Stochastic models for SARS-CoV-2 epidemics

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Compartmental epidemiological models

- models for spread of the epidemics in population divided into several disjoint compartments or classes (e.g. susceptible S, exposed E, infected I and recovered R individuals)
- population is of either constant size N or it could vary with time $(N_t,\, t \geq 0)$
- deterministic case - e.g. systems of difference equations; systems of ODEs
- stochastic case - e.g. multidimensional Markov chains in discrete or continuous time; systems of SDEs governed by Brownian motion or some other type of process
- models depend of several parameters - the most important is the per-capita transmission rate $\beta > 0$ which governs the dynamics of transition from class S to class E

SEIR model

- system of ODEs

$$
\begin{aligned}
dS(t) &= \left(\Lambda - \left(\frac{\beta}{N(t)} I(t) + \mu\right) S(t)\right)\, dt \\
dE(t) &= \left(\frac{\beta}{N(t)} I(t) S(t) - (\kappa + \mu) E(t)\right)\, dt \\
dI(t) &= (\kappa E(t) - (\gamma + \delta) I(t))\, dt \\
dR(t) &= (\gamma I(t) - \mu R(t))\, dt
\end{aligned}
$$

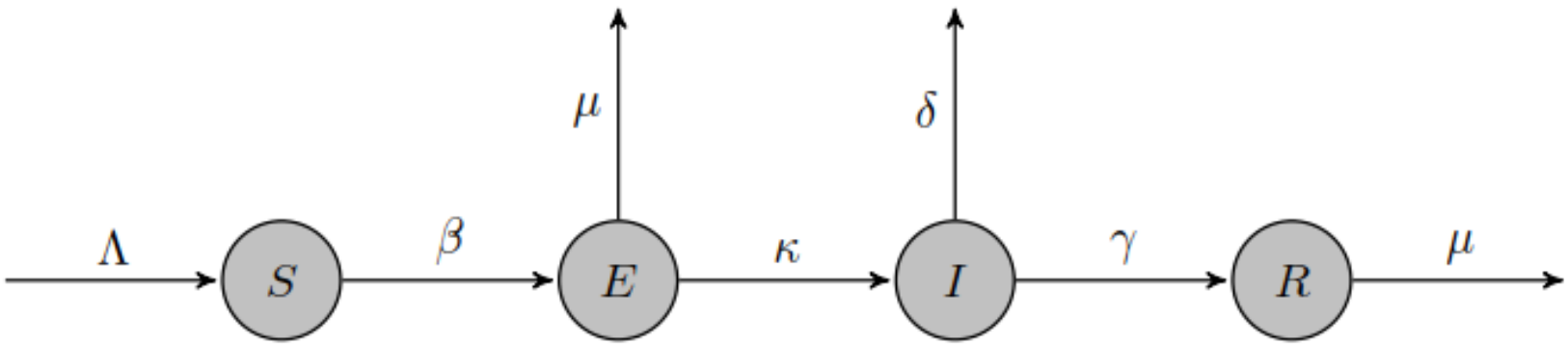


Figure 1: SEIR model scheme

- is it sensible to identify more compartments within the population?

SEIPHAR model - compartments

the human population is divided into seven mutually exclusive compartments:

- S - susceptible individuals
- E - individuals exposed to the virus SARS-CoV-2, but not yet infectious to others
- I - symptomatic infectious individuals
- P - infectuous superspreaders
- A - asymptomatic infectious individuals
- H - hospitalized infected individuals
- R - recovered individuals
- the total population size at time t is given by

$$N(t) = S(t) + E(t) + I(t) + P(t) + A(t) + H(t) + R(t), \quad t \geq 0$$

SEIPHAR model - parameters

Parameter	Description	Units
Λ	Estimated daily number of newborns in Wuhan in 2019	per day
β	Transmission coefficient due to infected individuals	per day
l	Relative transmissibility from hospitalized individuals	—
β'	Transmission coefficient due to superspreaders	per day
κ	Rate at which exposed individuals become infectious	per day
ρ_1	Proportion of transitions from exposed do infected class	—
ρ_2	Proportion of transitions from exposed to superspreaders	—
γ_a	Hospitalization rate	per day
γ_r	Recovery rate for hospitalized patients	per day
γ_i	Recovery rate for non-hospitalized patients	per day
k_1	Weight for recovery rate due to infected class	—
k_2	Weight for recovery rate due to superspreaders	—
δ_i	Disease induced death rate for infected class	per day
δ_p	Disease induced death rate for superspreaders	per day
δ_h	Disease induced death rate for hospitalized class	per day
μ	Natural death rate	per day

