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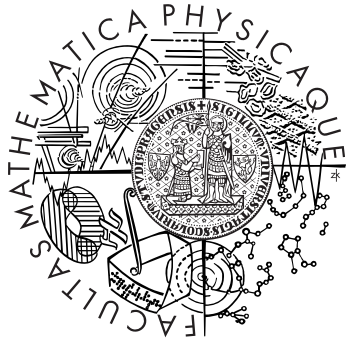

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Deterministic and stochastic epidemic models

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Field of study: Probability and Mathematical Statistics

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I declare that this thesis was written by myself and using the quoted references. I agree with using this thesis for study purposes.

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Abstract: Kermack-McKendrick model and its version with vaccination are presented. First, we introduce a model with vaccination and then a numerical study that includes comparison of different vaccination strategies and searching for optimal vaccination strategy is presented. We proceed to introduce a stochastic model with migration and consequently we suggest its generalization and prove the existence and uniqueness of a solution to the stochastic differential equation (henceforth SDE) describing this model. Three stochastic versions of Kermack-McKendrick model with vaccination are suggested and compared. A procedure of finding the optimal vaccination strategy is presented. We also prove the theorem on the existence and uniqueness of a solution to the SDE that drives a model with multiple pathogens. Finally, the stochastic differential equation describing the general model is presented. We study properties of a solution to this SDE and present sufficient conditions for the existence of a solution that is absorbed by the natural barrier of the model.

Keywords: absorption, differential equation, SIR epidemic models, stochastic differential equation, stochastic epidemic models, strong solution, uniqueness of solution to SDE, vaccination, vaccination strategy.

Chapter 1

Introduction

With massive growth of traveling, the danger of spread of infection diseases increases. Therefore, it is necessary to keep on improving healing methods and choosing new methods of prevention, hence it is necessary to keep on enlarging our knowledge of behavior of diseases. One of the tool which helps us to understand the behavior of diseases are mathematical models for spreading of epidemics.

This work presented both deterministic and stochastic model which are described by differential equations (DE) and by stochastic differential equations (SDE), respectively, and we study the properties of solutions to these equations.

In chapter 2, the Kermack-McKendrick model and its generalization with vaccination are presented. Both these deterministic models are suitable for modeling the spread of highly infection disease with fast recovery, hence we can consider constant size of population as the observation time period is short. The typical example of such a disease is influenza. For more general model with vaccination, we prove the theorem about the existence and uniqueness of a solution to DE and present the formulas for computing the maximum of infectives and the number of individuals which were infected during the running time of epidemics. In the last part of this chapter, we compare different vaccination strategies and choose the optimal vaccination strategy by using numerical method.

In chapter 3, we present a few stochastic models which are described by stochastic differential equations. The first model first presented by Štěpán and Hlubinka in [17] is a Kermack-McKendrick model with stochastic migration. We present a version with a little more general susceptibles-infectives contact rate β. In the second part of this section, we discuss the way, how to establish a stochastic version on the Kermack-McKendrick model with vaccination and present some numerical results for these versions, including the choice of optimal vaccination strategy. In the third part, we introduce the model with multiple pathogens which was introduced by Allen and Kirupaharas in [1]. This model

describes a behavior of epidemics like HIV-AIDS. This model assumes changing size of population, and includes births and deaths, as the observation time period is long. In this model, both the horizontal transmission (i.e. the transmission from infected individual to susceptible individual) and the vertical transmission (i.e. the transmission from infected mother to offspring) are considered. The theorem on the existence and uniqueness of a solution to SDE which describes this model is presented. In the last part of this chapter, we present the $(d+1)$-dimensional stochastic differential equation which describes the general epidemic model. We look for the conditions which provide the model with required properties, e.g. nonnegative solution, the existence and uniqueness of a solution which is absorbed by the natural barrier or that all solutions are absorbed by the natural barrier. We also present a few examples which illustrate the implication of the proved results.

Chapter 2

Deterministic models

In this chapter, we will present two deterministic models describing the spread of a highly infection disease with short healing time (few days) and very short incubation time which is omitted in the models. A typical example of such a disease is influenza. The first model is the Kermack-McKendrick model and the second one is its generalization which describes the situation when vaccination is considered.

2.1 Kermack-McKendrick model

The Kermack-McKendrick model was presented in 1927 by W. O. Kermack and A. G. McKendrick in [9] and since that time, it has been widely used. In this model, we assume a homogenously mixed population with constant size n which is divided into three sub-population changing their sizes in the running time:

- "susceptibles"... the individuals who are not infected, but who can be infected by the disease, denoted in the model by x_t,
- "infectives"... the infected individuals, who are able to spread the disease, denoted y_t,
- "removals"... the individuals who were infected, but who are not able to spread the infection further or get themselves infected again, denoted z_t. In this sub-population there are people who were recovered and have become immune, die or have been isolated.

The model is described by the following two dimensional differential equation:

$$\begin{aligned} dx_t &= -\beta x_t y_t dt, & x_0 > 0, \\ dy_t &= \beta x_t y_t dt - \gamma y_t dt, & y_0 > 0, \\ dz_t &= \gamma y_t dt, & z_0 = 0, \end{aligned} \tag{2.1.0.1}$$

where $\beta > 0$ is a susceptibles-infectives contact rate and $\gamma > 0$ is a recovery rate. Note that the size of β depends on the rate of infectivity of the disease and also on the density of population, therefore β is higher for more infectious disease or when modeling the population in a city and on the other hand lower for a population living in the countryside. γ^{-1} is the average time of duration of the disease or more precisely of "being in infectives".

Obviously, $n = x_t + y_t + z_t = x_0 + y_0 + z_0$ for all $t \geq 0$, x_t is nonincreasing function and z_t is nondecreasing function. It is possible to prove that equation (2.1.0.1) has a unique solution, there exist limits x_t, y_t and z_t at infinity and x_t, y_t and z_t are nonnegative functions, but unfortunately the equation (2.1.0.1) has no explicit solution. For further details see [4].

From the equation

$$dy_t = y_t(\beta x_t - \gamma)dt$$

it is possible to see, that y_t is decreasing for all $t \geq 0$ if and only if $x_0 < \frac{\gamma}{\beta} = \rho$ and y_t has maximum (if it is not decreasing for all $t \geq 0$) in time when $x_t = \rho$. Therefore the size of relative removals rate ρ seems to be reasonable measure of the virulence of an epidemics. One can see from the Figure 2.1 that the epidemics is weak when ρ is approximately the same as x_0. On the other hand, if ρ is twice smaller than x_0 then the epidemics is very serious.

Remark 2.1 *If we choose constant β, we assume that the population is not only homogenously mixed, but also that each member of the population has the same level of immunity. However this is not very realistic assumption, because for example children have lower level of immunity than adults, and therefore the probability of infection is higher for children than for adults . Hence during the running time the proportion of the individuals with lower level of immunity in susceptibles will be decreasing and therefore, it is reasonable to expect that β is decreasing during the running time. This choice of β was presented in [17].*

2.2 Kermack-McKendrick model with vaccination

This model is a generalization of Kermack-McKendrick model. We choose more general β and we added vaccination by the natural way, because we wanted a model of epidemics

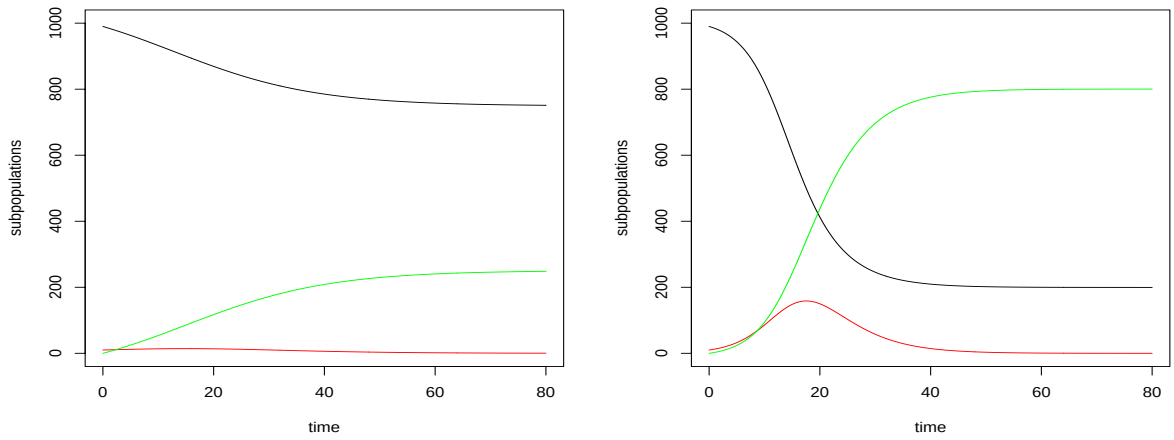

Figure 2.1:
Behavior of an epidemic with the parameters $\beta = 0.0005$, $\gamma = 0.45$ (left) and $\beta = 0.0005$, $\gamma = 0.25$ (right). The black line describes the size of susceptibles, the red line the size of infectives and the green line the size of removals. In both cases, the initial conditions are $x_0 = 990$, $y_0 = 10$ and $z_0 = 0$.

which allows us to control epidemics by a vaccination, to study the effect of vaccination and which allows us to compare different vaccination strategy.

We consider (like in the previous model) constant size of population n which is divided into three sub-populations ("susceptibles","infectives","removals"). The model is described by the following differential equations (see [19]):

$$\begin{aligned} dx_t &= -\beta(z_t)y_t \ [x_t - \vartheta(z_t)]^+ dt, & x_0 > 0, \\ dy_t &= \beta(z_t)y_t \ [x_t - \vartheta(z_t)]^+ dt - \gamma y_t dt, & y_0 > 0, \\ dz_t &= \gamma y_t dt, & z_0 = 0, \end{aligned} \tag{2.2.0.2}$$

where $\beta(z_t)$ is a susceptibles-infectives contact rate that is time dependent through z_t, where γ is a recovery rate of the infection, and finally, $\vartheta(z_t)$ is the size of vaccinated susceptibles sub-population controlled by z_t again.

We shall assume that $\beta(z) : \mathbb{R} \to \mathbb{R}^+$ is a nonincreasing continuous function, $\gamma > 0$ and that $\vartheta(z) : \mathbb{R} \to \mathbb{R}^+$ is a nondecreasing continuous function. From the assumptions, we know that $x_t + y_t + z_t = n = x_0 + y_0$ for all $t \geq 0$.

It means that the size of individuals newly infected during the time interval $(t, t + \triangle)$ is approximately equal to the product $y_t[x_t - \vartheta(z_t)]^+\beta(z_t)\triangle$, where $y_t[x_t - \vartheta(z_t)]^+$ is the number of all possible contacts between infective and susceptible nonvaccinated people

(i.e. the number of all possible pairs) in time t, and $\beta(z_t)$ is a probability that a randomly chosen susceptible nonvaccinated person is infected by a randomly chosen infective person during the time interval $(t, t+1)$. Because the population consists of people with different rate of immunity (e.g. children are more inclined to diseases then adults) and people with weaker immunity fall ill more easily than strong immune people, the rate of immunity of susceptibles grows with increasing z_t. Therefore the susceptibles-infectives contact rate β is a nonincreasing function of removals.

After the consultation with practitioners in medicine, the function of vaccinated susceptibles ϑ is also considered to be a function of the removals, because the number of the removals is usually known and also because it is an indicator of the extent of the epidemics used in practice. Moreover, if we choose ϑ as an increasing linear function of vaccinated individuals, then we vaccinate more people in the case when we have more infected individuals, because the increment of removals is proportional to the number of infectives.

2.2.1 Theoretical resuls

In this section, we will speak about a solution to differential equation. By the solution to DE we mean the classical solution, i.e. we use the definition of a solution as introduced in [2], p.67.

Lemma 2.1 follows from more general results, e.g. Corollary 16.10, p.219, in [2], but it could be unnoticed when using it for our case. Therefore we show more intuitive proof without using any special theorems.

Lemma 2.1 *If $l_t = (x_t, y_t, z_t)$ is a solution to (2.2.0.2), then $l_t \in [0, n]^3$ for all $t \geq 0$. Moreover, x_t is a nonincreasing function and z_t is an increasing function.*

Proof. From (2.2.0.2), we can get

$$y_t = y_0 \exp\left\{ \int_0^t \beta(z_s)[x_s - \vartheta(z_s)]^+ - \gamma ds, \right\},$$

therefore $y_t > 0$ for all t.

Further, $z_t = z_0 + \int_0^t \gamma y_s ds$, therefore we get z_t as a nonnegative increasing function as $y_t > 0$.

The size of susceptibles x_t is obviously a nonincreasing function.

If we denote by $\tau_v := \inf\{t \in \mathbb{R}^+ : x_t \leq \vartheta(z_t)\}$ the first time, when susceptibles are completely vaccinated, then

$$dx_t = -\beta(z_t)y_t[x_t - \vartheta(z_t)]dt \tag{2.2.1.1}$$

for $t \in [0, \tau_v]$. Moreover, as x_t is nonincreasing and z_t is increasing, we have for all $t > \tau_v$ that $x_t \leq \vartheta(z_t)$ and

$$dx_t = 0.$$

Solving equation (2.2.1.1) we get

$$x_t = \left[x_0 + \int_0^t \beta(z_s)\vartheta(z_s)y_s \exp\left\{\int_0^s \beta(z_u)y_u du\right\} ds\right] \exp\left\{-\int_0^t \beta(z_s)y_s ds\right\} \quad \geq 0.$$

Since $x_t = x_{\tau_v}$ for all $t \in (\tau_v, \infty)$, x_t is nonnegative function.

We proved that any solution $l_t = (x_t, y_t, z_t)$ to (2.2.0.2) maps $[0, \infty)$ into the first octant. As $x_t \geq 0$, $y_t \geq 0$ and $z_t \geq 0$ for all $t \geq 0$ and $x_t + y_t + z_t = n$ it follows that $l_t \in [0, n]^3$. □

As ϑ is nondecreasing and $x(.)$ is nonincreasing, then using τ_v from the previous proof we can rewrite (2.2.0.2) to the form

$$\begin{aligned} dx_t &= -\beta(z_t)y_t\left[x_t - \vartheta(z_t)\right]dt, & x_0 &> 0, \\ dy_t &= \beta(z_t)y_t\left[x_t - \vartheta(z_t)\right]dt - \gamma y_t dt, & y_0 &> 0, \\ dz_t &= \gamma y_t dt, & z_0 &= 0, \end{aligned} \tag{2.2.1.2}$$

for $t \in [0, \tau_v]$ and

$$\begin{aligned} dx_t &= 0, \\ dy_t &= -\gamma y_t dt, \\ dz_t &= \gamma y_t dt, \end{aligned} \tag{2.2.1.3}$$

for $t \in [\tau_v, \infty)$.

Lemma 2.2 *Let β and ϑ be Lipschitz bounded functions. Then the equation* (2.2.1.2) *has a unique solution on the interval* $[0, \tau_v]$.

Proof. Denote

$$f(x,y,z) = (-\beta(z)[x-\vartheta(z)]y, \beta(z)[x-\vartheta(z)]y - \gamma y, \gamma y)$$

and

$$\tilde{f}(l) = f(\tilde{x},\tilde{y},\tilde{z}),$$

where $\tilde{x} = (x \vee -2n) \wedge 2n$. Then, using Lemma 2.1 and the fact that the unique solution to

$$dl = \tilde{f}(l),\ l_0 = (x_0, y_0, z_0)$$

is the unique solution to (2.2.1.2) on the interval $[0, \tau_v]$, Lemma 2.2 follows from more general theorem 7.6 in [2], p.100.

□

Define $\tau_Y := \arg\max y_t$, i.e. $\tau_Y = \{t \in [0,\infty) : y_t = \max\limits_{s\in[0,\infty)} y_s\}$ the time of culmination of the epidemics. Below we show that the time τ_Y is unique.

The following theorem is the main result of this chapter.

Theorem 2.3 *Let β and ϑ satisfy the conditions of Lemma 2.2 Then*

(i) the equation (2.2.0.2) *has a unique solution in the time interval* $[0,\infty)$*,*

(ii) there exist limits of x, y, z at infinity, $y_\infty = 0$. If $\tau_v = \infty$ then z_∞ is a solution to the equation $z = n - X(z)$, where

$$X(z) = \left[x^0 + \int_0^z \frac{\beta(u)}{\gamma}\vartheta(u)\exp\left\{\frac{\int_0^u \beta(s)ds}{\gamma}\right\}du\right]\exp\left\{\frac{-\int_0^z \beta(u)du}{\gamma}\right\},$$

(iii) the size of infectives sub-population y_t has a unique maximum y_{τ_Y}.
If $\beta(z_0)[x_0 - \vartheta(z_0)] - \gamma > 0$, then $\beta(z_{\tau_Y})[x_{\tau_Y} - \vartheta(z_{\tau_Y})] = \gamma$.
If $\beta(z_0)[x_0 - \vartheta(z_0)] - \gamma \le 0$, then $\tau_Y = 0$.

Proof.

