery rate for hospitalized patients	0.5 [5]
γ_i	Recovery rate for non-hospitalized patients	0.27 [5]
δ_i	Disease induced death rate for infected class	1/23 [5]
δ_p	Disease induced death rate for superspreaders	1/23 [5]
δ_h	Disease induced death rate for hospitalized class	1/23 [5]
μ	Natural death rate	0.00714 [7]
k_1	Weight for recovery rate due to infected class	0.85 [a]
k_2	Weight for recovery rate due to superspreaders	0.95 [a]
σ_1	Intensity of Brownian motion B_1 due to infected class	0.0005 [a]
σ_2	Intensity of Brownian motion B_2 due to superspreaders	0.001 [a]

Parameters values are based either on the epidemics in Wuhan (January 4 - March 9, 2020) or rationally assumed ($k_1, k_2, \sigma_1, \sigma_2$)

SEIPHAR system od SDEs, basic reproduction number, extinction and persistence of the virus

Existence and uniqueness of solution of the SEIPHAR SDEs system

Theorem 1 *For any initial value $(S(0), E(0), I(0), P(0), H(0), A(0), R(0)) \in \mathbb{R}^7_+$ there exists a unique solution*

$$\{(S(t), E(t), I(t), P(t), H(t), A(t), R(t)),\ t \geq 0\}$$

of the SEIPHAR system of SDEs, which almost surely remains positive for all $t > 0$. Moreover, since $N(t) = S(t) + E(t) + I(t) + P(t) + A(t) + H(t) + R(t)$ we have that

$$\frac{\Lambda}{\delta} = \liminf_{t\to\infty} N(t) \leq \limsup_{t\to\infty} N(t) = \frac{\Lambda}{\mu},$$

where $\delta = \max\{\delta_i, \delta_p, \delta_h\}$.

Positively invariant set for the SEIPHAR system:

$$\Gamma^\star = \{(S(t), E(t), I(t), P(t), H(t), A(t), R(t)) : S(t) > 0, E(t) > 0,$$

$$I(t) > 0, P(t) > 0, H(t) > 0, A(t) > 0, R(t) > 0, N(t) \leq \Lambda/\mu\}$$

If the system starts from $\Gamma^\star$, it never leaves $\Gamma^\star$

Basic reproduction number R_0^D related to deterministic SEIPHAR model

- the basic reproduction number R_0^D is the expected number of secondary infections generated by one infected individual in a fully susceptible population
- R_0^D for deterministic SEIPHAR model:

$$R_0^D = \frac{\kappa}{\kappa + \mu} \frac{\omega_h(\beta\rho_1\omega_p + \beta'\rho_2\omega_i) + l\beta\gamma_a(\rho_1\omega_p + \rho_2\omega_i)}{\omega_h\omega_i\omega_p}$$

$$\omega_i = \gamma_a + k_1\gamma_i + \delta_i, \quad \omega_p = \gamma_a + k_2\gamma_i + \delta_p, \quad \omega_h = \gamma_r + \delta_h$$

- R_0^D is an epidemiologically significant threshold - it determines the potential of an infectious disease to spread in a population
- if $R_0^D < 1$ the disease-free equilibrium of deterministic (ODE) SEIPHAR system is locally asymptotically stable and if $R_0^D > 1$ the system has locally asymptotically stable endemic equilibrium with all positive components
- it is well known that extinction of the epidemics appears if $R_0^D < 1$, while persistence occurs when $R_0^D > 1$

Extinction

The virus is extinct in the population if

$$E(t) + I(t) + P(t) + H(t) + A(t) \to 0 \quad \mathbb{P} - \text{a.s. as } t \to \infty.$$

Theorem 2 *If σ_1 and σ_2 satisfy*

$$\frac{1}{2(\kappa + \mu)}\left(\frac{\beta^2}{\sigma_1^2} + \frac{(\beta')^2}{\sigma_2^2}\right) < 1,$$

than for any initial value $(S(0), E(0), I(0), P(0), H(0), A(0), R(0)) \in \mathbb{R}^7_+$ such that the solution of the SEIPHAR system od SDEs is in $\Gamma^\star$

$$E(t) + I(t) + P(t) + H(t) + A(t) \to 0 \quad \mathbb{P} - a.s. \ \ as\ t \to \infty,$$

while

$$\limsup_{t\to\infty} S(t) = \frac{\Lambda}{\mu} \quad \mathbb{P} - a.s.$$

Threshold R_0^S, often called "the stochastic basic reproduction number", related to stochastic SEIPHAR system:

$$R_0^S = \frac{(\beta + \beta')\frac{\Lambda}{\mu}}{\kappa + \mu + \frac{1}{2}(\sigma_1^2 + \sigma_2^2)\frac{\Lambda^2}{\mu^2}}$$