SEIPHAR model - scheme

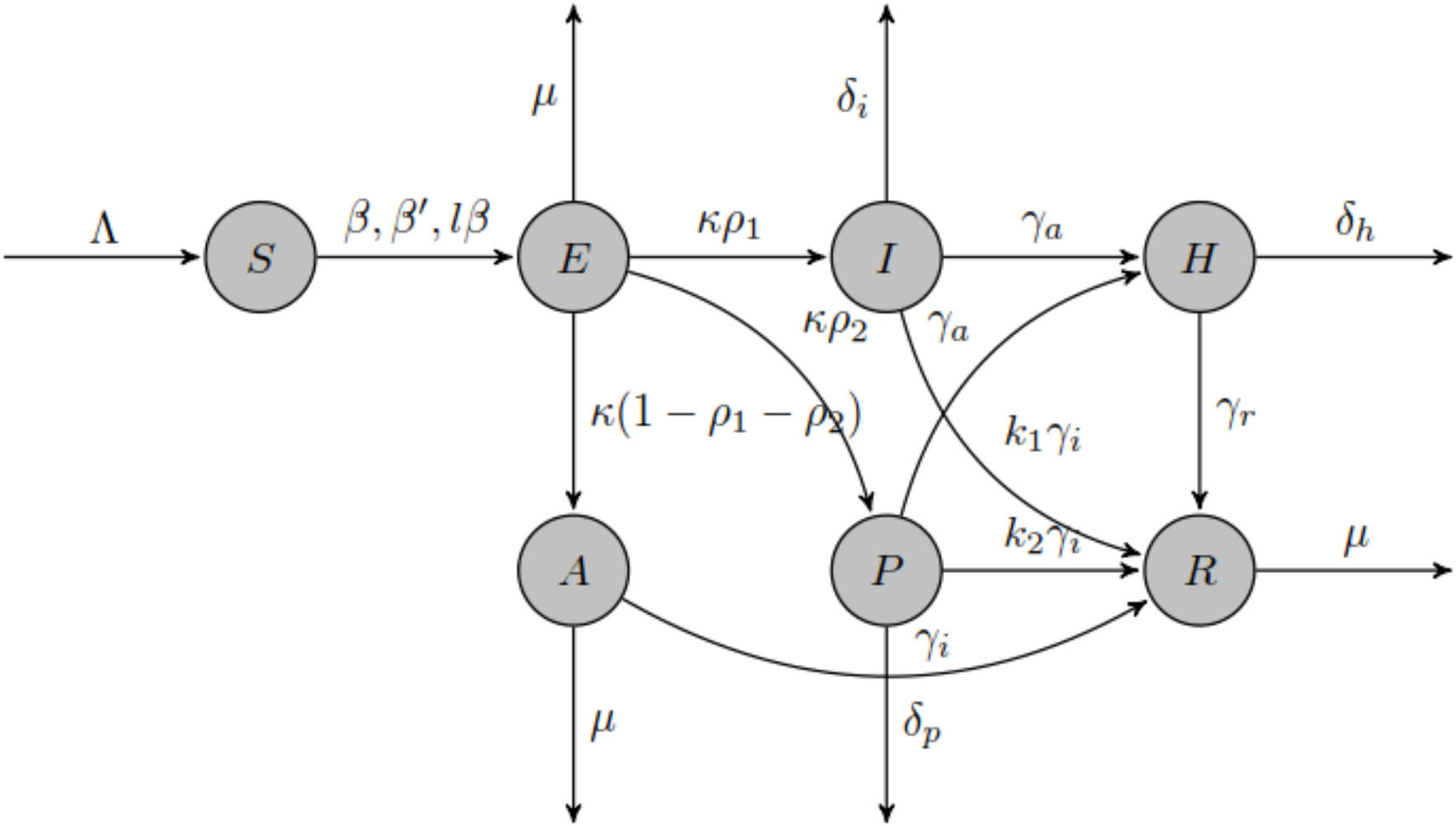


Figure 2: SEIPHAR model scheme

SEIPHAR model - ODEs dynamics

$$
\begin{aligned}
dS(t) &= \left(\Lambda - \left(\frac{\beta}{N(t)}\left(I(t) + lH(t)\right) + \frac{\beta'}{N(t)}P(t) + \mu\right)S(t)\right)dt \\
dE(t) &= \left(\frac{\beta}{N(t)}\left(I(t) + lH(t)\right)S(t) + \frac{\beta'}{N(t)}P(t)S(t) - (\kappa + \mu)E(t)\right)dt \\
dI(t) &= \left(\kappa\rho_1 E(t) - (\gamma_a + k_1\gamma_i + \delta_i)I(t)\right)dt \\
dP(t) &= \left(\kappa\rho_2 E(t) - (\gamma_a + k_2\gamma_i + \delta_p)P(t)\right)dt \\
dH(t) &= \left(\gamma_a(I(t) + P(t)) - (\gamma_r + \delta_h)H(t)\right)dt \\
dA(t) &= \left(\kappa(1 - \rho_1 - \rho_2)E(t) - (\gamma_i + \mu)A(t)\right)dt \\
dR(t) &= \left(\gamma_i(A(t) + k_1 I(t) + k_2 P(t)) + \gamma_r H(t) - \mu R(t)\right)dt
\end{aligned}
$$