(i) The existence and uniqueness of a solution to ((2.2.1.2)) in the time interval $[0, \tau_v]$ follows from Lemma 2.2. Therefore we need to prove its existence and uniqueness in the time interval $[\tau_v, \infty]$ in the case $\tau_v < \infty$. Because the equation (2.2.1.3) with the initial conditions $x(\tau_v) = \tilde{x}(\tau_v), y(\tau_v) = \tilde{y}(\tau_v), z(\tau_v) = \tilde{z}(\tau_v)$, where $(\tilde{x},\tilde{y},\tilde{z})$ is

a solution to (2.2.1.2) in the time interval $[0, \tau_v]$, has a unique solution, it follows that

$$\begin{aligned} x(t) &= x_{\tau_v}, \\ y(t) &= y_{\tau_v} - e^{-\gamma\tau_v} + e^{-\gamma t}, \\ z(t) &= n - x_{\tau_v} - y_{\tau_v} + e^{-\gamma\tau_v} - e^{-\gamma t} \end{aligned}$$

holds for all $t \in [\tau_v, \infty)$.

Joining these solutions, we get a unique solution to ((2.2.0.2)) on the time interval $[0, \infty)$. Indeed, if we denote

$$\begin{aligned} \hat{l}_t = (\hat{x}_t, \hat{y}_t, \hat{z}_t) \qquad &= (\tilde{x}_t, \tilde{y}_t, \tilde{z}_t) \qquad && t \in [0, \tau_v], \\ &= (x, y, z) && t \in (\tau_v, \infty), \end{aligned}$$

then

$$\begin{aligned} \hat{x}_t &= \hat{x_0} - \int_0^t \beta(\hat{z}_s)\hat{y}_s[\hat{x}_s - \vartheta(\hat{z}_s)]^+ ds, \\ \hat{y}_t &= \hat{y_0} + \int_0^t \beta(\hat{z}_s)\hat{y}_s[\hat{x}_s - \vartheta(\hat{z}_s)]^+ - \gamma\hat{y}_s ds, \\ \hat{z}_t &= \int_0^t \gamma\hat{y}_s ds. \end{aligned}$$

Therefore $\hat{l}$ is a solution to (2.2.0.2).

(ii) Functions x and z are monotone and bounded, therefore they have their limits x_∞, z_∞ at infinity. Because $y_t = n - x_t - z_t$ for all $t \in [0, \infty)$, the existence of the limits x_∞ and z_∞ implies the existence of the limit y_∞. Since $z_\infty < \infty$, we get $y_\infty = 0$. Indeed, if $y_\infty > 0$, then there exists a time $T \in [0, \infty)$ and a constant $a > 0$ such that $y_t \geq a$ for all $t > T$. Therefore

$$z_\infty = \int_0^\infty \gamma y_s ds \geq \int_0^T \gamma y_s ds + \int_T^\infty \gamma a ds = \infty.$$

Hence $y_\infty = 0$.

As z_t is a continuous differentiable mapping from $[0, \infty)$ on $[0, z_\infty]$ with positive derivation, it has continuously differentiable inverse z_t^{-1}, we can set $X(z) = x(z_t^{-1})$ and (2.2.1.2) implies

$$\frac{dX}{dz}(z) = \frac{\frac{dx_t}{dt}}{\frac{dz_t}{dt}} = \frac{-\beta(z_t)Y(z_t)[X(z_t) - \vartheta(z_t)]}{\gamma Y(z_t)}, \quad X(z_0) = x_0,$$

therefore

$$X(z) = \left[x^0 + \int_0^z \frac{\beta(u)}{\gamma}\vartheta(u)\exp\left\{\frac{\int_0^u \beta(s)ds}{\gamma}\right\}du\right]\exp\left\{\frac{-\int_0^z \beta(u)du}{\gamma}\right\}. \quad (2.2.1.4)$$

Finally, let $t \to \infty$ in $z(t) = n - x(t) - y(t)$ to get the equation $z_\infty = n - x_\infty = n - X(z_\infty)$.

(iii) Because $\beta(z_t)$ and x_t are nonincreasing functions of t and ϑ a nondecreasing function of t, it follows that $\beta(z_t)[x_t - \vartheta(z_t)]$ is nonincreasing. Hence $\beta(z_0)[x_0 - \vartheta(z_0)] - \gamma \le 0$ implies $dy_t \le 0$ for all $t \ge 0$, and y_t is nonincreasing. Thus, $\tau_Y = 0$. If $\beta(z_0)[x_0 - \vartheta(z_0)] - \gamma > 0$, then y_t is increasing in neighborhood of zero and because moreover $y_0 > y_\infty = 0$, we have $0 < \tau_Y < \infty$. Hence continuity and the existence of derivative of y_t imply that $y'_{\tau_Y} = 0$, therefore $\beta(z_{\tau_Y})[x_{\tau_Y} - \vartheta(z_{\tau_Y})] - \gamma = 0$.

Consider the case $\beta(z_{\tau_Y})[x_{\tau_Y} - \vartheta(z_{\tau_Y})] = \gamma$. Denote
$T := \inf\{t \ge 0 : \beta(z_t)[x_t - \vartheta(z_t)] = \gamma\}$. From (2.2.0.2) and $y_{\tau_Y} \ge y_0 > 0$ it follows that x_t is decreasing in T, and so there is no other time t satisfying $\beta(z_t)[x_t - \vartheta(z_t)] = \gamma$. Therefore $\tau_Y = T$ is unique. In the case $\beta(z_0)[x_0 - \vartheta(z_0)] - \gamma < 0$, the uniqueness of τ_Y is obvious.

□

Example 2.1 *We shall scrutinize the equation $z_\infty = n - X(z_\infty)$ (see Theorem 2.3 (ii)) and assume β to be a constant and $\vartheta(z)$ a general function, later on a linear function.*

We apply (2.2.1.4) to get

$$z_\infty = n - \left[x^0 + \int_0^{z_\infty} \frac{\beta}{\gamma}\vartheta(u)\exp\left\{\frac{\int_0^u \beta ds}{\gamma}\right\}\right]\exp\left\{\frac{-\int_0^{z_\infty} \beta du}{\gamma}\right\}. \quad (2.2.1.5)$$

Denoting $\rho = \beta/\gamma$ then (2.2.1.5) yields

$$z_\infty = n - e^{-\rho z_\infty}\left[x^0 + \rho\int_0^{z_\infty} \vartheta(u)e^{\rho u}du\right].$$

Choosing a linear vaccination, i.e. $\vartheta(z) = \vartheta_0 + \vartheta_1 z$, where $\vartheta_0 \ge 0$ a $\vartheta_1 \ge 0$, we have

$$C_1 z_\infty = C_2 - C_3 e^{-\rho z_\infty}, \quad (2.2.1.6)$$

where

$$C_1 = 1 + \vartheta_1,$$
$$C_2 = n - \vartheta_0 + \vartheta_1/\rho,$$
$$C_3 = x^0 - \vartheta_0 + \vartheta_1/\rho.$$

The uniqueness of a solution to equations (2.2.1.5) depends on the choice of functions $\beta(z)$, $\vartheta(z)$ and initial conditions. If we have more then one solution to the equation, we have to decide which of them is z_∞.

To illustrate it, go back to the equation (2.2.1.6). What we know is that $C_1 > 0$ and $C_2 > C_3$ hold.

If $C_3 \leq 0$ then the number of vaccinated at $t = 0$ is larger than or equal to the number of susceptibles, hence $\tau_v = 0$ and the assumption of Theorem 2.3 (ii) is not satisfied. In practice, this choice is not very realistic, mathematically it leads to $z_\infty = y_0$ by (2.2.1.3) and, of course, to $y_\infty = 0$.

If $C_3 > 0$ then (2.2.1.6) possesses two solutions, but only one positive. It follows that (2.2.1.6) has a unique solution $z_\infty \in [0, n]$.

Example 2.2 *Consider again constants β, γ and a linear ϑ in a way that $\tau_v = \infty$ and $\tau_Y \neq 0$. Theorem 2.3 (iii) yields*

$$[x_{\tau_Y} - \vartheta(z_{\tau_Y})] = \frac{\gamma}{\beta}. \tag{2.2.1.7}$$

Computing

$$\begin{aligned} X(z) &= \left[x^0 + \int_0^z \frac{\beta}{\gamma}\vartheta(u) \exp\left\{\frac{\int_0^u \beta ds}{\gamma}\right\}\right] \exp\left\{\frac{-\int_0^z \beta du}{\gamma}\right\} \\ &= \left[x^0 + \frac{\beta}{\gamma}\int_0^z (\vartheta_0 + \vartheta_1 u) e^{\frac{\beta u}{\gamma}}\right] e^{-\frac{\beta z}{\gamma}} \\ &= \left(\vartheta_0 - \frac{\vartheta_1}{\rho}\right) + \vartheta_1 z + \left(x^0 + \frac{\vartheta_1}{\rho} - \vartheta_0\right) e^{-\rho z} \end{aligned} \tag{2.2.1.8}$$

by (2.2.1.4) and substituting $X(z)$ into (2.2.1.7), we arrive at

$$\left(\vartheta_0 - \frac{\vartheta_1}{\rho}\right) + \vartheta_1 z_{\tau_Y} + \left(x^0 + \frac{\vartheta_1}{\rho} - \vartheta_0\right) e^{-\rho z_{\tau_Y}} - \vartheta_0 - \vartheta_1 z_{\tau_Y} = \frac{1}{\rho}.$$

This implies

$$z_{\tau_Y} = \frac{1}{\rho}\left[\log\left(x^0 + \frac{\vartheta_1}{\rho} - \vartheta_0\right) - \log\left(\frac{1+\vartheta_1}{\rho}\right)\right]. \tag{2.2.1.9}$$

Finally, having on mind that $n = x + y + z$, we get

$$y_{max} = y_{\tau_Y} = n - X(z_{\tau_Y}) - z_{\tau_Y}, \tag{2.2.1.10}$$

where z_{τ_Y} and $X(z_{\tau_Y})$ are given by (2.2.1.9) and (2.2.1.8), respectively.

2.2.2 Numerical results

This part deals with several problems that arise when one is trying to get some usable results concerning the time of culmination of the epidemics, the largest number of those infected, the influence of vaccination, the comparison of various vaccination strategies and the choice of the "optimal" vaccination strategy.

First, we consider a constant $\beta > 0$ and a linear vaccination, i.e. $\vartheta(z) = \vartheta_0 + \vartheta_1 z$. Having made this choice, we replace the differential equation (2.2.0.2) by the equation

$$\begin{aligned} x_{n+1} &= x_n - \beta(z_n) y_n \max\{[x_n - \vartheta(z_n)], 0\}\Delta, & x_0 &= x^0 > 0, \\ y_{n+1} &= y_n + (\beta(z_n) y_n \max\{[x_n - \vartheta(z_n)], 0\} - \gamma y_n)\Delta, & y_0 &= y^0 > 0, \\ z_{n+1} &= z_n + \gamma y_n \Delta, & z_0 &= 0, \end{aligned} \tag{2.2.2.1}$$

where Δ is a difference step.

We solved the equation (2.2.2.1) with the number of steps 5000 and the difference step $\Delta = 0.016$, because we observed that a choice of smaller step does not change the results significantly. This corresponds to the time interval $(0, 80)$. We decided to use these values, because on this interval, the behavior of the epidemics can be well graphically shown (see Figure 2.2). We choose the initial conditions $x^0 = 990$, $y^0 = 10$, what means that at the beginning, 1% of population suffers from the disease, and we observed the behavior of the epidemics with several choices of $\gamma, \beta, \vartheta_0$ and ϑ_1. All computations and graphic results were made by software R.[1]

Figure 2.2 shows the differences in behavior of epidemics for different vaccinations. Although in the first case ($\vartheta_0 = 0$ and $\vartheta_1 = 1$), we have vaccinated 443 individuals by the time $t = 80$, while choosing $\vartheta_0 = 300$ and $\vartheta_1 = 0.2$ we have vaccinated only 363 individual in the same time interval, the evolution of epidemics is less favourable in the

[1] Version R 2.3.1 was used.

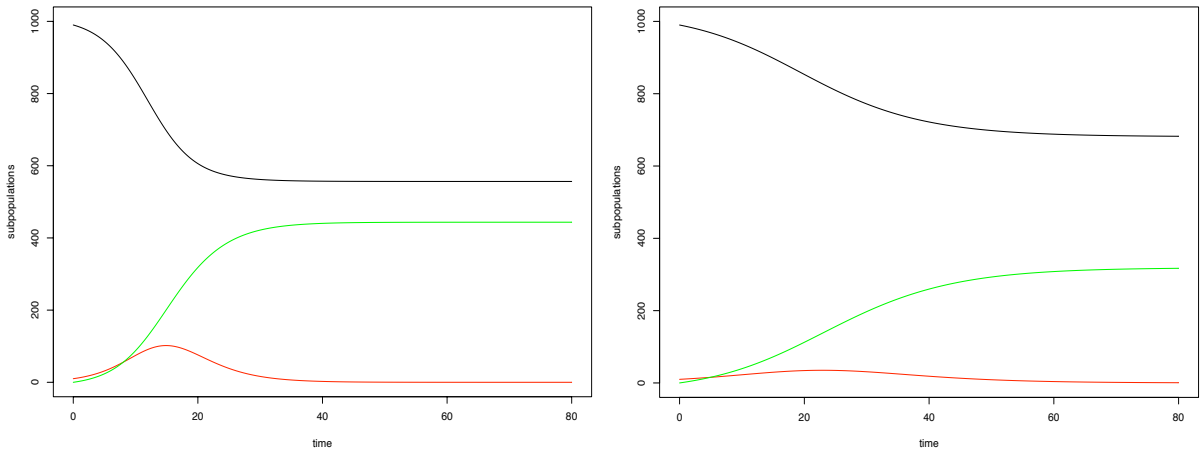

Figure 2.2:
Behavior of epidemics with $\beta = 0.0005$, $\gamma = 0.25$ and the vaccination either $\vartheta_0 = 0$, $\vartheta_1 = 1$(left) or $\vartheta_0 = 300$, $\vartheta_1 = 0.2$ (right). The black line describes the size of susceptibles, the red line the size of infectives and the green line the size of removals.

former case than in the latter one in the sense that the number of removals for the first choice is 443 in comparison with 317 for the second choice. Moreover, the maximal size of infected individuals (35) is also in favor of the latter vaccination compared with the former one (101).

Figure 2.3 shows how the vaccination affects the size of removals at time $t = 200$ and a global maximum of infectives. The blue line describes the effect of linear vaccination, the black line the effect of pre-vaccination.

Table 2.1 summarizes the values obtained by solving equation (2.2.2.1) for several pairs of the coefficients ϑ_0 and ϑ_1. Here, we approximated x_∞ and z_∞ by x_{12500} and z_{12500}, respectively. The approximation should be a satisfactory one as already the values y_{12500} are observed to be close to zero. To get the results, we produced 12500 steps with difference step $\Delta = 0.016$ (i.e. we observed the time interval $(0, 200)$), choosing β and γ as before, i.e. $\beta = 0.0005$, $\gamma = 0.25$. The initial conditions were again $x^0 = 990$ and $y^0 = 10$. The table lists the final values of x, y and z, i.e. the numbers of the susceptibles, infectives and removals at time $t = 200$, the total number of vaccinated individuals by the time $t = 200$, the size of maxima of infected individuals and the time of maxima.

Numerical results have confirmed our expectations that having determined to provide a fixed number of vaccinations, an epidemic has a better evolution if choosing a more robust pre-vaccination (larger ϑ_0) because it decreases both the number and the global maximum of the infected individuals (see Figure 2.3). Moreover, comparing 5th and 10th row in Table 2.1, we can see that for the same running of epidemics (in the mean of remained susceptibles), much less (almost one half) people need to be vaccinated in the

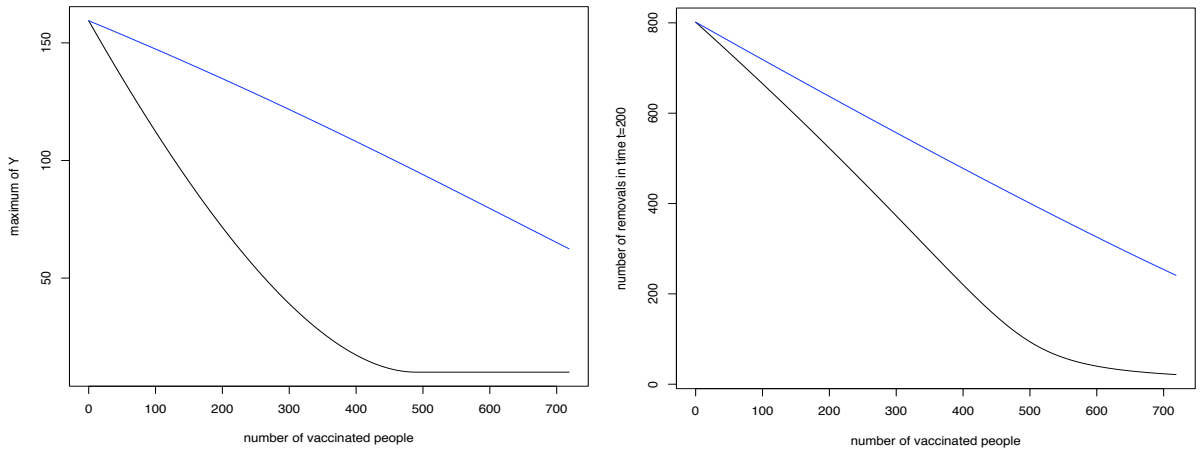

Figure 2.3:
The comparison of the effect of pre-vaccination (the black line) and linear vaccination (the blue line).