Alternative conditions for extinction based on R_0^S:

If $\sigma_1^2 \leq \beta\frac{4\mu}{\Lambda}\max\{1, l\}$, $\sigma_2^2 \leq \beta'\frac{4\mu}{\Lambda}$ and $R_0^S < 1$, than the virus is P-a.s. extinct in the population

Persistence in mean

The virus remains persistent in population if there is at least one individual in one of the I, P, H, A classes

The solution of SEIPHAR system is persistent in mean if

$$\liminf_{t\to\infty}\, [I(s) + P(s) + H(s) + A(s)] > 0 \qquad \mathbb{P} - \text{a.s.}$$

$$[I(s) + P(s) + H(s) + A(s)] = \frac{1}{t}\int_0^t (I(s) + P(s) + H(s) + A(s))\, ds$$

Theorem 3 *Let initial value $(S(0), E(0), I(0), P(0), H(0), A(0), R(0)) \in \mathbb{R}^7_+$, such that the solution of the SEIPHAR system of SDEs is in $\Gamma^\star$, where μ, β, β' and l satisfy the relation*

$$\Lambda > \left(\frac{\beta}{N(t)}(I(t) + lH(t)) + \frac{\beta'}{N(t)}P(t) + \mu\right) S(t), \quad \forall t \geq 0$$

and where $c > 0$ is a constant such that $\inf_{t\geq 0} E(t)/N(t) \geq c$. If σ_1 and σ_2 satisfy the condition

$$\sigma_1^2 + \sigma_2^2 <$$

$$c\kappa\left(\rho_1\frac{\gamma_r + \gamma_a + \delta_p}{(\gamma_a + k_1\gamma_i + \delta_i)(\gamma_r + \delta_p)} + \rho_2\frac{\gamma_r + \gamma_a + \delta_p}{(\gamma_a + k_2\gamma_i + \delta_p)(\gamma_r + \delta_p)} + \frac{1 - \rho_1 - \rho_2}{\gamma_i + \mu}\right),$$

then

$$\liminf_{t\to\infty}[I(t) + P(t) + A(t) + H(t)] \geq$$

$$c\left(\kappa\rho_1\frac{\gamma_r + \gamma_a + \delta_p}{(\gamma_a + k_1\gamma_i + \delta_i)(\gamma_r + \delta_p)} + \kappa\rho_2\frac{\gamma_r + \gamma_a + \delta_p}{(\gamma_a + k_2\gamma_i + \delta_p)(\gamma_r + \delta_p)} + \right.$$

$$\left. + \frac{\kappa(1 - \rho_1 - \rho_2)}{\gamma_i + \mu} - \frac{(\sigma_1^2 + \sigma_2^2)}{c}\right) > 0.$$

Alternative condition for persistence in mean based on R_0^S:

If $R_0^S > 1$, the solution $\{(S(t), E(t), I(t), P(t), A(t), H(t), R(t)),\ t \geq 0\}$ of SEIPHAR system is persistent in mean

Sensitivity analysis of R_0^D and R_0^S

Thresholds R_0^D and R_0^S are analyzed regarding the values of the **normalized forward sensitivity indices (NFSI)** $\Upsilon_\theta^{R_0^i}$, $i \in \{D, S\}$ (parameter values are given in the table above).

NFSI is the ratio of the relative change in the basic reproduction number R_0^i as a function of the parameter θ to the relative change in the parameter θ, assuming that R_0^i is differentiable with respect to parameter: $\Upsilon_\theta^{R_0^i} = \dfrac{dR_0^i}{d\theta}\dfrac{\theta}{R_0^i}$

NFSI is used to discover parameters that have a high impact on R_0^i and should be **targeted by specific epidemiological intervention strategies.**

Sensitivity analysis of R_0^D

- R_0^D is most sensitive to change in values of parameters β, ρ_1, l, γ_i and γ_r
- change of $R_0^D = 4.5206$ under the 10% increase in value of parameters β, ρ_1, l, γ_i and γ_r is given in the following table:

Parameter	Value of R_0^D	Relative change in R_0^D (%)
β	4.9720	+9.98
ρ_1	4.9715	+9.97
l	4.8501	+7.29
γ_i	4.4366	−1.86
γ_r	4.2429	−6.14

Sensitivity analysis of R_0^S

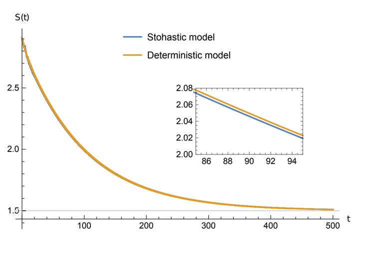
- R_0^S is most sensitive to change in values of parameters β, β', σ_1 and σ_2
- change of $R_0^S = 1.0298$ under the 10% increase in value of parameters β', β, σ_1 and σ_2 is given in the following table:

Parameter	Value of R_0^S	Relative change in R_0^S (%)
β'	1.1071	+7.51
β	1.0556	+2.51
σ_1	0.9883	−4.03
σ_2	0.8817	−14.38

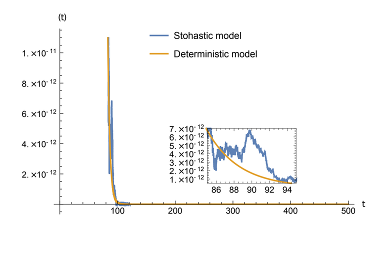
Simulation results

Extinction and persistence in mean, for reasonable set of parameter values for which the unique global positive solution of the SEIPHAR system of SDEs exists, are verified in the simulation study. Parameter values for simulation are adjusted from the table above, in order to satisfy the theoretical assumptions of extinction and persistence theorems. Simulations confirm that the trajectories of the stochastic model either oscillate around (on the short time-scale) or are close to (on the long time-scale) the trajectories of the deterministic model

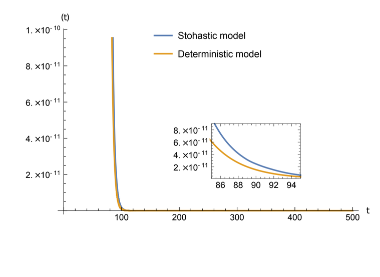
Extinction



Susceptibles



Exposed



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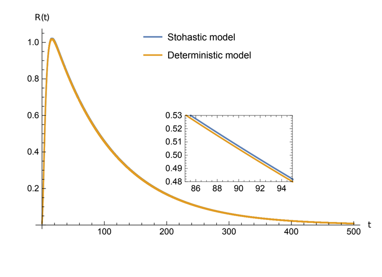
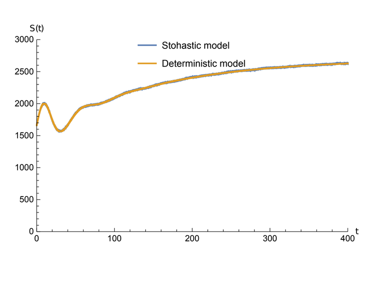


Recovered

Persistence in mean



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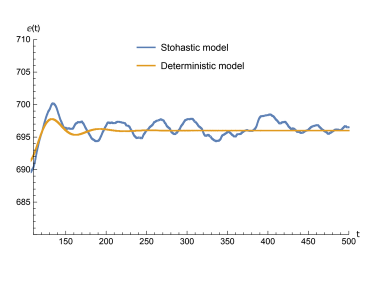

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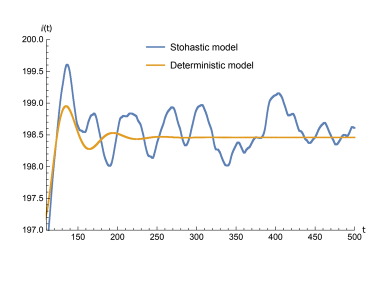
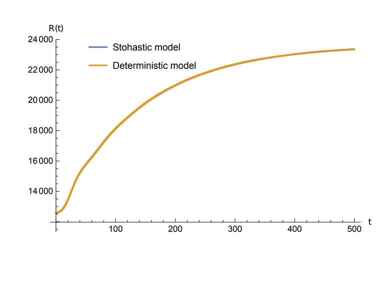


Infected



Recovered

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