SEIPHAR model (ODEs) - R_0

- the basic reproduction number R_0 - the expected number of secondary cases generated by one infected individual during its lifespan as infectious in a fully susceptible population
- deterministic SEIPHAR model R_0:

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

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

- R_0 - a threshold value that is epidemiologically significant and determines the potential of an infectious disease to spread in a population

SEIPHAR model - SDEs dynamics

- stochastic SEIPHAR model - constructed as system of SDEs by introducing the perturbation in the form of the environmental white noise in transmission coefficients β and β'

$$\beta\, dt \to \beta\, dt + \sigma_1 dB_1(t), \quad \sigma_1 > 0$$

$$\beta'\, dt \to \beta'\, dt + \sigma_2 dB_2(t), \quad \sigma_2 > 0$$

where $B_1 = \{B_1(t),\, t \geq 0\}$ and $B_2 = \{B_2(t),\, t \geq 0\}$ are independent standard Brownian motions with intensities $\sigma_1 > 0$ and $\sigma_2 > 0$

SEIPHAR model - SDEs dynamics

$$
\begin{aligned}
dS(t) &= \left(\Lambda - \left(\frac{\beta}{N(t)}\left(I(t)+lH(t)\right)+\frac{\beta'}{N(t)}P(t)+\mu\right)S(t)\right)dt \\
&\quad -\frac{\sigma_1}{N(t)}\left(I(t)+lH(t)\right)S(t)dB_1(t) - \frac{\sigma_2}{N(t)}P(t)S(t)dB_2(t) \\
dE(t) &= \left(\frac{\beta}{N(t)}\left(I(t)+lH(t)\right)S(t)+\frac{\beta'}{N(t)}P(t)S(t)-(\kappa+\mu)E(t)\right)dt \\
&\quad +\frac{\sigma_1}{N(t)}\left(I(t)+lH(t)\right)S(t)dB_1(t)+\frac{\sigma_2}{N(t)}P(t)S(t)\,dB_2(t) \\
dI(t) &= \left(\kappa\rho_1 E(t)-(\gamma_a+k_1\gamma_i+\delta_i)I(t)\right)dt \\
dP(t) &= \left(\kappa\rho_2 E(t)-(\gamma_a+k_2\gamma_i+\delta_p)P(t)\right)dt \\
dH(t) &= \left(\gamma_a(I(t)+P(t))-(\gamma_r+\delta_h)H(t)\right)dt \\
dA(t) &= \left(\kappa(1-\rho_1-\rho_2)E(t)-(\gamma_i+\mu)A(t)\right)dt \\
dR(t) &= \left(\gamma_i(A(t)+k_1I(t)+k_2P(t))+\gamma_r H(t)-\mu R(t)\right)dt
\end{aligned}
\tag{1}
$$

SEIPHAR model - probability space and space of values

- complete filtered probability space $(\Omega, \mathcal{F}, \mathbb{F}, \mathbb{P})$
- filtration $\mathbb{F} = \{\mathcal{F}_t,\, t \geq 0\}$ is generated by natural filtrations of Brownian motions B_1 and B_2
- space of values of the process $\{(S(t), E(t), I(t), P(t), H(t), A(t), R(t))\,,\, t \geq 0\}$:

$$\mathbb{R}^7_+ = \{(x_1, x_2, x_3, x_4, x_5, x_6, x_7) : x_i > 0,\, \forall i = 1, \ldots, 7\}$$

SEIPHAR model - SDEs solution

Theorem

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 SDE system (1) *for every* $t > 0$*, 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 $\delta = \max\{\delta_i, \delta_p, \delta_h\}$.