ϑ_0	ϑ_1	x_{12500}	z_{12500}	y_{12500}	Vaccinated	max. y	τ_Y
0	0	199.5697	800.4303	$5.3\ e-10$	0	158.6046	17.552
0	0.2	313.1946	686.8054	$5.1\ e-11$	137.3611	141.9416	16.848
0	0.5	432.0209	567.9791	$3.1\ e-12$	283.9895	123.0361	15.984
0	1	557.2330	442.7670	$9.8\ e-14$	442.7670	101.3385	14.832
0	2	690.4325	309.5675	$1.0\ e-15$	619.1350	76.0882	13.200
100	0.2	430.9243	569.0757	$2.2\ e-09$	213.8151	99.6202	18.752
100	0.5	530.3573	469.6427	$2.3\ e-10$	334.8214	86.0446	17.648
100	1	634.6346	365.3654	$1.4\ e-11$	465.3654	70.7635	16.192
100	2	744.7960	255.2041	$3.1\ e-13$	610.4081	53.3868	14.112
300	0.2	681.4626	318.5374	$1.2\ e-05$	363.7075	34.9557	22.896
300	0.5	736.9506	263.0494	$2.8\ e-06$	431.5247	30.6612	20.704
300	1	794.3346	205.6654	$4.1\ e-07$	505.6654	26.0612	17.952
300	2	854.0339	145.9661	$2.0\ e-08$	591.9322	21.1174	14.304

Table 2.1: For several choices of ϑ_0 and ϑ_1 the table summarizes the values of $x_{12500}, y_{12500}, z_{12500}$, the number of vaccinated individuals, maximum of y and τ_Y obtained from (2.2.2.1), with difference step $\Delta = 0.016$, $\beta = 0.0005$, and $\gamma = 0.25$ and initial condition $x^0 = 990$ and $y^0 = 10$.

	$\vartheta_1 = 0$	$\vartheta_1 = 0.2$	$\vartheta_1 = 0.5$	$\vartheta_1 = 1$	$\vartheta_1 = 2$
$\vartheta_0 = 0$	800.2034	686.5820	567.7654	442.5726	309, 4061
$\vartheta_0 = 100$		568.9032	469.4815	365.2218	255.0868
$\vartheta_0 = 300$		318.4655	262.9839	205.6079	145.9184

Table 2.2: Values of z_∞ for several choices of ϑ_0 and ϑ_1 with $\beta = 0.0005$, $\gamma = 0.25$ and initial condition $x^0 = 990$ and $y^0 = 10$.

	$\vartheta_1 = 0$	$\vartheta_1 = 0.2$	$\vartheta_1 = 0.5$	$\vartheta_1 = 1$	$\vartheta_1 = 2$
$\vartheta_0 = 0$	158.4516	141.7980	122.90494	101.2239	75.9957
$\vartheta_0 = 100$		99.5348	85.9673	70.6963	53.3324
$\vartheta_0 = 300$		34.9380	30.6450	26.0467	21.1049

Table 2.3: Maxima of y for several choices of ϑ_0 and ϑ_1 with $\beta = 0.0005$, $\gamma = 0.25$ and initial condition $x^0 = 990$ and $y^0 = 10$.

case of pre-vaccination. On the other hand, we can see that while vaccination during the time shorts the time of culmination τ_Y, pre-vaccination makes this time higher, therefore if we want only to short the time of culmination, it is suitable to choose vaccination during the time (nonzero ϑ_1) without pre-vaccination.

In Table 2.2, there are values of z_∞, that we receive as a solution to equation (2.2.1.6) in Example 2.1. We choose again $\beta = 0.0005$, $\gamma = 0.25$, $x^0 = 990$ and $y^0 = 10$ and the vaccination which enters Table 2.1. We solved the equation by using the divising interval method, we look for a solution in the interval $[0, 1000]$ and we require the error to be less then 0.001.

Comparing the values delivered by Table 2.1 with those delivered by Table 2.2, the differences are observed to be less than 0.3.

The values of maxima of infected individuals received by the formula (2.2.1.10) in Example 2.2 are presented by Table 2.3 choosing β, γ and the initial conditions as above.

Comparing Table 2.1 and Table 2.3, the differences are seen to be less than 0.2. Hence, we can conclude that (2.2.2.1) provides approximations close enough to the theoretical values.

In the last part of this chapter, we introduce how to find the "optimal" vaccination strategy. As it was possible to see in Figure 2.2 and Figure 2.3, different vaccination strategies have different effects, by the mean that the number of removals, the time of culmination and the time of the end of the epidemics are changing. Therefore, it is natural question how to choose the suitable vaccination strategy.

In general, we choose penalization function f and we look for the vaccination strategy among all considered strategies which minimizes the function f. This strategy is the optimal.

In our case, we consider linear vaccination as in Example 2.2 and choose the final time $T > 0$. For simplicity, we concern only the number of removals at the time T, the number of people, who have been vaccinated by the time T and the number of pre-vaccinated people. The time of culmination or the time of the end of the epidemics is not important for us. Therefore, we define a "penalization" function by $f = c*(y_T+z_T)+c_0*v_0+c_1*v_1$, where

- $y_T + z_T$ is the number of people, who have been infected by the time T ,
- v_0 is the number of people, who have been pre-vaccinated,
- v_1 is the number of people vaccinated during the time interval $(0, T)$,
- c is a penalization for one person who was infected,
- c_0, c_1 are penalizations for one pre-veccinated and vaccinated person, respectively.

One possible interpretation of this penalization function can be such that c is a cost of healing procedure for one infected individual, c_0 is the cost of pre-vaccination and c_1 is the cost of vaccination during running the epidemics, therefore f is the sum of money which were expended for healing and vaccination.

When we choose a linear vaccination $\vartheta(z) = \vartheta_0 + \vartheta_1 * z$, then it means that $v_0 = \vartheta_0$ and $v_1 = \vartheta_1 * z_T$ and the vaccination strategy is uniquely represented by choice ϑ_0 and ϑ_1 . Thus, if we want to find the optimal strategy, we have to find the minimum of f dependently on ϑ_0 and ϑ_1 and such $(\vartheta_0, \vartheta_1)$ represent our optimal strategy . Without lost of generality, we can consider $c = 1$, hence we get $f = y_T + z_T + c_0 * \vartheta_0 + c_1 * \vartheta_1 * z_T$. Because we look for the minimum of f numerically, we choose ϑ_0^m and ϑ_1^m and we find $\min_{(\vartheta_0,\vartheta_1)\in[0,\vartheta_0^m]\times[0,\vartheta_1^m]} f$. While the natural choice of ϑ_0^m is $\vartheta_0^m = n$, because we can not vaccinate more people (n is size of population), the choice of ϑ_1^m is more complicated.

Figure 2.4 shows a graph of a penalization function f dependently on ϑ_0 and ϑ_1 with two different choices of (c_0, c_1). The left picture represents an interesting situation, when the optimal choice of θ_0 and θ_1 is neither on the axe $\vartheta_0 = 0$ nor on the axe $\vartheta_1 = 0$. The right one represents more common situation, when the optimal strategy lies on one of the axes $\vartheta_0 = 0$, $\vartheta_1 = 0$.

Figure 2.5 shows the areas, where the optimal strategy is $\vartheta_1 = 0$ (area **I**), the optimal strategy is $\vartheta_0 = 0$ (area **II**) and where the optimal strategy is nonzero ϑ_0 and ϑ_1. Therefore, if we want to determine optimal strategy for c_0 and c_1 from the area **I**, we

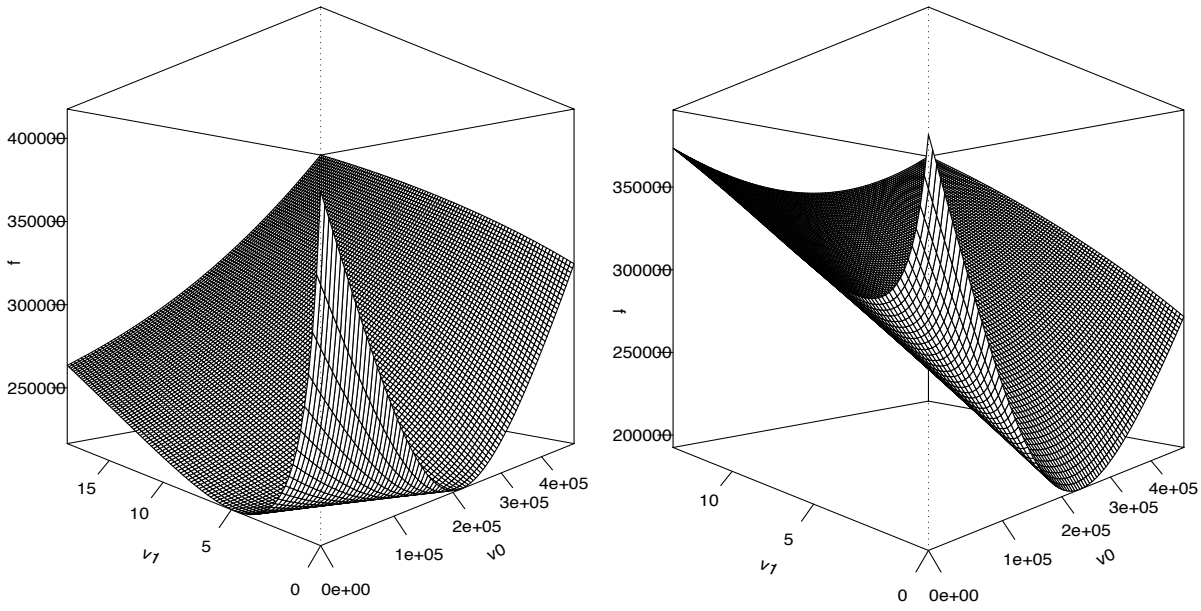

Figure 2.4:
The value of f dependently on ϑ_0 and ϑ_1. $\beta = 0.3 * 10^{-6}$, $\gamma = 0.25$ and initial condition $x_0 = 990000$ and $y_0 = 10000$ are same for both of picture. The value $c_0 = 0.607$ and $c_1 = 0.3061$ are chosen at left picture, $c_0 = c_1 = 0.5$ at the right one.

know that $\min_{(\vartheta_0,\vartheta_1)\in[0,\vartheta_0^m]\times[0,\vartheta_1^m]} f = \min_{(\vartheta_0,\vartheta_1)\in[0,\vartheta_0^m]\times 0} f$ which makes our case more easy. It is not surprising that for fixed c_1, if the cost of pre-vaccination (c_0) is increasing, the optimal pre-vaccination (ϑ_0) is decreasing, and the same holds for ϑ_1. The smallest value of c_0 for which it is not reasonable to use pre-vaccination is $c_0 = 1.576$ and the smallest value of c_1 is $c_1 = 0.838$ and it is possible to say the same about $c_1 > 0.838c$. Thus, if the pre-vaccination costs 1.576 times more than the healing procedure, it is not reasonable (by the mean of the optimal strategy, presented by f) to produce vaccine for pre-vaccination. Therefore, the left picture of Figure 2.5 shows the whole reasonable area for (c_0, c_1). However, since the area **III** is not visible in this picture, we add the right picture which provide a better idea, how big the area **III** is.

To get the plots presented in Figure 2.4 and Figure 2.5, we choose $T = 150$, $\beta = 0.3*10^{-6}$, $\gamma = 0.25$ and initial condition $x_0 = 990000$ and $y_0 = 10000$, thus the size of population is 10^6 which is approximately the same number of people as the number of people living in Prague. The value z_{150} was approximated by solving (2.2.2.1) with number of steps 2000, therefore the difference step was $\Delta = 0.075$. This choice of β and γ describes the epidemics, when without any vaccination, approximately 35% people will be infected ($z_{150} = 347430$, $y_{150} = 135$).

Even though there exists the area **III**, where it is optimal to use both pre-vaccination and vaccination, this area is too narrow, so the optimal strategy for $(c_0, c_1) \in$ **III** is not much

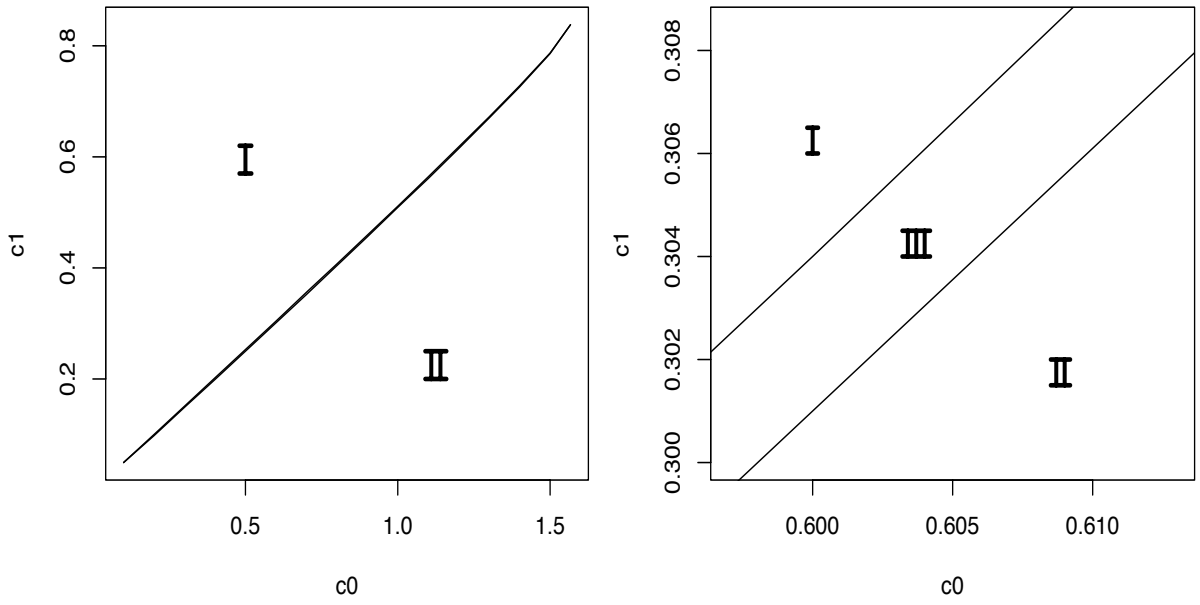

Figure 2.5:
In area **I**, the optimal vaccination strategy has $\vartheta_1 = 0$, in area **II**, has $\vartheta_0 = 0$. In area **III** the optimal strategy has nonzero ϑ_0 and ϑ_1.

better than the optimal strategy which is given by $\min_{(\vartheta_0,\vartheta_1)\in[0,\vartheta_0^m]\times 0} f$ or $\min_{(\vartheta_0,\vartheta_1)\in 0\times[0,\vartheta_1^m]} f$, (e.g. with choice of $c_0 = 0.607$ and $c_1 = 0.3061$, presented by the left picture in Figure 2.4, the optimal strategy is $(\vartheta_0, \vartheta_1) = (111000, 2.34)$ and minimum of the penalization function f is equal to 216464 while if we consider only pre-vaccination, we get the optimum as $\vartheta_0 = 219000$ and minimum of f is equal to 216566 and in the case we consider only vaccination during running the epidemics, we get optimal vaccination $\vartheta_1 = 4.86$ and minimum of f is equal to 216550.) These differences are so small that they can be caused by numerical deviation, therefore we can omit the existence of the area **III** and we can look for the optimal strategy only on the axes $\vartheta_0 = 0$ and $\vartheta_1 = 0$.

Chapter 3

Stochastic models

3.1 Stochastic model with migration

A stochastic version of Kermack-McKendrick model was introduced by Štěpán and Hlubinka in [17]. In this model the spread of an infection is the same as that one introduced in classical Kermack-McKendrick model, but the size of population (N_t) is a martingale which solves Engelbert-Schmidt stochastic differential equation. The model is given by the following SDE:

$$\begin{aligned} dX_t &= -\beta(X_t, Y_t, Z_t)X_tY_tdt + X_t\sigma(N_t)dW_t, & X_0 = x_0 \quad &> 0, \\ dY_t &= \beta(X_t, Y_t, Z_t)X_tY_tdt - \gamma Y_tdt + Y_t\sigma(N_t)dW_t, & Y_0 = y_0 \quad &> 0, \\ dZ_t &= \gamma(N_t)dt + \sigma(N_t)dW_t, & Z_0 = z_0 \quad &= 0, \end{aligned} \tag{3.1.0.1}$$

where X_t, Y_t and Z_t are stochastic processes, X_t describes the number of "susceptibles", Y_t denotes the number of "infectives" and Z_t is the number of "removals". The susceptibles-infectives contact rate is supposed to be a nonnegative function $\beta : \mathbb{R}^3 \to \mathbb{R}^+$, $\gamma > 0$ denotes a recovery rate and $\sigma : \mathbb{R}^3 \to \mathbb{R}^+$ is the intensity of migration which satisfies that $\text{supp}(\sigma) \subseteq [a, b]$, where $0 \leq a \leq n_0 \leq b < \infty$ and $n_0 = x_0 + y_0$ is the size of population at time $t = 0$.

The migration affects only the size of the population, but not the proportions of the sub-populations. Therefore, the model describes the situation, when the migration is considered only at the area, where the epidemics is spreading homogeneously, and we observe the situation only at some smaller sub-area.

It is obvious, that the size of population $N_t = X_t + Y_t + Z_t$ is a solution to the equation

$$dN_t = N_t\sigma(N_t)dW_t, \quad N_0 = n_0 = x_0 + y_0 > 0. \tag{3.1.0.2}$$

More details about this model can be found in [17].

Here we show that using the same method introduced in [17], we can prove the existence and uniqueness theorem for a little more general model which considers β as a previsible path functional[1] from $\mathcal{C}(\mathbb{R}^+, \mathbb{R}^3) \times \mathbb{R}^+$ to $\mathbb{R}^+$. The main idea of choosing β as a functional is to obtain a model which can describe the epidemics with nonzero incubation time.

Therefore, the model is given by the equation

$$\begin{aligned} dX_t &= -\beta(X_\cdot, Y_\cdot, Z_\cdot)X_tY_tdt + X_t\sigma(N_t)dW_t, & X_0 = x_0 \quad &> 0, \\ dY_t &= \beta(X_\cdot, Y_\cdot, Z_\cdot)X_tY_tdt - \gamma Y_tdt + Y_t\sigma(N_t)dW_t, & Y_0 = y_0 \quad &> 0, \\ dZ_t &= \gamma Y_tdt + Z_t\sigma(N_t)dW_t, & Z_0 = z_0 \quad &= 0. \end{aligned} \tag{3.1.0.3}$$

We consider, as in the previous model, $0 < a \leq n_0 \leq b < \infty$, σ is bounded measure function which satisfies that $\text{supp}(\sigma) \subseteq [a, b]$ and $\gamma > 0$.

Note $\triangle_{ab} := \{(x_\cdot, y_\cdot, z_\cdot) \in \mathcal{C}(\mathbb{R}^+, \mathbb{R}^3) : a \leq x_t + y_t + z_t \leq b \text{ and } x_t, y_t, z_t \geq 0 \ \forall t \geq 0\}$. Consider that β and σ satisfy following conditions:

(i) $\beta(x_\cdot, y_\cdot, z_\cdot, t)$ is previsible path functional from $\mathcal{C}(\mathbb{R}^+, \mathbb{R}^3) \times \mathbb{R}^+$ to $\mathbb{R}^+$,

(ii) β is bounded and locally Lipschitz on $\triangle_{ab}$, i.e. $\forall N \in \mathbb{N}$ there exists a constants K_N and K such that $\forall l_\cdot, \tilde{l}_\cdot \in \triangle_{ab}$ which satisfy $||l||_s^* \vee ||\tilde{l}||_s^* \leq N$ and $0 \leq s \leq N$, it holds that

$$|\beta(l_\cdot, s) - \beta(\tilde{l}_\cdot, s)| \leq K_N||l - \tilde{l}||_s^*,$$
$$|\beta(l_\cdot, s)| \leq K,$$

where $l_\cdot = (x_\cdot, y_\cdot, z_\cdot)$ is continuous function from $\mathbb{R}^+$ to $\mathbb{R}^3$, $|\cdot|$ is Euclide norm on $\mathbb{R}^3$ and $||f||_s^* \equiv \sup\{|f(t)| : t \leq s\}$ is the sub-norm in $\mathcal{C}([0, s], \mathbb{R}^3)$,

(iii) σ is a bounded measure function on $\mathbb{R}^+$ which satisfies that $\text{supp}(\sigma) \subset [a, b]$,

(iv) σ is locally Lipschitz on $\mathbb{R}^+$.

Theorem 3.1 *Assume that β and σ satisfy conditions (i)-(iv). Then, the equation (3.1.0.3) has a unique strong solution and arbitrary solution $L_t = (X_t, Y_t, Z_t)$ is non-negative process on $(0, \infty)$.*

[1]The definition of the previsible path functional is possible to find on p.122 in [12].

Proof. Let φ_1 and φ_2 are locally Lipschitz previsible path functionals from $\mathcal{C}(\mathbb{R}^+, \mathbb{R}^3) \times \mathbb{R}^+$ to $\mathbb{R}$ which satisfy

$$\begin{aligned}\varphi_1(x_\cdot, y_\cdot, z_\cdot, t) &= -\beta(x_\cdot, y_\cdot, z_\cdot, t) \cdot y_t, \\ \varphi_2(x_\cdot, y_\cdot, z_\cdot, t) &= \beta(x_\cdot, y_\cdot, z_\cdot, t) \cdot x_t - \gamma\end{aligned}$$

for all $(x_\cdot, y_\cdot, z_\cdot, t)$ such that, $a \leq x_{\tilde{t}} + y_{\tilde{t}} + z_{\tilde{t}} \leq b$ and $x_{\tilde{t}}, y_{\tilde{t}}, z_{\tilde{t}} \geq 0$ $\forall \tilde{t} \in [0, t]$. By using the condition (ii), we get that $\forall l_\cdot, \tilde{l}_\cdot \in \triangle_{ab}$ which satisfy $||l||_s^* \vee ||\tilde{l}||_s^* \leq N$ and $0 \leq s \leq N$

$$\begin{aligned}|\varphi_1(l_\cdot, s) - \varphi_1(\tilde{l}_\cdot, s)| =& |\beta(\tilde{l}_\cdot, s)\tilde{y}_s - \beta(l_\cdot, s)y_s| \\ =& |(\beta(\tilde{l}_\cdot, s) - \beta(l_\cdot, s))\tilde{y}_s + \beta(l_\cdot, s)(\tilde{y}_s - y_s)| \\ \leq& K_N||l - \tilde{l}||_s^*||\tilde{y}||_s^* + K||\tilde{y} - y||_s^* \\ \leq& (K_N N + K)||l - \tilde{l}||_s^*\end{aligned}$$

holds, therefore the definition of φ_1 is correct. Using the same way, we can verify the correctness of the definition of φ_2.

Assume the following stochastic differential equation:

$$\begin{aligned} d\tilde{X}_t &= \varphi_1(\tilde{X}_\cdot, \tilde{Y}_\cdot, \tilde{Z}_\cdot, t)\tilde{X}_t dt + \tilde{X}_t \sigma(\tilde{N}_t) dW_t, & \tilde{X}_0 &= x_0 \\ d\tilde{Y}_t &= \varphi_2(\tilde{X}_\cdot, \tilde{Y}_\cdot, \tilde{Z}_\cdot, t)\tilde{Y}_t dt + \tilde{Y}_t \sigma(\tilde{N}_t) dW_t, & \tilde{Y}_0 &= y_0 \\ d\tilde{Z}_t &= \gamma \tilde{Y}_t dt + \tilde{Z}_t \sigma(\tilde{N}_t) dW_t, & \tilde{Z}_0 &= 0. \end{aligned} \tag{3.1.0.4}$$

Then, if we denote $\tilde{L}_t = (\tilde{X}_t, \tilde{Y}_t, \tilde{Z}_t)$, we can rewrite the equation 3.1.0.4 by

$$d\tilde{L}_t = b(\tilde{L}_\cdot, t)dt + a(\tilde{L}_t)dB_t, \quad \tilde{L}_0 = (x_0, y_0, 0), \tag{3.1.0.5}$$

where

$$b(l_\cdot, t) = \begin{pmatrix} b_1(l_\cdot, t) \\ b_2(l_\cdot, t) \\ b_3(l_\cdot, t) \end{pmatrix} = \begin{pmatrix} \varphi_1(l_\cdot, t)x_t \\ \varphi_2(l_\cdot, t)y_t \\ \gamma y_t \end{pmatrix} : \quad \mathbb{R}^3 \to \mathbb{R}^3,$$

$$a(l) = \begin{pmatrix} x\sigma(x+y+z) & 0 & 0 \\ y\sigma(x+y+z) & 0 & 0 \\ z\sigma(x+y+z) & 0 & 0 \end{pmatrix} : \quad \mathbb{R}^3 \to \mathbf{M}^3.$$

$\mathbf{M}^3$ denotes the space of real matrices 3×3, and $B_t = (W_t, W_t^2, W_t^3)$ is a three-dimensional Brownian motion. It is easy to verify that $b(l_\cdot, t)$ is previsible path functional

$$b : \mathcal{C}(\mathbb{R}^+, \mathbb{R}^3) \times \mathbb{R}^+ \to \mathbb{R}^3$$

and $a(l)$ is a measurable function

$$a : \mathbb{R}^3 \to \mathbf{M}^3.$$

Coefficients $a(l)$ and $b(l.,t)$ are locally Lipschitz as σ and $\varphi_i(l.,t)$ are bounded and locally Lipschitz. Moreover, it is possible to show, that for arbitrary N and $0 \leq t \leq N$,

$$|a(l)| + |b(l.,t)| \leq C_N ||l.||_t^*,$$

holds, where the constant $C_N \in \mathbf{R}^+$ depends on N.

Using Theorem 12.1, p.132, in [12], we get the existence and uniqueness of a strong solution to (3.1.0.5), hence the equation (3.1.0.4) has also a unique strong solution.

Now, we show that the solution $(\tilde{X}_t, \tilde{Y}_t, \tilde{Z}_t)$ to the equation (3.1.0.4) is nonnegative. We show that

$$\tilde{X}_t = x_0 \exp\left\{ \int_0^t \varphi_1(\tilde{X}_., \tilde{Y}_., \tilde{Z}_., u) - \frac{1}{2}\sigma^2(\tilde{N}_u)du + \int_0^t \sigma(\tilde{N}_u)dW_u \right\} > 0$$

almost surely.

Denote $U_t := \int_0^t \varphi_1(\tilde{X}_., \tilde{Y}_., \tilde{Z}_., u) - \frac{1}{2}\sigma^2(\tilde{N}_u)du$, $V_t := \int_0^t \sigma(\tilde{N}_u)dW_u$, and $\hat{X}_t = x_o \exp\{U_t + V_t\}$ and using Itô formula, Theorem 17.18, p.340, in [7] we get

$$\begin{aligned} d\hat{X}_t &= x_0 \exp\{U + V\} \left(dU_t + dV_t + \frac{1}{2}d\langle U\rangle_t + \frac{1}{2}\langle V\rangle_t + \langle U, V\rangle_t \right) \\ &= \tilde{X}_t(dU_t + dV_t + d\langle V\rangle_t) = \tilde{X}_t(\varphi_1(\tilde{X}_., \tilde{Y}_., \tilde{Z}_., t)dt + \sigma(\tilde{N}_t)dW_t), \end{aligned}$$

therefore, $\hat{X}_t$ is a solution to the first equation of (3.1.0.4) and from the uniqueness of the equation, we get $\tilde{X}_t = \hat{X}_t$ a.s. In the same way, we can verify that

$$\tilde{Y}_t = y_0 \exp\left\{ \int_0^t \varphi_2(\tilde{X}_., \tilde{Y}_., \tilde{Z}_., u) - \frac{1}{2}\sigma^2(\tilde{N}_u)du + \int_0^t \sigma(\tilde{N}_u)dW_u \right\} > 0 \quad \text{a.s.}$$

Now, denote $U_t := \int_0^t \gamma\tilde{Y}_u du$, $V_t := \int_0^t \sigma(\tilde{N}_u)dW_u$, $S_t := \exp\left\{V_t - V_0 - \frac{1}{2}\langle V\rangle_t\right\}$ and $R_t := \int_0^t S_u^{-1}dU_u - \int_0^t S_u^{-1}d\langle U, V\rangle_u$. Then using Theorem 2.2.13, p.292, in [5], we get that $\hat{Z}_t := S_t R_t$ is a solution to the equation

$$\hat{Z}_t = U_t + \int_0^t \hat{Z}_u dV_u = \int_0^t \gamma\tilde{Y}_u du + \int_0^t \hat{Z}_u \sigma(\tilde{N}_u)dW_u. \tag{3.1.0.6}$$

Because the equation (3.1.0.6) corresponds to the third equation of (3.1.0.4) which has a unique strong solution then $\tilde{Z}_t = \hat{Z}_t$ almost surely. Therefore

$$\begin{aligned}\tilde{Z}_t =& \hat{Z}_t = S_t R_t = \exp\left\{V_t - V_0 - \frac{1}{2}\langle V\rangle_t\right\} \cdot \int_0^t S_u^{-1} dU_u \\ =& \exp\left\{V_t - \frac{1}{2}\langle V\rangle_t\right\} \cdot \int_0^t \exp\left\{-V_u + \frac{1}{2}\langle V\rangle_u\right\} \gamma \tilde{Y}_u du \\ =& \exp\left\{\int_0^t \sigma(\tilde{N}_u) dW_u - \frac{1}{2}\int_0^t \sigma^2(\tilde{N}_u) du\right\} \cdot \\ & \cdot \int_0^t \exp\left\{-\int_0^u \sigma(\tilde{N}_w) dW_w + \frac{1}{2}\int_0^u \sigma^2(\tilde{N}_w) dw\right\} \cdot \gamma \tilde{Y}_u du,\end{aligned}$$

holds almost surely, hence $\tilde{X}_t, \tilde{Y}_t, \tilde{Z}_t > 0$ a.s. $\forall t \geq 0$.

Note $\triangle^{ab} := \{(x, y, z) \in [0, b]^3, a \leq x + y + z \leq b\}$ and define $\tau := \inf\{t > 0 : \tilde{L}_t \notin \triangle^{ab}\}$ the time of the first exit of $\tilde{L} = (\tilde{X}, \tilde{Y}, \tilde{Z})$ from the set $\triangle^{ab}$. Then we get

$$\begin{aligned}\tilde{X}_{t\wedge\tau} &= x_0 + \int_0^{t\wedge\tau} -\beta(\tilde{X}_\cdot, \tilde{Y}_\cdot, \tilde{Z}_\cdot, u)\tilde{X}_u\tilde{Y}_u du + \int_0^{t\wedge\tau} \tilde{X}_u \sigma(\tilde{N}_u) dW_u \\ &= x_0 + \int_0^{t\wedge\tau} \varphi_1(\tilde{X}_\cdot, \tilde{Y}_\cdot, \tilde{Z}_\cdot, u)\tilde{X}_u du + \int_0^{t\wedge\tau} \tilde{X}_u \sigma(\tilde{N}_u) dW_u \\ \tilde{Y}_{t\wedge\tau} &= y_0 + \int_0^{t\wedge\tau} \left(\beta(\tilde{X}_\cdot, \tilde{Y}_\cdot, \tilde{Z}_\cdot, u)\tilde{X}_u\tilde{Y}_u - \gamma\tilde{Y}_u\right) du + \int_0^{t\wedge\tau} \tilde{Y}_u \sigma(\tilde{N}_u) dW_u \\ &= y_0 + \int_0^{t\wedge\tau} \varphi_2(\tilde{X}_\cdot, \tilde{Y}_\cdot, \tilde{Z}_\cdot, u)\tilde{Y}_u du + \int_0^{t\wedge\tau} \tilde{Y}_u \sigma(\tilde{N}_u) dW_u \\ \tilde{Z}_{t\wedge\tau} &= \gamma \int_0^{t\wedge\tau} \tilde{Y}_u du + \int_0^{t\wedge\tau} \tilde{Z}_u \sigma(\tilde{N}_u) dW_u.\end{aligned}$$

From the existence of the unique solution to (3.1.0.4), we get the existence of the unique solution to (3.1.0.3) in the time interval $[0, \tau)$.

It remains to prove, that $\tau = \infty$ almost surely. Let us suppose that there exists a time $t > 0$ such that $\tilde{N}_t > b$ and denote τ_b the time of the last enter of the process $\tilde{N}$ to b on $[0, t]$, i.e. $\tau_b := \sup\{s \geq 0 : \tilde{N}_s = b\}$, then

$$\begin{aligned}\tilde{N}_t &= n_0 + \int_0^t \tilde{N}_u \sigma(\tilde{N}_u) dW_u = b + \int_{\tau_b}^t \tilde{N}_u \sigma(\tilde{N}_u) dW_u \\ &= b + \int_{\tau_b}^t 0 dW_u = b \ a.s.,\end{aligned}$$

therefore, $\tilde{N}_t \leq b \ \forall t \geq 0$ a.s. In the same way, we get $\tilde{N}_t \geq a \ \forall t \geq 0$ a.s., hence $a \leq \tilde{N}_t \leq b \ \forall t \geq 0$ a.s. Because moreover $\tilde{X}_t, \tilde{Y}_t, \tilde{Z}_t > 0 \ \forall t \geq 0$ a.s., we get $\tau = \infty$ a.s. □

Remark 3.1 *When we consider β in one of the following forms*

$$\beta \in \mathbf{R}^+,\ \beta \in \mathcal{C}(\mathbf{R}, \mathbf{R}^+),\ \beta \in \mathcal{C}(\mathbf{R}^3, \mathbf{R}^+),\ \beta \in \mathcal{C}(\mathbf{R}^3 \times \mathbf{R}^+, \mathbf{R}^+),$$

we can rewrite them to the functional form and thus, the previous theorem may be applied to all these choices of β.

In the model described by (3.1.0.1), the number of the newly infected people at time t depends only on the state at time t, but in fact, the number of newly infected people can depend also on the size of X, Y, Z during some time period before the time t. The choice of β as a functional allows us to describe the situations when the disease has longer incubational time period during which the disease can burn up.