SEIPHAR model - space of values

- positively invariant set of the system (1):

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

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

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

SEIPHAR model - persistence in mean

- the virus remains persistent in population if there is at least one symptomatic infectious, asymptomatic infectious, hospitalized individual or super-spreader
- persistence in mean - we say that the system (1) is persistent in mean if

$$[I(s) + P(s) + A(s) + H(s)] > 0 \qquad \mathbb{P} - \text{a.s.}, \tag{2}$$

where

$$[I(s) + P(s) + A(s) + H(s)] =$$

$$= \lim_{t\to\infty} \frac{1}{t} \int_0^t (I(s) + P(s) + A(s) + H(s))\ ds$$

SEIPHAR model - persistence in mean

Theorem

Let initial value $(S(0), E(0), I(0), P(0), A(0), H(0), R(0)) \in \mathbb{R}_+^7$, *such that the solution of the system* (1) *is in* $\Gamma^\star$, *where* μ, β, β' *and* l *satisfy the relation*

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

and where c *is a small fixed constant such that* $\inf_{t \geq 0} E(t)/N(t) \geq c$. *If we assume that noises satisfy the condition*

$$\sigma_1^2 + \sigma_2^2 < c\kappa \left(\rho_1 \frac{\gamma_r + \gamma_a + \delta_p}{(\gamma_a + k_1\gamma_i + \delta_i)(\gamma_r + \delta_p)} + \right.$$

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

SEIPHAR model - persistence in mean

Theorem

then the solution $\{(S(t), E(t), I(t), P(t), A(t), H(t), R(t)),\ t \geq 0\}$ *has the property*

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

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

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

SEIPHAR model - persistence in mean

- alternative condition for persistence in mean is based on the so-called stochastic R_0:

$$R_0^S = \frac{(\beta + \beta') \frac{\Lambda}{\mu}}{\kappa + \mu + \frac{1}{2}\left(\sigma_1^2 + \sigma_2^2\right) \frac{\Lambda^2}{\mu^2}} \tag{3}$$

- 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 system (1) is persistent in mean

SEIPHAR model - extinction

Theorem

If noises satisfy that

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

than for any initial value $(S(0),E(0),I(0),P(0),A(0),H(0),R(0))\in\mathbb{R}_+^7$, *such that the solution of the system* (1) *is in* $\Gamma^\star$, *it follows that*

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

while

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

SEIPHAR model - extinction

- alternative conditions for extinction in mean are also based on R_0^S given by (3)

- 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 disease P-a.s. goes to extinction

SEIPHAR model - parameter values

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]
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]
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 [6]
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]

Table 1: Parameters values, either based on the epidemics in Wuhan in the period January 4 - March 9, 2020, or rationally assumed ($k_1, k_2, \sigma_1, \sigma_2$)

SEIPHAR model - sensitivity analysis

- R_0^D and the stochastic model related threshold R_0^S are compared regarding the values of the normalized forward sensitivity indices (NFSI)
- 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:

$$\Upsilon_\theta^{R_0^i} = \frac{dR_0^i}{d\theta}\frac{\theta}{R_0^i}, \quad i \in \{D, S\}$$

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

SEIPHAR model - R_0^D sensitivity analysis

- R_0^D is the 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

SEIPHAR model - R_0^S sensitivity analysis

- R_0^S is the most sensitive to change in values of parameters β, β', σ_1 and σ_2

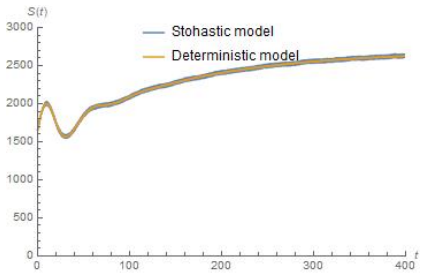
- change of $R_0^S = 1.0298$ under the 10% increase in value of parameters β', β, σ_1 and σ_2 is given in the following table:

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

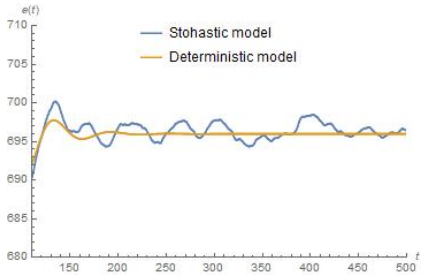
SEIPHAR model - simulation parameters

- theoretical results (persistence, extinction) are, for reasonable set of values of model parameters for which the global positive solution of system (1) exists, verified within the simulation study
- simulation parameters - adjusted values from Table 1 in order to satisfy the theoretical assumptions of persistence and extinction 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, showing the robustness of such stochastic model to the Brownian noise