Example 3.1 *Consider a disease which has the incubation time period of the length $\widetilde{t}$. It means that during this time period, the disease can burn up with constant intensity. Then a possible choice of the coefficient $\beta(.)$ is*

$$\beta(x_., y_., z_., t) = C \int_{t-\widetilde{t}}^{t} \frac{x_u y_u}{(x_u + y_u + z_u)^2} du.$$

Choosing such a coefficient $\beta(.)$, the number of newly infected people at time t depends on the size of X_t and Y_t and on the size of the rates $\frac{X}{N}$ and $\frac{Y}{N}$ for the whole time period $(t - \widetilde{t}, t)$.

Another possible choices of $\beta(.)$ are

$$\beta(x_., y_., z_., t) = C \int_{t-\tilde{t}}^{t} \frac{y_u}{x_u + y_u + z_u} du,$$
$$\beta(x_., y_., z_., t) = C \int_{t-\tilde{t}}^{t} y_u du.$$

It is possible to check that all the introduced choices of β satisfy the conditions (i) and (ii).

Remark 3.2 *It seems that for example the choice of drift at the form $\int_{t-\tilde{t}}^{t} \beta X_s Y_s ds$ instead of $\beta(X_., Y_., Z_., t) X_t Y_t$ could be also suitable. However, even though the equation with this drift has a unique solution, the solution does not need to be nonnegative, therefore it is not reasonable to consider any more general drift than $\beta(X_., Y_., Z_., t) X_t Y_t$.*

3.2 Stochastic models with vaccination

In the first part of this chapter, we presented the stochastic version of Kermack-McKendrick model, where the stochastic part simulates the effect of migration, therefore it does not affect the spread of epidemics, but affects only the size of population.

Now, we introduce a stochastic version of Kermack-McKendrick model or more precisely, a more general stochastic version of the model described by (2.2.0.2), where the stochastic part has a significant effect to spread of the epidemics. We take the deterministic part from (2.2.0.2) and choose the diffusion coefficient as a square root of the trend coefficient. Then the model is described by following stochastic differential equation:

$$\begin{aligned} dX_t &= -\beta(Z_t)Y_t[X_t - \vartheta(Z_t)]dt + \sqrt{\beta(Z_t)Y_t[X_t - \vartheta(Z_t)]}dW_t^1, \\ dY_t &= \beta(Z_t)Y_t[X_t - \vartheta(Z_t)]dt - \gamma Y_t dt - \sqrt{\beta(Z_t)Y_t[X_t - \vartheta(Z_t)]}dW_t^1 + \sqrt{\gamma Y_t}dW_t^2, \\ dZ_t &= \gamma Y_t dt - \sqrt{\gamma Y_t}dW_t^2 \end{aligned} \tag{3.2.0.7}$$

in the time interval $[0, \tau)$. Here τ is the first time, when either no one is infected or all susceptibles are vaccinated. It means that $\tau := \min\{\tau^X, \tau^Y\}$, where τ^Y is a stopping time of the first entry of the process Y to zero, i.e. $\tau^Y = \inf\{t \geq 0, Y_t = 0\}$, and τ^X is a stopping time defined by $\tau^X = \inf\{t \geq 0, X_t = \vartheta(Z_t)\}$, meaning that τ^X is the first time, when there are no susceptibles which are not vaccinated. As well as in the previous model, X_t is the number of susceptible, Y_t the number of infectives, Z_t the number of removals and the size of population N is constant. Further, we consider β to be a continuous function from $\mathbb{R}$ to $\mathbb{R}^+$, ϑ a nondecreasing continuous function from $\mathbb{R}$ to $\mathbb{R}^+$, $\gamma > 0$ and $W_t = (W_t^1, W_t^2)$ is a Wiener process satisfying that W^1 and W^2 are independent. We also assume initial conditions $X_0 = x^0 > 0,\ Y_0 = y^0 > 0,\ Z_0 = z^0 \geq 0$. The interpretation of β, γ and ϑ is the same as that one introduced in the deterministic model with vaccination.

A heuristic interpretation of the choice of the stochastic part as the square root of the deterministic one is following. Assume that the size of population is large and that every non-vaccinated susceptible can be infected with the same probability. Then the number of newly infected people in time interval $[t, t + \Delta]$, where $\Delta > 0$ is small, has approximately Poisson distribution with parameter $\lambda = Y_t[X_t - \vartheta(Z_t)]\Delta$. Because the variance of the Poisson distribution is equal to λ, we choose the diffusion coefficient so that the variance of the number of newly infected people on the interval $[t, t + \Delta]$ is approximately equal to λ. This leads us to choose the diffusion coefficient as introduced in the equation (3.2.0.7).

The model is defined only on the interval $[0, \tau)$, because after the time τ the situation is

not interesting. However, if we need a model defined on the whole time interval $[0, \infty)$, we can define the model after a time τ as follows.

In the time interval $[\tau, \tau^Y)$ (if it is nonempty), the model is given by the following SDE:

$$\begin{aligned} dX_t &= 0, \\ dY_t &= -\gamma Y_t dt + \sqrt{\gamma Y_t} dW_t^2, \\ dZ_t &= \gamma Y_t dt - \sqrt{\gamma Y_t} dW_t^2, \end{aligned} \tag{3.2.0.8}$$

with initial conditions $Y_\tau = Y_{\tau_-}$, $Z_\tau = Z_{\tau_-}$ and $X_\tau = X_{\tau_-}$. Consequently $X_t = X_{\tau_-}$ for all $t \geq \tau$.

And finally, in the time interval $[\tau^Y, \infty)$, we set $X_t = X_{\tau_-}, Y_t = Y_{\tau_-^Y}$ and $Z_t = Z_{\tau_-^Y}$.

It means that the process described by this model arises by joining the solution of (3.2.0.7) with the solution of (3.2.0.8) in the point $(\tau, X_{\tau_-}, Y_{\tau_-}, Z_{\tau_-})$ and by joining the solution of (3.2.0.8) with the process $L_t = (X_{\tau_-}, Y_{\tau_-^Y}, Z_{\tau_-^Y})$ in the point $(\tau^Y, X_{\tau_-}, Y_{\tau_-^Y}, Z_{\tau_-^Y})$.

For the equation (3.2.0.7), we can say the following theorem about the existence of the solution.

Theorem 3.2 *Let ϑ be a continuous function from $\mathbb{R}$ to $\mathbb{R}_+$ and β a continuous, bounded function from $\mathbb{R}$ to $\mathbb{R}_+$. Then there exists a stopping time $\widetilde{\tau}$ such that the equation (3.2.0.7) has a weak solution in the time interval $(0, \widetilde{\tau})$.*

Furthermore, let L_t be a solution to (3.2.0.7) and denote τ^N the stopping time of the first exit of process L from the set $[0, N]^3$. Then we can choose $\widetilde{\tau}$ such that $\tau^N \leq \widetilde{\tau}$ a.s.

Proof. The equation (3.2.0.7) can be rewritten to the form

$$dL_t = b(t, L)dt + \sigma(t, L)dW_t, \tag{3.2.0.9}$$

where $W_t = (W_t^1, W_t^2)'$, $L = (X, Y, Z)'$,

$$b(t, l) = b(l_t) = \begin{pmatrix} -\beta(z_t) y_t [x_t - \vartheta(z_t)] \\ +\beta(z_t) y_t [x_t - \vartheta(z_t)] - \gamma y_t \\ +\gamma y_t \end{pmatrix}$$

and

$$\sigma(t, l) = \sigma(l_t) = \begin{pmatrix} +\sqrt{\beta(z_t) y_t [x_t - \vartheta(z_t)]_+} & 0 \\ -\sqrt{\beta(z_t) y_t [x_t - \vartheta(z_t)]_+} & +\sqrt{\gamma y_t} \\ 0 & -\sqrt{\gamma y_t} \end{pmatrix}.$$

Let $K > N$ and denote $l^{Kbound} = ((x \vee -K) \wedge K, (y \vee -K) \wedge K, (z \vee -K) \wedge K)$.

Consider the equation

$$d\widetilde{L} = \widehat{b}(t, \widetilde{L})dt + \widehat{\sigma}(t, \widetilde{L})dW_t, \tag{3.2.0.10}$$

with initial condition $\widetilde{L}_0 = (x^0, y^0, z^0)$, where $\widehat{b}(t, l) = b(t, l^{Kbound})$ and $\widehat{\sigma}(t, l) = \sigma(t, l^{Kbound})$.

Denote $\widehat{a} = \widehat{\sigma}\widehat{\sigma}'$ and consider $\widehat{\sigma}$ to be a bounded, progressive function such that for all $t \in \mathbb{R}_+$, $\widehat{\sigma}(t, .)$ is continuous on $\mathbf{C}(\mathbb{R}_+, \mathbb{R}^3)$. Consequently, $\widehat{a}$ is a bounded, progressive function such that $\widehat{a}(t, .)$ is a continuous function on $\mathbf{C}(\mathbb{R}_+, \mathbb{R}^3)$ for all $t \in \mathbb{R}_+$.

Consider $\widehat{b}$ to be a bounded, progressive function such that $\widehat{b}(t, .)$ is bounded for an arbitrary $t \in \mathbb{R}_+$. Then from Theorem 21.9, p.419, in [7], we have a solution $P_{\delta_{\widetilde{l}_0}}$ of the martingale problem $(\widehat{a}, \widehat{b})$ with initial distribution $\delta_{\widetilde{l}_0}$, i.e. $\widetilde{l}_0 = (x_0, y_0, z_0)$ a.s.

Using the Theorem 21.7, p.418, in [7], we get the existence of a weak solution to the equation (3.2.0.10).

Because the initial conditions of equations (3.2.0.9) and (3.2.0.10) are equal to each other, $\widehat{\sigma}(t, L) = \sigma(t, L)$ and $\widehat{b}(t, L) = b(t, L)$ for $L_t \in [-K, K]^3$. Denote τ^K the first exit of the solution to (3.2.0.10) from the set $[-K, K]^3$. Then the solution to the equation (3.2.0.10) in the time interval $(0, \tau^K)$ is also a solution to the equation (3.2.0.9) in the time interval $(0, \tau^K)$. Because $K > N$, then $\tau^K \geq \tau^N$.

□

In the previous model, there are problems with the behavior of the processes Y and Z in the neighborhood of zero and with the behavior of the process X in the situation, where X is close to $\vartheta(Z)$, because in these cases, the diffusion coefficients are not Lipschitz. Moreover, it is possible that $Z_t < 0$ for some $t > 0$ which is not very realistic. Consequently, we can not use any standard theorem about existence and uniqueness of a solution.

However, we can easily modify this model and remove these problems by changing the diffusion coefficient in the neighborhood of zero as follows.

For the same $\epsilon > 0$, define the functions $g(z)$ and $h(z)$ by

$$\begin{aligned} g(z) &= 1 && z \notin (-\epsilon, \epsilon), \\ &= \frac{|z|}{\epsilon} && z \in (-\epsilon, \epsilon), \\ h(z) &= 1 && z \notin (-2\epsilon, 2\epsilon), \\ &= \left(\frac{|z| - \epsilon}{\epsilon}\right)^2 && z \in (-2\epsilon, -\epsilon) \cup (\epsilon, 2\epsilon), \\ &= 0 && z \in [-\epsilon, \epsilon]. \end{aligned}$$

The equation (3.2.0.7) will be modified to the equation

$$\begin{aligned} dX_t =& -\beta(Z_t)Y_t[X_t - \vartheta(Z_t)]dt + \sqrt{\beta(Z_t)Y_t[X_t - \vartheta(Z_t)]g(\beta(Z_t)Y_t[X_t - \vartheta(Z_t)])}dW_t^1, \\ dY_t =& \beta(Z_t)Y_t[X_t - \vartheta(Z_t)]dt - \gamma Y_t dt + \sqrt{\gamma Y_t g(Y_t)h(Z_t)}dW_t^2 \\ & - \sqrt{\beta(Z_t)Y_t[X_t - \vartheta(Z_t)]g(\beta(Z_t)Y_t[X_t - \vartheta(Z_t)])}dW_t^1, \\ dZ_t =& \gamma Y_t dt - \sqrt{\gamma Y_t g(Y_t)h(Z_t)}dW_t^2, \end{aligned} \tag{3.2.0.11}$$

and (3.2.0.8) will be modified to

$$\begin{aligned} dX_t &= 0, \\ dY_t &= -\gamma Y_t dt + \sqrt{\gamma Y_t g(Y_t)h(Z_t)}dW_t^2, \\ dZ_t &= \gamma Y_t dt - \sqrt{\gamma Y_t g(Y_t)h(Z_t)}dW_t^2, \end{aligned} \tag{3.2.0.12}$$

where β, γ, ϑ, W_t, τ, τ^Y and τ^X are defined as above.

Denote $L^1 = (X^1, Y^1, Z^1)$ a solution to (3.2.0.11) with the same initial conditions as in (3.2.0.7), and denote $L^2 = (X^2, Y^2, Z^2)$ a solution of (3.2.0.12) with the initial condition $L_\tau^2 = (X_\tau^2, Y_\tau^2, Z_\tau^2) = L_{\tau_-}^1$. Let L be defined by

$$\begin{aligned} L_t = (X_t, Y_t, Z_t) &= L_t^1, && t \in (0, \tau), \\ &= L_t^2, && t \in [\tau, \tau^Y), \\ &= (X_{\tau_-}^1, Y_{\tau_-^Y}^2, Z_{\tau_-^Y}^2), && t \in [\tau^Y, \infty). \end{aligned} \tag{3.2.0.13}$$

Then for the process L, it is possible to prove the following theorem about the existence, uniqueness and behavior of the process L.

Theorem 3.3 *Let β and ϑ be measurable, Lipschitz, bounded functions from $\mathbb{R}$ to $\mathbb{R}^+$. Then*

(i) if L is defined by (3.2.0.13), then L is a continuous process which satisfies that $L_t \in [0, N]^3$ for all $t \in \mathbb{R}^+$, where $N = x^0 + y^0 + z^0$;

(ii) for any set-up $(\Omega, \mathcal{F}_t, P, W)$, there exists exactly one semimartingale L defined by (3.2.0.13). It means, that if there exists another semimartingale $\tilde{L}$ satisfying (3.2.0.13), then $P[L_t = \tilde{L}_t, \forall t] = 1$;

(iii) X_t is a $\mathcal{F}_t-$supermartingale, Z_t is a $\mathcal{F}_t-$submartingale;

(iv) all the limits X_∞, Y_∞ and Z_∞ exist.

Proof.

(i) Continuity of the process L follows from continuity of solutions to (3.2.0.11) and (3.2.0.12). Because x^0 and y^0 are positive, X_t and Y_t are continuous and we stop the processes X_t and Y_t in zero, therefore the processes X_t and Y_t are nonnegative. Let $Z_t = 0$ for some time t. Then $Z_s = 0 + \int_t^s \gamma Y_u du \geq 0$ for all $s \in (t, \tau_\epsilon^t)$, where $\tau_\epsilon^t = \inf\{s > t; Z_s \geq \epsilon\}$, and therefore Z_t is nonnegative. Moreover, because $dX_t + dY_t + dZ_t = 0$ and therefore $X_t + Y_t + Z_t = N$, we get (i).

(ii) First, we prove the existence and uniqueness of a solution to (3.2.0.11). Rewrite (3.2.0.11) to the form:

$$dL_t = b(L_t)dt + \sigma(L_t)dW_t, \tag{3.2.0.14}$$

where

$$b(l) = \begin{pmatrix} -\beta(z)y[x - \vartheta(z)] \\ +\beta(z)y[x - \vartheta(z)] - \gamma y \\ +\gamma y \end{pmatrix}$$

and

$$\sigma(l) = \begin{pmatrix} +\sqrt{\beta(z)y[x - \vartheta(z)]g(\beta(z)y[x - \vartheta(z)])} & 0 \\ -\sqrt{\beta(z)y[x - \vartheta(z)]g(\beta(z)y[x - \vartheta(z)])} & +\sqrt{\gamma y g(y)h(z)} \\ 0 & -\sqrt{\gamma y g(y)h(z)} \end{pmatrix}.$$

Let $K > N$ and denote $l^{Kbound} = ((x \vee -K) \wedge K, (y \vee -K) \wedge K, (z \vee -K) \wedge K)$. Consider the equation

$$d\widetilde{L} = \widehat{b}(\widetilde{L})dt + \widehat{\sigma}(\widetilde{L})dW_t \tag{3.2.0.15}$$

with initial condition $\widetilde{L}_0 = (x^0, y^0, z^0)$, where $\widehat{b}(l) = b(l^{Kbound})$ and $\widehat{\sigma}(l) = \sigma(l^{Kbound})$. Because the functions β, ϑ, $\sqrt{zg(z)}$ and $\sqrt{h(z)}$ are Lipschitz, $\widehat{b}$ and $\widehat{\sigma}$ are also Lipschitz and we can apply the theorem 11.2, p.128, in [12] from which we get that the equation (3.2.0.15) has a pathwise unique strong solution.

From the fact that $\widehat{\sigma}(l) = \sigma(l)$ and $\widehat{b}(l) = b(l)$ for $l \in [-K, K]^3$ follows the existence and pathwise uniqueness of a strong solution to (3.2.0.14) in thetime interval $(0, \tau^K)$, where $\tau^K = \inf\{t > 0; L_t \notin [-K, K]^3\}$. But because $K > N$, then from (i) we get $\tau^K > \tau$, and therefore we have the existence and pathwise uniqueness of a strong solution to (3.2.0.14) in the time interval $(0, \tau]$.

In a similar way, we can prove the existence and pathwise uniqueness of a strong solution to (3.2.0.12).

The existence and uniqueness of L follows from existence and uniqueness of solutions to (3.2.0.11) and (3.2.0.12).

(iii) Let $s \in (0, \tau)$, $t > s$, and denote $f^1(x, y, z) = \beta(z)y[x - \vartheta(z)]$ and $f^2(x, y, z) = \sqrt{f^1(x, y, z)g(f^1(x, y, z))}$. Then

$$\begin{aligned} E[X_t|\mathcal{F}_s] &= E\left[x^0 - \int_0^{t\wedge\tau} f^1(X_u, Y_u, Z_u)du + \int_0^{t\wedge\tau} f^2(X_u, Y_u, Z_u)dW_u^1 \middle| \mathcal{F}_s\right] \\ &= X_s + E\left[-\int_s^{t\wedge\tau} f^1(X_u, Y_u, Z_u)du + \int_s^{t\wedge\tau} f^2(X_u, Y_u, Z_u)dW_u^1 \middle| \mathcal{F}_s\right] \\ &= X_s + E\left[-\int_s^{t\wedge\tau} f^1(X_u, Y_u, Z_u)du \middle| \mathcal{F}_s\right] \leq X_s \quad a.s., \end{aligned}$$

because $f^1(X_u, Y_u, Z_u) \geq 0$ for $u \in (0, \tau)$. If $s \geq \tau$, then $X_s = X_\tau = X_t$, and therefore X is a $\mathcal{F}_t-$supermartingale.

If we use the same procedure for Z_t with $f^1(x, y, z) = \gamma y$ and $f^2(x, y, z) = \sqrt{\gamma y g(y)h(z)}$, we get that Z_t is a $\mathcal{F}_t-$submartingale.

(iv) Because X_t is a continuous bounded $\mathcal{F}_t-$supermartingale, and Z_t is a continuous, bounded $\mathcal{F}_t-$submartingale, we get from Theorem 69.1, p.176, and Theorem 70.2, p.177, in [11], that the limits X_∞ and Z_∞ exist. The existence of Y_∞ follows immediately from the relation $Y_t = N - X_t - Z_t$ together with the existence of limits X_∞ and Z_∞.

□

Such a modification of the coefficients as introduced in (3.2.0.11) could seem to be unnatural. The most suitable stochastic version of the model with vaccination seems to be the model given be SDE:

$$\begin{aligned} dX_t =& -\beta(Z_t)Y_t[X_t - \vartheta(Z_t)]I_{[X_t>\vartheta(Z_t),Y_t>0]}dt + \sqrt{\beta(Z_t)Y_t[X_t - \vartheta(Z_t)]}I_{[X_t>\vartheta(Z_t),Y_t>0]}dW_t, \\ dY_t =& \beta(Z_t)Y_t[X_t - \vartheta(Z_t)]I_{[X_t>\vartheta(Z_t),Y_t>0]}dt \\ & - \gamma Y_t dt - \sqrt{\beta(Z_t)Y_t[X_t - \vartheta(Z_t)]}I_{[X_t>\vartheta(Z_t),Y_t>0]}dW_t, \\ dZ_t =& \gamma Y_t dt, \end{aligned} \tag{3.2.0.16}$$

where the diffusion coefficient affects only the spread of the infection, but not recovering. We assume initial conditions $X_0 = x^0 > 0,\ Y_0 = y^0 > 0,\ Z_0 = z^0 \geq 0$, W_t is a Brownian motion and β, γ and ϑ are the same as in the previous models.

For this model, it is possible to prove that the solution (X_t, Y_t, Z_t) never exits the cube $[0, N]^3$, X_t is a non-negative supermartingale with $X_t = 0$ for all $t \geq \tau_X$, the limits X_∞ and Y_∞ exist and $Y_\infty = 0$ a.s. Further, if we consider β and ϑ to be Lipschitz continuous, we can prove that the equation (3.2.0.16) has a unique solution which satisfies

$$\begin{aligned} X_t &= X_\tau \quad \text{for all} \quad t \geq \tau, \\ Y_t &= Y_{\tau_X} e^{-\gamma(t-\tau_X)} \quad \text{for all} \quad t \geq \tau_X, \\ Y_t &= 0 \quad \text{for all} \quad t \geq \tau_Y. \end{aligned}$$

All these results will be formulated in the last section of this chapter for more general model.

If we look back to the heuristic idea of the choice of diffusion coefficient, it seems that the effect of this coefficient should be weaker for bigger population and stronger for smaller one. Let us now to study this effect. Consider for simplicity a model without vaccination, i.e. $\vartheta = 0$, and constant susceptibles-infectives contact rate β. Further, assume that (X_t, Y_t, Z_t) is a solution to (3.2.0.16) and denote $(\widetilde{X}_t, \widetilde{Y}_t, \widetilde{Z}_t) = \left(\frac{X_t}{N}, \frac{Y_t}{N}, \frac{Z_t}{N}\right)$ the process of ratios of the sub-populations. For simpler notation, we consider $t < \tau$, where τ is the first time such that $X_t = 0$ or $Y_t = 0$. Then, we get

$$\begin{aligned} \widetilde{X_t} &= \frac{x_0}{N} - \int_0^t \beta N \left[\frac{X_s}{N}\frac{Y_s}{N}\right]^+ ds + \int_0^t \sqrt{\beta \left[\frac{X_s}{N}\frac{Y_s}{N}\right]^+} dW_s \\ &= \widetilde{x}_0 - \int_0^t \widetilde{\beta}[\widetilde{X}_s \widetilde{Y}_s]^+ ds + \int_0^t \sqrt{\frac{\widetilde{\beta}}{N}[\widetilde{X}_s \widetilde{Y}_s]^+} dW_s, \end{aligned}$$

where $\widetilde{\beta} = \beta N$. In the same way, we can write the equations for $\widetilde{Y}_t$ and $\widetilde{Z}_t$. If we look at these equations, we can see that the process $(\widetilde{X}_t, \widetilde{Y}_t, \widetilde{Z}_t)$ does not solve the equation (3.2.0.16), because the diffusion coefficient is $\sqrt{N}$-times smaller than it should be in comparison with the trend coefficient. This fact may be interpreted so that with growing size of population, the effect of diffusion becomes weaker. In Figure 3.4 and Figure 3.5, we can see the effect of diffusion in dependence on the size of the population.

3.2.1 Simulations

In this section, we show a few simulations of the models from the previous section. We compare the model described by (3.2.0.7) to its modification given by (3.2.0.11) and we

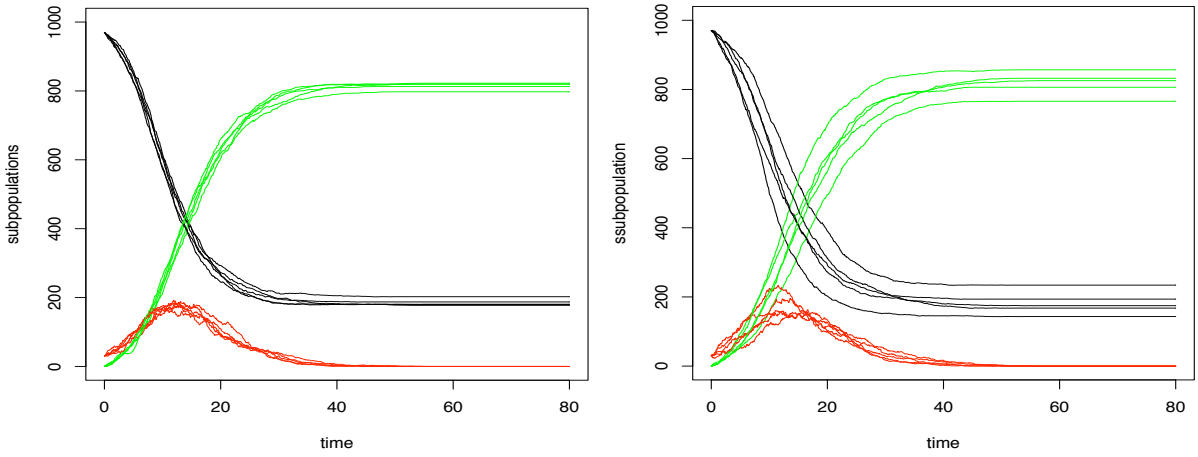

Figure 3.1:
Behavior of epidemics with $\beta = 0.0005$, $\gamma = 0.25$ and the vaccination $\vartheta = 0$ for the model given by (3.2.0.7) (left) and the model given by (3.2.0.11) (right). The black line describes the size of susceptibles, the red line the size of infectives and the green line the size of removals.

show a possible way how to establish the optimal vaccination strategy for the model defined by (3.2.0.16).

Simulations were produced by using explicit Euler method (see p.247 in [8]). All computations and graphic results were produced by software R.[2]

First, we show the behavior of the models given by (3.2.0.7) and (3.2.0.11). For these simulations, we choose $\beta = 0.0005$, $\gamma = 0.25$, initial conditions $x_0 = 990$, $y_0 = 10$, vaccination function $\vartheta = 0$ and $\epsilon = 0.01$. The length of the observation time period is equal to 80 because the epidemics with $\beta = 0.0005$ and $\gamma = 0.25$ has short running. The number of simulations is 5000 and the number of steps of Euler method is 2000.

Figure 3.1 shows five realizations of the model (3.2.0.7) (left picture) and the model (3.2.0.11) (right picture). It is possible to see that the behavior of both these models is very similar as we expected.

Figure 3.2 shows the density of maximum of infectives (left picture) and the density of culmination time (right picture), where the solid line describes the density for the model (3.2.0.7) and the dashed line the density for the model (3.2.0.11).

Left picture in Figure 3.3 shows the density of removals at time $t = 80$ which is approximately equal to the number of people infected till the time $t = 80$. There the solid line describes the density for the model (3.2.0.7) and the dashed line the density for the model

[2]Version R 2.3.1 was used.

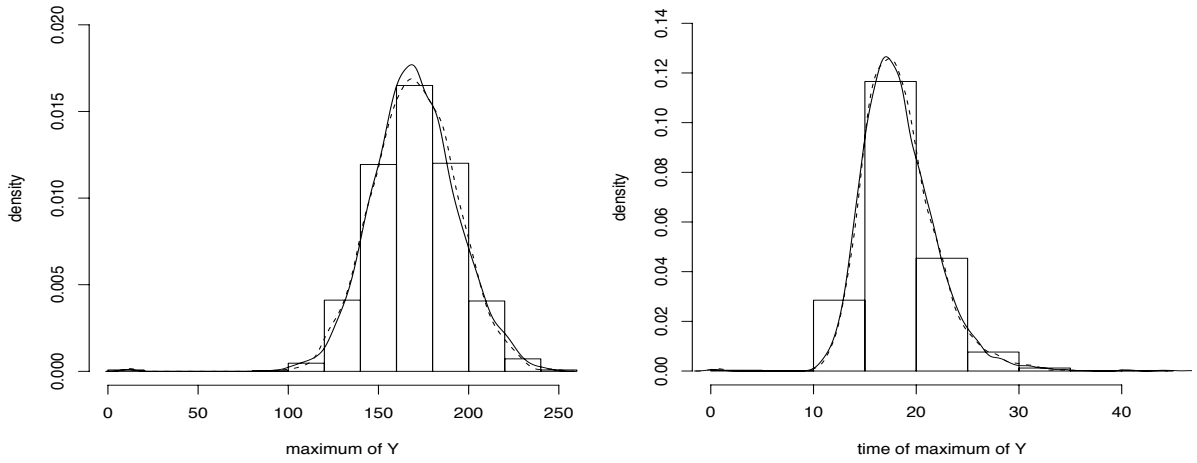

Figure 3.2:
The densities of maximum of Y (left) and of the time of culmination (right), solid line is used for the model (3.2.0.7), dashed line for the model (3.2.0.11).

(3.2.0.11). The right picture then shows the difference between the expected values of respective susceptibles, infectives and removals in the models (3.2.0.7) and (3.2.0.11).

As we can see in Figure 3.1, Figure 3.2 and Figure 3.3, the modified model (3.2.0.11) and the model (3.2.0.7) have very similar behavior. Therefore we can say that the modification which "improve" the theoretical properties of the model (3.2.0.7) does not change its behavior significantly.

Now, we examine the model given by (3.2.0.16). In the previous section, we have shown that the effect of diffusion depends on the size of population. Now, let us study, how strong is the effect for some choices of the size of population. As well as before, we choose $\gamma = 0.25$, $\beta = 0.5/N$, vaccination function $\vartheta = 0$, time interval $(0, 80)$, 5000 simulation and the number of steps equal to 2000.

Figure 3.4 shows the expected value of the solution to (3.2.0.16) (solid line) and the solution to equation (2.2.0.2) which describes the deterministic model with vaccination. Left picture shows the situation for the size of population equal to 100, the right one for the size of population $N = 1000$. We can see that while for the smaller size, the difference between the expected value and the solution to the deterministic model is essential (the stochastic model has milder running), the difference for bigger population is negligible.

Figure 3.5 shows five realizations of the model (3.2.0.16) (dashed lines) and its expected value (solid line) for the size of population $N = 1000$ (left picture) and $N = 100000$ (right picture). As we can see from the plots, for the populations of the size $N = 1000$, the effect of randomness is significant, therefore it can be useful to use the stochastic model. On the other hand, the influence of randomness for the size of population $N = 100000$ is

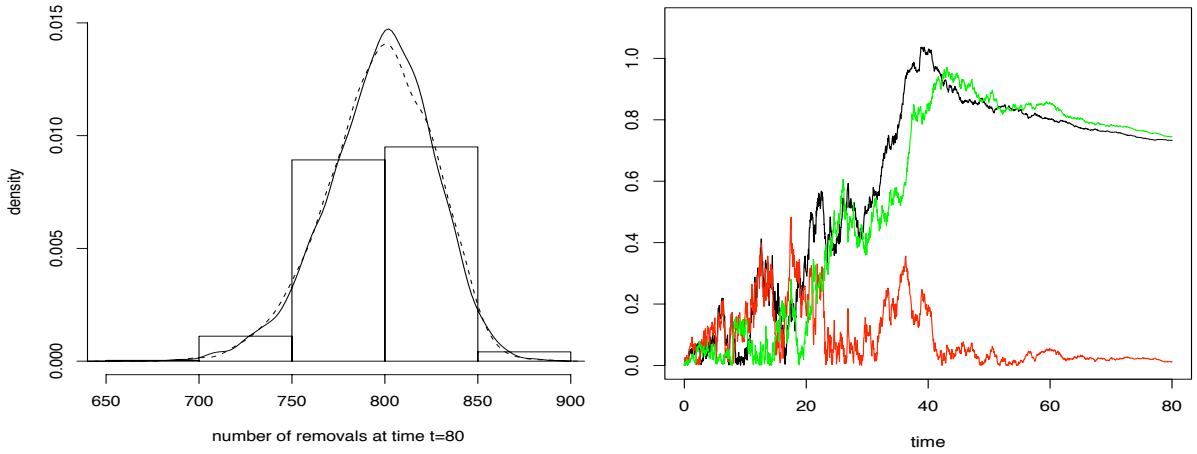

Figure 3.3:
Density of Z_{80} for the model (3.2.0.7) (solid line) and the model (3.2.0.11) (dashed line) (left picture), and the difference of the expected values of models (3.2.0.7) and (3.2.0.11) (right picture). The black line describes the size of susceptibles, the red line the size of infectives and the green line the size of removals.

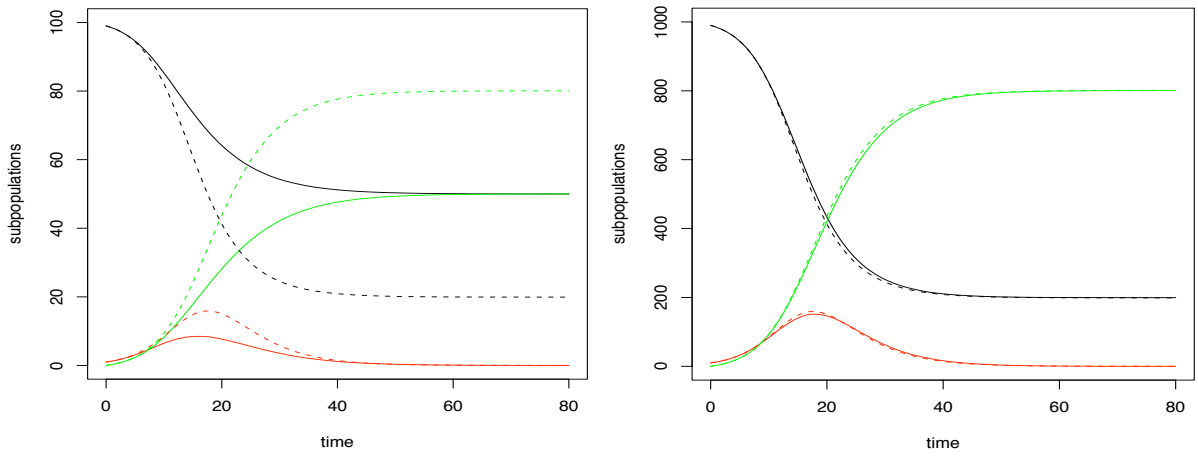

Figure 3.4:
Behavior of expected value of model (3.2.0.16) (solid line) and the deterministic model (dashed line). Left picture displays the situation with $N = 100$, the right one with $N = 1000$. On both the pictures, the black line describes the size of susceptibles, the red line the size of infectives and the green line the size of removals.