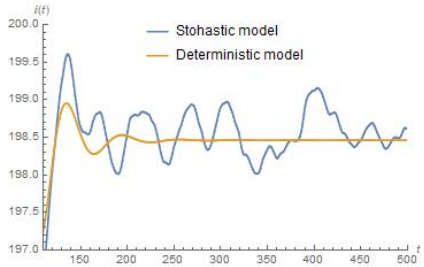
Persistence in mean



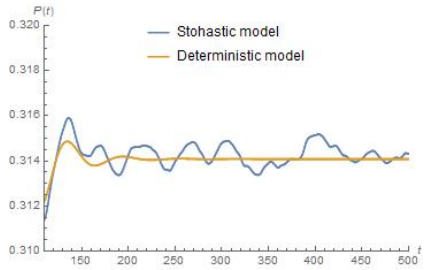
(a) susceptible



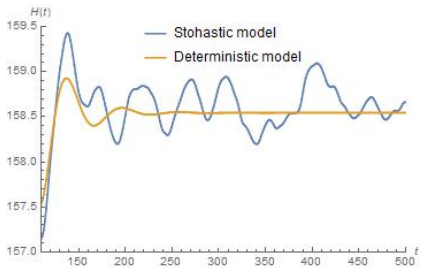
(b) exposed



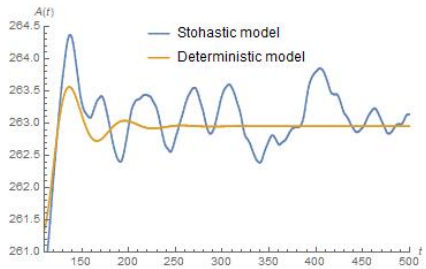
(c) infected



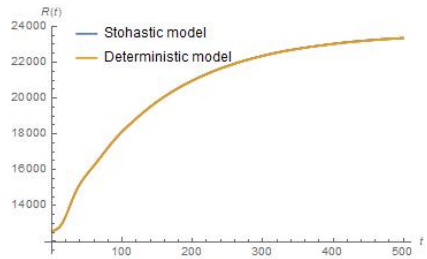
(d) superspreaders



(e) hospitalized



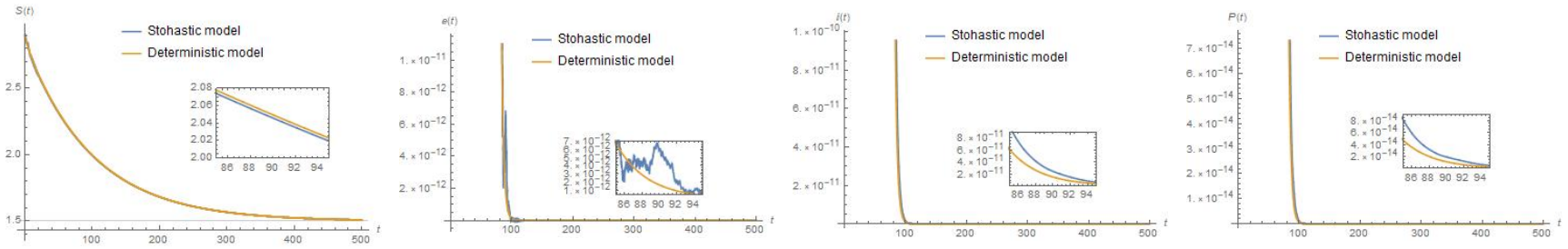
(f) asymptomatic



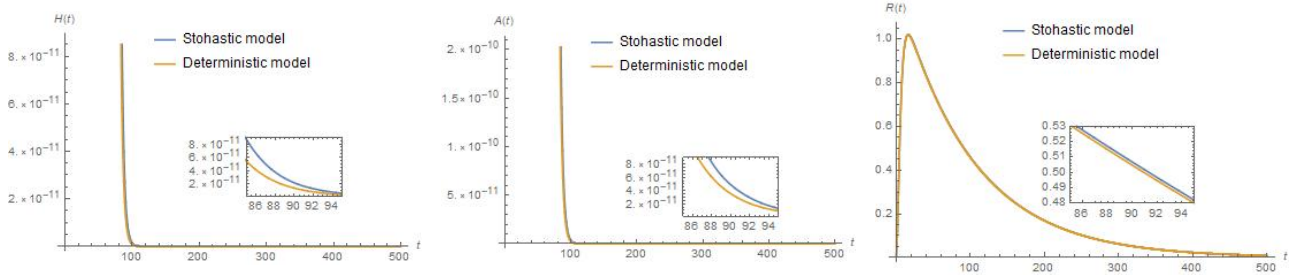
(g) recovered

Figure 3: Persistence - stochastic (blue) and deterministic (orange) model

Extinction



(a) susceptible (b) exposed (c) infected (d) superspreaders



(e) hospitalized (f) asymptomatic (g) recovered

Figure 4: Extinction - stochastic (blue) and deterministic (orange) model

Delayed SVEIR model - main characteristics

- V - vaccinated individuals (new compartment)
- cumulative number of exposed individuals by time $t > 0$ (A_* is a unit-rate Poisson process):