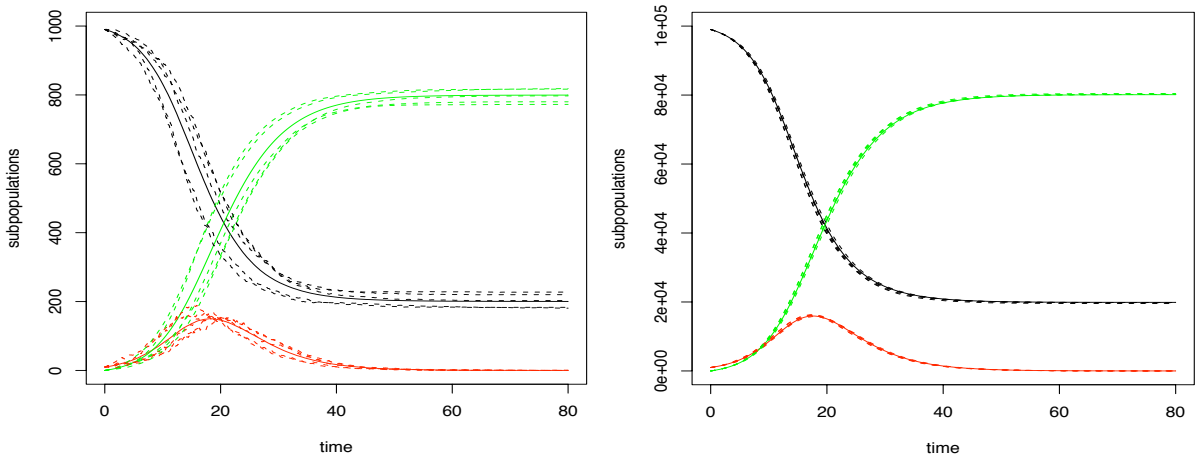

Figure 3.5:
Five realizations of the model (3.2.0.16) (dashed line) and expected value (solid line). Left picture displays the situation with $N = 1000$, the right one with $N = 10^5$. On both the pictures, the black line describes the size of susceptibles, the red line the size of infectives and the green line the size of removals.

very small (meaning that all the realizations are similar) and when we choose $N = 10^6$, it is difficult to distinguish one realization from another. It means that for larger size of population, the stochastic model gives the same result as the deterministic one, hence it is not reasonable to use it.

At the last part of this section, we will present one possible way how to find the optimal vaccination strategy. We will choose a penalization function and define the optimal vaccination strategy as a strategy for which the penalization function is minimal. The choice of the penalization function follows from the same idea as described in Section 2.2.2, therefore we choose

$$f = E[c * (Y_T + Z_T) + c_0 * v_0 + c_1 * V_1 + c_2 * T_{ep}], \tag{3.2.1.1}$$

where c, c_0, c_1 and v_0 has the same meaning as the corresponding coefficients described in Section 2.2.2, and moreover

- $Y_T + Z_T$ is the number of people, who have been infected by the time T ,
- V_1 is the number of people vaccinated during the time interval $(0, T)$,
- T_{ep} it the length of the time period (or sum of separated periods), when the number of infectives is being greater than some chosen bound,
- c_2 is a penalization for one time unit in which the number of infected people gets over the chosen bound.

The interpretation of T_{ep} and c_2 is the following. When the number of infectives overgrows some bound, it is necessary to do some general equipments (like closing schools etc.). Value c_2 is the loss per each day, when it is needed to keep these equipments, and T_{ep} is the total number of these days. Thus, f may be interpreted as an expected value of the loss caused by the disease and optimal strategy is that one which minimizes this loss.

Because it is very difficult to compute the expected value from (3.2.1.1), we use simulations to get an approximate value of f. In our case, we look for the optimal linear vaccination as described in Section 2.2.2., i.e. $\vartheta(z) = \vartheta_0 + \vartheta_1 * z$, and therefore, for given initial conditions and given c_0, c_1, c_2 and T, we can consider the penalization function f to be a function of $(\vartheta_0, \vartheta_1)$, i.e.

$$f(\vartheta_0, \vartheta_1) = E[c * (Y_T + Z_T) + c_0 * \vartheta_0 + c_1 * \vartheta_1 * Z_T + c_2 * T_{ep}.$$

Then the optimal vaccination strategy is given by $(\vartheta_0, \vartheta_1) = \arg\min f(\vartheta_0, \vartheta_1)$.

Figure 3.6 shows the approximate value of f for two different choices of c, c_0, c_1 and c_2, the first one is $c = 1$, $c_0 = 0.3$, $c_1 = 0.4$ and $c_2 = 0.5$ (left picture), the second one is $c = 1$, $c_0 = 0.6$, $c_1 = 0.304$ and $c_2 = 0$ (right picture). In both cases, we choose the size of population $N = 1000$, $\beta = 0.3 * 10^{-3}$, $\gamma = 0.25$, $T = 150$, $x_0 = 990$, $y_0 = 10$. The number of simulations as well as the number of steps of Euler method is 1000. The first choice represents more common situation, when the optimal strategy satisfies that either $\vartheta_0 = 0$ or $\vartheta_1 = 0$. In this situation, we do not need too much simulation to establish the optimal vaccination. In the second case, the situation is more complicated, because the plot of f is not smooth enough to establish the optimal vaccination strategy. In these situations, we need more simulations which could have high computational complexity. On the other hand, although in this situation we can get the optimal strategy which is not close enough to the real optimal strategy, the effect of this strategy, in meaning of the penalization function f, is close to the effect of the real optimal strategy. So we get the strategy which is nearly as good as the real one.

3.3 Model with multiple pathogens

In this section, we present a model with multiple pathogens which was introduced by Allen and Kirupaharan in [1]. The models with multiple pathogens are suitable for example for modelling the spread of influenza, HIV-AIDS or malariri. This model assumes that nobody is infected by two or more pathogen strains and somebody infected by some pathogen strain is immune for the other pathogen strains. This situation is called the cross immunity. As we want to model the disease such as AIDS, the observation time interval is long, therefore it is necessary to add births and deaths to the model. Then the size of population is not constant. Moreover, we suppose that everyone, who have been infected by some pathogen can not be recovered.

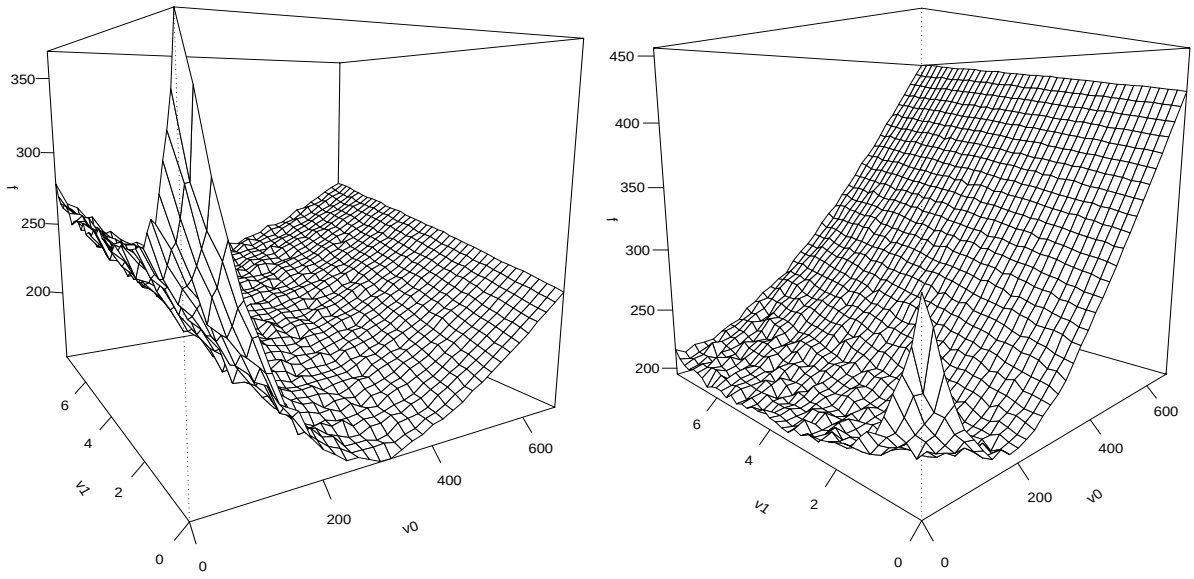

Figure 3.6:
Penalization function $f = E[Z_{150} + 0.3 * \vartheta_0 + 0.4 * \vartheta_1 * Z_{150} + 0.5 * T_{ep}]$ (left picture) and $f = E[Z_{150} + 0.6 * \vartheta_0 + 0.304 * \vartheta_1 * Z_{150}]$ (right picture).

Therefore, we consider a model of epidemics with unstable size of the population N_t and suppose the population being divided into $d+1$ sub-populations: X_t is the size of susceptibles and $Y_t^j,\ j = 1, ..., d$, is the size of population which is infected by the j-th pathogen strain $j = 1, ..., d$. We consider the end of epidemics as the stopping time τ_f when some of processes X_t, Y_t^j enters to zero or to N_b, where $N_b > N_0$ is a chosen (constant) upper bound for the size of population. The first condition means that there are no people who can be infected or that some pathogen strain has finished, so we stop the model. The second condition means that the size of population overgrows some reasonable bound. The model is given by the following $(d+1)$-dimensional stochastic differential equation:

$$
\begin{aligned}
dX_t &= X_t \left(b - d(N_t) - \sum_{k=1}^{d} \frac{\beta_k Y_t^k}{N_t} \right) dt + \sum_{k=1}^{d} b_k Y_t^k dt + \sum_{k=1}^{d+1} B_{1.k}(L_t) dW_t^k, \\
dY_t^j &= Y_t^j \left(b - b_j - d(N_t) - \alpha_j + \frac{\beta_j X_t}{N_t} \right) dt + \sum_{k=1}^{d+1} B_{j+1.k}(L_t) dW_t^k, \quad j = 1, \ldots, d,
\end{aligned}
\tag{3.3.0.2}
$$

for $t \in (0, \tau_f)$, with initial condition $X_0 = x_0 > 0$, $Y_0^1 = y_0^1 > 0$,...,$Y_0^d = y_0^d > 0$ where b is the per capita birth rate, the function $d(.)$ is the per capita death rate, and

for $j = 1, \ldots, d$, $b_j \leq b$ is the birth rate of health offspring to parents infected by j-th pathogen, α_j is the j-th pathogen-related per capita death rate, and β_j is the transmission rate for j-th pathogen. Therefore $(b-b_j)/b$ is possible to be interpreted as the probability that the parent infected by the j-th pathogen will have infected offspring. In other words $(b-b_j)/b$ is a probability of vertical transmission for j-th pathogen strain. Further, $W_t^k,\ k = 1, ..., d+1$, are independent Wiener processes, $L_t = (X_t, Y_t^1, ..., Y_t^d)$ and $B(L_t) = \sqrt{C(L_t)}$, where $C(L_t)$ is a $(d+1) \times (d+1)$-matrix which is symmetric, positive definite and is defined by

$$C(L_t) = \begin{pmatrix} 0 & \sigma_{1.2}(L_t) & \cdots & \sigma_{1.d+1}(L_t) \\ \sigma_{2.1}(L_t) & 0 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ \sigma_{d+1.1}(L_t) & 0 & \cdots & 0 \end{pmatrix} + \mathrm{diag}(\sigma_{11}(L_t), \ldots, \sigma_{d+1,d+1}(L_t)),$$

where

$$\begin{aligned} \sigma_{1.1}(L_t) &= X\left(b + d(N) + \sum_{k=1}^{d} \frac{\beta_k Y^k}{N}\right) + \sum_{k=1}^{d} b_k Y^k, \\ \sigma_{j+1.j+1}(L_t) &= Y^j\left(b - b_j + d(N) + \alpha_j + \beta_j \frac{X}{N}\right), \quad j = 1, ..., d, \\ \sigma_{1.j+1}(L_t) &= -\beta_j \frac{XY^j}{N} = \sigma_{j+1.1}, \quad j = 1, ..., d. \end{aligned}$$

Matrix $C(L_t)$ is the covariance matrix for the change in the population sizes. For $j, k = 2, ..., d$, the coefficients $\sigma_{1,k}(L_t)$ describe the interaction between X_t and Y_t^{k-1} and $\sigma_{j,k}(L_t) = 0$ for $j \neq k$ because of the cross immunity. It can be proved that $C(L_t)$ is strictly positive definite if and only if $X, Y^j > 0$ and $b, d(N), b - b_j, \alpha_j > 0$ holds. Under these conditions $C(L_t)$ is positive definite, and therefore it has a unique positive definite square root matrix $B(L_t)$.

For this model, it is possible to prove the following theorem on the existence and uniqueness of a solution to (3.3.0.2).

Theorem 3.4 *Let $d(.)$ is a bounded local Lipschitz function and $b, d(N), b - b_j, \alpha_j > 0$. Then there exists a stopping time τ, such that the equation (3.3.0.2) has a unique solution for $t \in (0, \tau)$. If $L_t = (X_t, Y_t^1, ..., Y_t^d)$ is a solution to (3.3.0.2), a possible choice of τ is $\tau = \tau_f$, where τ_f is described above.*

Proof. The equation (3.3.0.2) can be rewritten as

$$dL_t = a(L_t)dt + B(L_t)dW_t, \tag{3.3.0.3}$$

where $W_t = (W_t^1, ..., W_t^{d+1}),\ a(L_t) = (a^1(L_t), ..., a^{d+1}(L_t))$ and

$$a^1(L_t) = X_t\left(b - d(N_t) - \sum_{k=1}^{d}\frac{\beta_k Y_t^k}{N_t}\right) + \sum_{k=1}^{d} b_k Y_t^k,$$
$$a^j(L_t) = Y_t^j\left(b - b_j - d(N_t) - \alpha_j + \frac{\beta_j X_t}{N_t}\right), \quad j = 2, .., d+1.$$

Let $1 > \epsilon > 0$. Denote $\widehat{l} = ((l_1 \vee \epsilon) \wedge N_b, ..., (l_{d+1} \vee \epsilon) \wedge N_b)$ for some vector $l = (l_1, \ldots, l_{d+1})$. Define a map $\widehat{C} : \mathbf{R}_+^{d+1} \to \mathbf{M}^{d+1\times d+1}$ so that $\widehat{C}(l) = C(\widehat{l})$. Then $\widehat{C}(l)$ is everywhere strictly positive definite, and from Theorem 12.12, p.134, in [12], the map $\widehat{B} := \widehat{C}^{\frac{1}{2}}$ is local Lipschitz. Thus, for all N there exists K_N such that

$$|\widehat{B}(l) - \widehat{B}(\widetilde{l})| \leq K_N |l - \widetilde{l}| \tag{3.3.0.4}$$

holds for all $l, \widetilde{l}$ satisfying $|l|, |\widetilde{l}| \leq N$, where $|\widehat{B}(l)| \equiv \sqrt{\text{trace}(\widehat{B}(l)\widehat{B}(l)^T)}$ and $|l|$ is Euclidean norm of l.

Because for all $j = 1, ..., d+1$, $a^j(l)$ are local Lipschitz, we get that $a(l)$ is local Lipschitz, and so for all N, there exists K_N such that

$$|a(l) - a(\widetilde{l})| \leq K_N |l - \widetilde{l}| \tag{3.3.0.5}$$

holds for all $l, \widetilde{l}$ satisfying $|l|, |\widetilde{l}| \leq N$.

Since $d(.) \leq K_{death}$ for some $K_{death} < \infty$, then

$$|a(l)| \leq \sqrt{\left(\sum_{k=1}^{d}(\beta_k + b_k) + b + K_{death}\right)^2 + \sum_{k=1}^{d}(b - b_k + K_{death} + \alpha + \beta)^2}|l| \leq K|l| \tag{3.3.0.6}$$

holds for some $K < \infty$.