$$A_E^n(t) = A_* \left(n \int_0^t \beta(t) S^n(s) I^n(s)\, ds \right)$$

- cumulative number of vaccinated individuals by time $t > 0$, independent of $(A_E^n(t),\, t \geq 0)$:

$$A_V^n(t) = A_* \left(n \int_0^t \alpha(t) S^n(s)\, ds \right)$$

Delayed SVEIR model - scheme

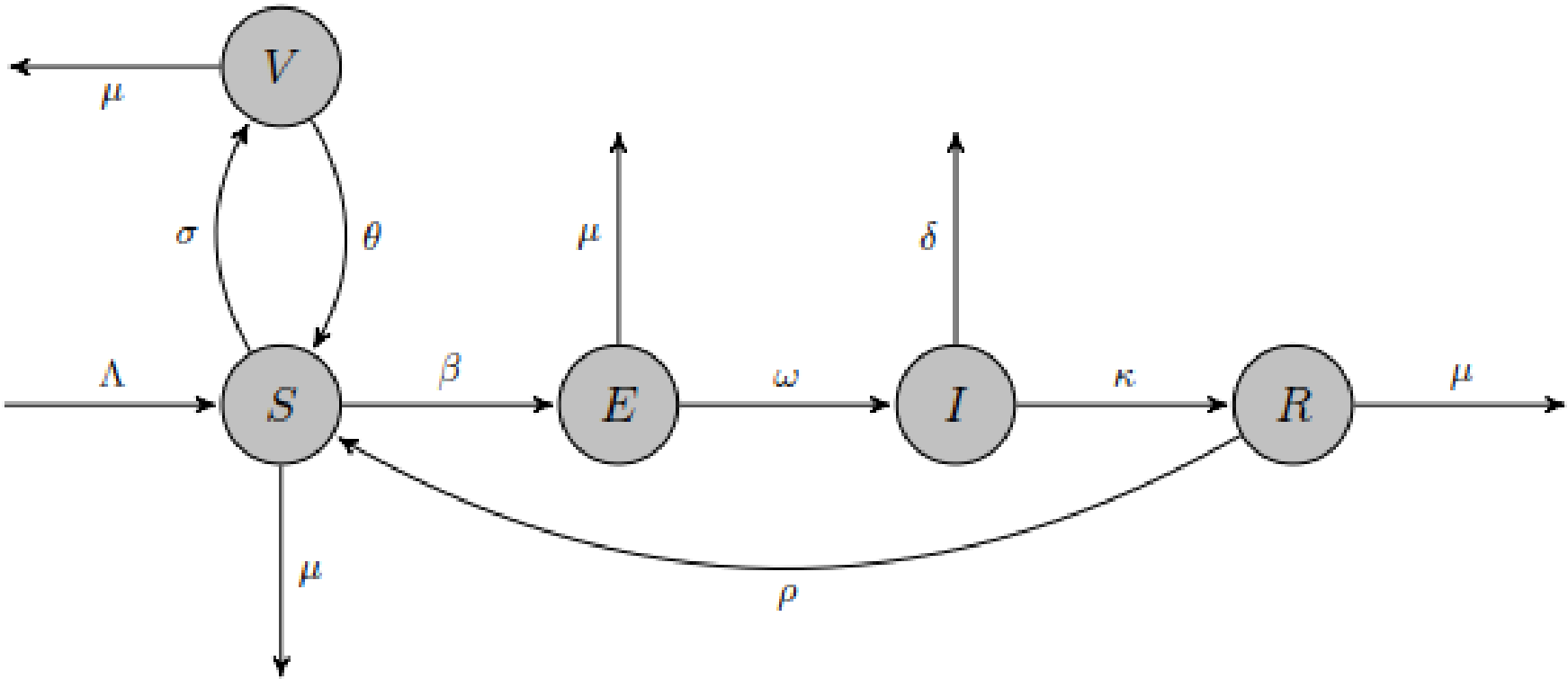


Figure 5: SVEIR model scheme

Delayed SVEIR model - delays

- the individual i going through the $S - E - I - R$ path has the following time epochs: τ_i, $\tau_i + \mathcal{E}_i$, $\tau_i + \mathcal{E}_i + \mathcal{I}_i$, $\tau_i + \mathcal{E}_i + \mathcal{I}_i + \mathcal{W}_i$, representing the times of becoming exposed, infected, immune and then again susceptible
- $\mathcal{E}_i$ is the exposure period, $\mathcal{I}_i$ is the infectious period and $\mathcal{W}_i$ is the natural immunity period
- an individual can initially be exposed $(\mathcal{E}_i^0)$, infected $(\mathcal{I}_i^0)$ or recovered (W_i^0)

Delayed SVEIR model - distributions of delays

$$G^c(t) = P(t < \mathcal{E}_i) \qquad G_0^c(t) = P(t < \mathcal{E}_i^0)$$
$$\Psi(t) = P(\mathcal{E}_i \le t < \mathcal{E}_i + \mathcal{I}_i), \qquad \Psi_0(t) = P(\mathcal{E}_i^0 \le t < \mathcal{E}_i^0 + \mathcal{I}_i)$$
$$\Phi(t) = P(\mathcal{E}_i + \mathcal{I}_i \le t < \mathcal{E}_i + \mathcal{I}_i + \mathcal{W}_i), \qquad \Phi_0(t) = P(\mathcal{E}_i^0 + \mathcal{I}_i \le t < \mathcal{E}_i^0 + \mathcal{I}_i + \mathcal{W}_i)$$
$$\Xi(t) = P(\mathcal{E}_i + \mathcal{I}_i + \mathcal{W}_i \le t) \qquad \Xi_0(t) = P(\mathcal{E}_i^0 + \mathcal{I}_i + \mathcal{W}_i \le t)$$

$$G_1^c(t) = P(t < \mathcal{I}_i^0),$$
$$\Phi_1(t) = P(\mathcal{I}_i^0 \le t < \mathcal{I}_i^0 + \mathcal{W}_i) \qquad G_2^c(t) = P(t < \mathcal{W}_i^0)$$
$$\Xi_1(t) = P(\mathcal{I}_i^0 + \mathcal{W}_i \le t) \qquad G_2(t) = P(\mathcal{W}_i^0 \le t).$$

Delayed SVEIR model - counting process

- denote the proportion of individuals at time t in compartment X by $X^n(t)$
- the counting process

$$(S^n(t), V^n(t), E^n(t), I^n(t), R^n(t),\ t \geq 0)$$

is given as follows:

$$\begin{aligned} S^n(t) &= S^n(0) + \sum_{i=1}^{V^n(0)} \mathrm{I}_{\{\mathcal{Y}_i^0 \leq t\}} + \sum_{i=1}^{E^n(0)} \mathrm{I}_{\{\mathcal{E}_i^0 + \mathcal{I}_i + \mathcal{W}_i \leq t\}} + \sum_{i=1}^{I^n(0)} \mathrm{I}_{\{\mathcal{I}_i^0 + \mathcal{W}_i \leq t\}} + \\ &\quad + \sum_{i=1}^{R^n(0)} \mathrm{I}_{\{\mathcal{W}_i^0 \leq t\}} + \sum_{i=1}^{A_V^n(t)} \mathrm{I}_{\{T_i + \mathcal{Y}_i \leq t\}} + \sum_{i=1}^{A_E^n(t)} \mathrm{I}_{\{\tau_i + \mathcal{E}_i + \mathcal{I}_i + \mathcal{W}_i \leq t\}} - \\ &\quad - A_E^n(t) - A_V^n(t) \end{aligned}$$

$$V^n(t) = \sum_{i=1}^{V^n(0)} \mathrm{I}_{\{\mathcal{Y}_i^0 > t\}} + \sum_{i=1}^{A_V^n(t)} \mathrm{I}_{\{T_i + \mathcal{Y}_i > t\}}$$

$$E^n(t) = \sum_{i=1}^{E^n(0)} \mathrm{I}_{\{\mathcal{E}_i^0 > t\}} + \sum_{i=1}^{A_E^n(t)} \mathrm{I}_{\{\tau_i + \mathcal{E}_i > t\}}$$

Delayed SVEIR model - counting process

$$
\begin{aligned}
I^n(t) &= \sum_{i=1}^{I^n(0)} \mathrm{I}_{\{\mathcal{I}_i^0 > t\}} + \sum_{i=1}^{E^n(0)} \mathrm{I}_{\{\mathcal{E}_i^0 \le t < \mathcal{E}_i^0 + \mathcal{I}_i\}} + \sum_{i=1}^{A_E^n(t)} \mathrm{I}_{\{\tau_i + \mathcal{E}_i \le t < \tau_i + \mathcal{E}_i + \mathcal{I}_i\}} \\
R^n(t) &= \sum_{i=1}^{R^n(0)} \mathrm{I}_{\{\mathcal{W}_i^0 > t\}} + \sum_{i=1}^{I^n(0)} \mathrm{I}_{\{\mathcal{I}_i^0 \le t < \mathcal{I}_i^0 + \mathcal{W}_i\}} + \sum_{i=1}^{E^n(0)} \mathrm{I}_{\{\mathcal{E}_i^0 + \mathcal{I}_i \le t < \mathcal{E}_i^0 + \mathcal{I}_i + \mathcal{W}_i\}} + \\
&\quad + \sum_{i=1}^{A_E^n(t)} \mathrm{I}_{\{\tau_i + \mathcal{E}_i + \mathcal{I}_i \le t < \tau_i + \mathcal{E}_i + \mathcal{I}_i + \mathcal{W}_i\}}
\end{aligned}
$$

Delayed SVEIR model - system of Volterra integral equations

- according to [6], we want to prove that the law of large number limit of the above described counting system is the unique solution of the following system of deterministic Volterra integral equations:

$$
\begin{aligned}
S(t) &= S(0) + V(0)\Upsilon_0(t) + E(0)\Xi_0(t) + I(0)\Xi_1(t) + R(0)G_2(t) - \\
&\quad - \int_0^t (\beta(s)S(s)I(s)(1-\Xi(t-s)) + \alpha(s)S(s)\Upsilon(t-s) - \\
&\quad - V(s)\Upsilon(t-s) - R(s)\Xi^c(t-s))\, ds \\
V(t) &= V(0)\Upsilon_0^c(t) + \int_0^t (\alpha(s)S(s)\Upsilon^c(t-s) - V(s)\Upsilon(t-s))\, ds \\
E(t) &= E(0)G_0^c(t) + \int_0^t \beta(s)S(s)I(s)G^c(t-s)\, ds \\
I(t) &= I(0)G_1^c(t) + E(0)\Psi_0(t) + \int_0^t \beta(s)S(s)I(s)\Psi(t-s)\, ds \\
R(t) &= R(0)G_2^c(t) + I(0)\Phi_1(t) + E(0)\Phi_0(t) + \\
&\quad + \int_0^t (\beta(s)S(s)I(s)\Phi(t-s) - R(s)\Xi(t-s))\, ds
\end{aligned}
\tag{4}
$$

Delayed SVEIR model - stochastic perturbation

- transmission coefficient $\beta(t)$ - Ornstein-Uhlenbeck process $\beta = (\beta(t),\, t \geq 0)$ given by the stochastic differential equation (SDE)

$$d\beta(t) = \theta\left(\beta_e - \beta(t)\right) dt + \sigma dB(t), \quad t \geq 0,$$

  where β_e is the mean of the stationary Gaussian distribution with variance $\sigma/\sqrt{2\theta}$, $\theta > 0$ determines the speed of the mean reversion, σ is the intensity of volatility and Brownian motion $B = (B(t),\, t \geq 0)$ is the driving process

- explicit solution:

$$\beta(t) = \beta_e + \left(\beta(0) - \beta_e\right) e^{-\theta t} + \sigma \int_0^t e^{-\theta(t-s)}\, dB(s),$$

$$\sigma \int_0^t e^{-\theta(t-s)}\, dB(s) \sim \mathcal{N}\left(0, \frac{\sigma^2}{2\theta}(1 - e^{-2\theta t})\right)$$

- existence of unique positive solution, analysis of persistence and extinction of the disease

Bibliography

1. Y. Cai, J. Jiao, Z. Gui, Y. Liu, W. Wang (2018) *Environmental variability in a stochastic epidemic model*, Applied Mathematics and Computation, 329, 210–226
2. J. Đorđević, I. Papić, N. Šuvak (2021) *A two diffusions stochastic model for the spread of the new corona virus SARS-CoV-2*, Chaos, Solitons and Fractals, 148: 110991,
3. J. Đorđević, B. Jovanović, J. Manojlović, N. Šuvak (2022) *Analysis of stability and sensitivity of deterministic and stochastic models for the spread of the new corona virus SARS-CoV-2*, Filomat (to appear)
4. A. Idris, Modu G.U. et al. (2021) *A mathematical model of coronavirus disease (COVID-19) containing asymptomatic and symptomatic classes*, Results in Physics 21: 103776
5. F. Ndaïrou, I. Area, J.J. Nieto, D.F.M. Torres (2020) *Mathematical modeling of COVID-19 transmission dynamics with a case study of Wuhan*, Chaos, Solitons and Fractals 135: 109846
6. Pang G., Pardoux E. (2022) *Functional Limit Theorems for Non-Markovian Epidemic Models*, arXiv:2003.03249v3
7. Statista https://www.statista.com/statistics/250650/number-of-births-in-china