Now, we show that $b_{i.j}$ are bounded for all $i, j = 1, \ldots, d+1$. Denote $\mathbf{1} = (1, ..., 1)$ the $d+1$ dimensional vector. Then $\widehat{B}(\mathbf{1}) = B(\mathbf{1})$, $\sigma_{i.j}(\mathbf{1})$ are bounded constants for all $i, j = 1, ..., d+1$ and $\sigma_{i.i} > 0$ for all $i = 1, ..., d+1$. From the Cholesky decomposition (p.235 in [6]), we have:

$$\widehat{b}_{i,i}(\mathbf{1}) = b_{i.i}(\mathbf{1}) = \sqrt{\sigma_{i.i}(\mathbf{1}) - \sum_{k=1}^{i-1} b_{i.k}^2(\mathbf{1})},$$
$$\widehat{b}_{k,i}(\mathbf{1}) = b_{j.i}(\mathbf{1}) = \left(\sigma_{j.i}(\mathbf{1}) - \sum_{k=1}^{i-1} b_{j.k}(\mathbf{1}) b_{i.k}(\mathbf{1})\right)/b_{i.i}(\mathbf{1}), \qquad \text{if} \quad b_{i,i}(\mathbf{1}) > 0,$$
$$\widehat{b}_{k,i}(\mathbf{1}) = b_{j.i}(\mathbf{1}) = 0, \qquad \text{if} \quad b_{i,i}(\mathbf{1}) = 0.$$

As $\sigma_{i,j}$ are bounded for all $i,j = 1,...,d+1$ then from the Cholesky decomposition, we get that $b_{j,i}(\mathbf{1})$ are bounded for all $i,j = 1,...,d+1$, and therefore, there exists a constant $C_B < \infty$ satisfying

$$|\widehat{B}(\mathbf{1})| \leq C_B < \infty. \tag{3.3.0.7}$$

Using (3.3.0.4) and (3.3.0.7) we get that for all N, there exists K_N such that

$$|\widehat{B}(l)| \leq |\widehat{B}(l) - \widehat{B}(\mathbf{1}) + \widehat{B}(\mathbf{1})| \leq K_N|l - \mathbf{1}| + C_B \leq C_N(1 + |l|) \tag{3.3.0.8}$$

holds for all l satisfying $|l| \leq N$. Since $\widehat{B}(l) = \widehat{B}(\widehat{l})$, $|\widehat{l}| \leq \sqrt{d+1}N_b$ and using (3.3.0.8) we get that

$$|\widehat{B}(l)| \leq K(1 + |l|) \tag{3.3.0.9}$$

holds for some $K < \infty$. Using the properties (3.3.0.4),(3.3.0.5), (3.3.0.6) and (3.3.0.9), then due to Theorem 12.1, p.132, in [12], the equation

$$dL_t = a(L_t)dt + \widehat{B}(L_t)dW_t$$

has a unique solution. Note that the stopping time τ_ϵ is the time of the first output of the process L_t from the interval $(\epsilon, N_b)^{[d+1]}$. Then because

$$L_{t\wedge\tau_\epsilon} = L_0 + \int_0^{t\wedge\tau_\epsilon} a(L_s)ds + \int_0^{t\wedge\tau_\epsilon} \widehat{B}(L_s)dW_s = L_0 + \int_0^{t\wedge\tau_\epsilon} a(L_s)ds + \int_0^{t\wedge\tau_\epsilon} B(L_s)dW_s,$$

the equation (3.3.0.2) has a unique solution in the period $[0, \tau_\epsilon]$. Finally, for $\epsilon \to 0$ we get the unique solution to (3.3.0.2) in the time period $[0, \tau_f)$.

□

More information about epidemic models with multiple pathogen, including a deterministic model and numerical examples can be found in [1].

3.4 General epidemic model

The problems which arose in Section 3.2, when the coefficients of SDE are not Lipschitz, led us to study this situation in details for a more general model. Therefore, we construct the model which mainly generalizes the models described in the previous section. All results in this section follow from [18]. However, as we want to obtain a model which includes as sub-models the models with vaccination as well as the models with multiple pathogens, we need to construct a little more general model than that one described in [18], and hence some proofs from [18] must be modified.

Consider $(\Omega, \mathcal{F}, P)$ a complete probability space and $(\mathcal{F}_t, t \geq 0)$ a P-complete right continuous filtration. Then the model is given by $(d+1)$-dimensional stochastic differential equation

$$\begin{aligned} dX_t &= -\sum_{i=1}^{d} \varphi^i(X_t, Y_t)dt + \sum_{i=1}^{d} \psi^i(X_t, Y_t)dW_t^i, & X_0 &= x_0 \geq 0, \\ dY_t^1 &= \varphi^1(X_t, Y_t)dt - \gamma^1 Y_t^1 dt - \psi^1(X_t, Y_t)dW_t^1, & Y_0^1 &= y_0^1 \geq 0, \\ &\vdots \\ dY_t^d &= \varphi^d(X_t, Y_t)dt - \gamma^d Y_t^d dt - \psi^d(X_t, Y_t)dW_t^d, & Y_0^d &= y_0^d \geq 0, \end{aligned} \tag{3.4.0.10}$$

where $Y_t = (Y_t^1, ..., Y_t^d)$ and W_t^i denotes independent $\mathcal{F}_t$-Brownian motions.

Further, we shall assume

$$\begin{aligned} &\forall i : 1, ..., d, \quad \varphi^i, \psi^i : \mathbb{R}^{d+1} \to \mathbb{R} \text{ are borel functions,} \\ &n_0 = x_0 + \sum_{i=1}^{d} y_0^i, \varphi^i \geq 0 \text{ on } [0, n_0]^{d+1}, \quad \gamma^i > 0. \end{aligned} \tag{3.4.0.11}$$

Denote $y = (y_1, ..., y_d)$ and assume further that for all $i = 1, ..., d$,

$$\varphi^i(x, y) = \psi^i(x, y) = 0 \quad \forall (x, y) \in (-\infty, 0] \times \mathbb{R}^d \text{ or } (x, y) \in \mathbb{R}^{d+1} : y_i \in (-\infty, 0] \tag{3.4.0.12}$$

and $B \subseteq \mathbb{R}^{d+1}$ is an open set such that if $(x, y) \in \partial B \cap [0, n_0]^{d+1}$ then $(x, \widetilde{y}) \notin B$ for all $\widetilde{y} \in [0, y_1] \times \ldots \times [0, y_d]$.

This model describes the spread of disease with d pathogens, φ^i is a function of intensity of speed of transfer in the direction $X \to Y^i$, γ^i is again the intensity of recovering for the i-th pathogen strain and ψ^i describes the randomness of exchange between X and Y^i. The assumption (3.4.0.12) means that no one can be infected by the i-th pathogen if there are no susceptibles or people infected by the i-th pathogen strain. B is the set, where the infection can be spread. For example, if we consider a model with vaccination as introduced in Section 3.2, then B is a set, where the number of susceptibles is bigger than the number of vaccinated individuals, therefore $B := \{(x, y) \in \mathbb{R}^2 : x > \vartheta(N - x - y)\}$ (N denotes the size of population and therefore $N - x - z$ is the size of removals). In this model, we do not define the removal, but if it is needed, we can define the removals by

$$Z_t := N - X_t - \sum_{i=1}^{d} Y_t^i = n_0 - X_t - \sum_{i=1}^{d} Y_t^i = \sum_{i=1}^{d} \int_0^t \gamma^i Y_s^i ds. \tag{3.4.0.13}$$

Consider (X_t, Y_t) a fixed solution to the equation (3.4.0.10), and define the $\mathcal{F}_t$-stopping times τ_X, τ_B and τ_Y^i by:

$$\begin{aligned}\tau_X &:= \inf\{t \geq 0 : X_t \leq 0\}\\ \tau_B &:= \inf\{t \geq 0 : (X_t, Y_t) \notin B \cap (0,\infty) \times \mathbb{R}^d\},\\ \tau_Y^i &:= \inf\{t \geq 0 : Y_t \leq 0\}.\end{aligned}$$

τ_B is interpreted as the time of the end of epidemics, τ_Y^i is the first time, when no one is infected by the i-th pathogen strain and τ_X is the first time, when the process X_t enters to zero. It is obvious that $\tau_X \geq \tau_B$.

We say that the solution (X_t, Y_t) to (3.4.0.10) is absorbed by the natural barrier, if outside P-null set, (X_t, Y_t) satisfies that

$$\begin{aligned}X_t = X_{\tau_B} \quad \text{and} \quad Y_t^i = Y_{\tau_B}^i e^{-\gamma_i(t-\tau_B)} \quad \text{for all} \quad t \geq \tau_B,\\ Y_t^i = 0 \quad \text{for all} \quad t \geq \tau_Y^i.\end{aligned} \tag{3.4.0.14}$$

The property (3.4.0.14) is natural for epidemics, so we want to find the sufficient conditions for equation (3.4.0.10) which provides this behavior. We also want to find a condition for a nonnegative solution or the solution which never exits the set $[0, n_0]^{d+1}$. These questions are solved in the following section.

Now, we show the connection between a partial differential equation and expected value of X_t and Y_t^i or more generally, expected value of $f(X_t, Y_t)$, where $f \in \mathcal{C}^2(\mathbb{R}^{d+1})$.

In [10], this theory for SDE with Lipschitz coefficients is presented. Since in our model, we do not require this condition, we show the way of work with more general coefficients in the following paragraphs.

First, we rewrite the equation (3.4.0.10) to the following equation which is more suitable for this problem:

$$\begin{aligned}dY_t^1 &= b^1(Y_t, Z_t)dt + \sigma^1(Y_t, Z_t)dW_t^1, & Y_0^1 &= y_0^1 > 0,\\ &\vdots\\ dY_t^d &= b^d(Y_t, Z_t)dt + \sigma^d(Y_t, Z_t)dW_t^1, & Y_0^d &= y_0^d > 0,\\ dZ_t &= b^{d+1}(Y_t, Z_t)dt, & Z_0 &= z_0 = 0,\end{aligned} \tag{3.4.0.15}$$

where Z_t is defined by (3.4.0.13) and for $i = 1, \ldots, d$, $b^i(y,z) = \varphi^1(n_0 - z - \sum y^i, y) - \gamma^i y^i$, $\sigma^i(y,z) = -\psi^i(n_0 - z - \sum y^i, y)$ and $b^{d+1}(y,z) = \sum \gamma^i y^i$. Assume $u(s,y,z) \in \mathcal{C}^{1,2}(\mathbb{R}^+ \times \mathbb{R}^{d+1})$ and define a process M_s in time interval $[0,t]$ by

$$M_s = u(t-s, Y_s, Z_s).$$

Using Itô formula, Theorem 17.18, p.340, in [7], we get

$$\begin{aligned} dM_s = &- \frac{\partial}{\partial s}u(t-s,Y_s,Z_s)ds + \sum_{i=1}^{d}\frac{\partial}{\partial y^i}u(t-s,Y_s,Z_s)b^i(Y_s,Z_s)ds \\ &+ \frac{\partial}{\partial z}u(t-s,Y_s,Z_s)b^{d+1}(Y_s,Z_s)ds + \sum_{i=1}^{d}\frac{1}{2}\frac{\partial^2}{\partial^2 y_i}u(t-s,Y_s,Z_s)\sigma^i(Y_s,Z_s)ds \\ &+ \sum_{i=1}^{d}\frac{\partial}{\partial y^i}u(t-s,Y_s,Z_s)\sigma^i(Y_s,Z_s)dW_s^i, \end{aligned}$$

hence M_s is a martingale if u is a solution to the following partial differential equation (PDE):

$$\begin{aligned} \frac{\partial}{\partial s}u(s,y,z) =& \sum_{i=1}^{d}\frac{\partial}{\partial y^i}u(s,y,z)b^i(y,z) + \frac{\partial}{\partial z}u(s,y,z)b^{d+1}(y,z) \\ &+ \sum_{i=1}^{d}\frac{1}{2}\frac{\partial^2}{\partial^2 y_i}u(s,y,z)\sigma^i(y,z). \end{aligned} \tag{3.4.0.16}$$

Let $f \in \mathcal{C}^2(\mathbb{R}^{d+1})$ and assume further $u(0,y,z) = f(y,z)$, then we get

$$E[f(Y_t,Z_t)] = E[u(0,Y_t,Z_t)] = E[M_t] = E[M_0] = E[u(t,Y_0,Z_0)] = u(t,y_0,z_0).$$

Therefore, if we have the solution u to PDE (3.4.0.16) which satisfies initial condition $u(0,y,z) = f(y,z)$, then we have $E[f(Y_t,Z_t)] = u(t,y_0,z_0)$. Unfortunately, there is no general method for solving the PDE (3.4.0.16), and even if we choose $d = 1$, we do not know how to solve the equation (3.4.0.16) with choices of φ^1 and ψ^1 which we mostly use in epidemic models. On the other hand, as we do not know any method, for computing $E[f(Y_t,Z_t)]$, we must solve this problem numerically. Hence, this connection between PDE and expected value of $f(Y_t,Z_t)$ allows us to use the numerical method for solving PDE also for solving $E[f(Y_t,Z_t)]$.

3.4.1 Theoretical results

Lemma 3.5 *Let φ_i and ψ_i satisfies (3.4.0.11) and (3.4.0.12) and let $\tau_X^0 := \inf\{t \geq 0 : X_t < 0\}$, and for all $i = 1,...,d$ denote $\tau_{Y^i}^0 := \inf\{t \geq 0 : Y_t^i < 0\}$. Then $\lambda^0 := \min\{\tau_X^0, \tau_{Y^1}^0, ..., \tau_{Y^d}^0\} = \infty$ a.s., therefore $(X_t, Y_t, \sum \gamma_i \int_0^t Y_s^i ds)$ never exits the interval $[0,n_0]^{d+2}$.*

Proof. Assume to the contrary that $\lambda^0 < \infty$. Then there exists $t_0 > 0$ such that $X_{t_0} < 0$ or $Y^i_{t_0} < 0$ for some $i = 1, ..., d$. If $X_{t_0} < 0$, denote $s_0 := \sup\{0 \le s \le t_0 : X_s > 0\}$, therefore $X_s \le 0$ for all $s \in [s_0, t_0]$. Hence, according to (3.4.0.12),

$$X_{t_0} = X_{s_0} - \sum_{i=1}^{d} \int_{s_0}^{t_0} \varphi^i(X_s, Y_s)ds + \sum_{i=1}^{d} \int_{s_0}^{t_0} \psi^i(X_s, Y_s)dW^i_s = X_{s_0} \ge 0$$

and that is a contradiction.

If $Y^i_{t_0} < 0$ for some $i = 1, ..., d$, denote $s_0 = \sup\{0 \le s \le t_0 : Y^i_s > 0\}$, hence $Y^i_{s_0} = 0$ and $Y^i_s \le 0$ in the interval $[s_0, t_0]$. It follows again by (3.4.0.12) that

$$\begin{aligned} Y^i_t &= Y^i_{s_0} + \int_{s_0}^{t} \varphi^i(X_s, Y_s)ds - \int_{s_0}^{t} \psi^i(X_s, Y_s)dW^i_s - \gamma^i \int_{s_0}^{t} Y_s ds \\ &= -\gamma^i \int_{s_0}^{t} Y_s ds \ge 0 \end{aligned}$$

holds for $t \in [s_0, t_0]$ and therefore $Y^i_t = 0$ for arbitrary $t \in [s_o, t_0]$, hence a contradiction.

Because $X_t + \sum\limits_{i=1}^{d} Y^i_t + \sum\limits_{i=1}^{d} \int_0^t \gamma^i Y_s ds = n_0$ and $\sum\limits_{i=1}^{d} \int_0^t \gamma^i Y_s ds \ge 0$, the proof is complete. □

The following theorem presents conditions which guarantees that a solution (X, Y) is absorbed by the barrier $\{x = 0\}$ and has limits at infinity.

Theorem 3.6 *Assume (3.4.0.11) and (3.4.0.12), then X_t is a nonnegative $\mathcal{F}_t$-supermartingale and outside a P-null set the limits*

$$X_\infty = \lim_{t\to\infty} X_t, \quad Y^i_\infty = \lim_{t\to\infty} Y^i_t$$

exist and $Y^i_\infty = 0$ a.s. for all $i = 1, ..., d$.

Moreover,

$$\tau_X < \infty \Rightarrow X_t = 0 \quad \forall t \ge \tau_X \quad a.s.$$

Proof. It follows by (3.4.0.11) and Lemma 3.5 that

$$x_0 + \sum_{i=1}^{d} \int_0^t \psi^i(X_s, Y_s)dW^i_s = X_t + \sum_{i=1}^{d} \int_0^t \varphi^i(X_s, Y_s)ds$$

is a nonnegative martingale, hence X_t is a nonnegative supermartingale. These processes are known to have an integrable limits X_∞ and to be absorbed by $x = 0$. Let $i = 1, ..., d$, then by Lemma 3.5 we get $\gamma_i \int_0^\infty Y^i_s ds \le n_0$ and $Y^i_s \ge 0$, therefore $Y^i_\infty = 0$ a.s. □

Lemma 3.7 *Assume (3.4.0.11) and (3.4.0.12), then outside P-null set*

$$\tau_Y^i < \infty \Rightarrow \tau_Y^i \leq \tau_X$$

holds for all $i = 1, \cdots, d$.

Proof. Assume $\tau_X < \infty$ and $\tau_Y^i > \tau_X$, then by Theorem 3.6 and (3.4.0.12)

$$Y_t^i = Y_{\tau_X} - \int_{\tau_X}^t \gamma^i Y_s^i ds, \quad \text{a.s. }, \forall t > \tau_X.$$

Hence, Y_t^i is a solution to the equation

$$d\tilde{Y}_t = -\gamma^i \tilde{Y}_t dt, \quad \tilde{Y}_{\tau_X} = Y_{\tau_X},$$

which has a unique solution $\tilde{Y}_t = Y_{\tau_X} \exp\{-\gamma^i(t - \tau_X)\} > 0$, therefore $\tau_Y^i = \infty$ holds almost surely.

□

Now we can prove the following theorem about the existence and uniqueness of the process (X, Y) that solves the equation (3.4.0.10) and is absorbed by the natural barrier.

Theorem 3.8 *Let* $\varphi_i, \psi_i : \mathbb{R}^{d+1} \to \mathbb{R}$ *be locally Lipschitz on* $(0, n_0] \times [0, n_0]^{i-1} \times (0, n_0] \times [0, n_0]^{d-i} \cap B$ *such that* $\varphi_i = 0, \psi_i = 0$ *outside* B *and which satisfies (3.4.0.11) and (3.4.0.12). Then there exists a unique process* $(X, Y) \in [0, n_0]^{d+1}$ *satisfying (3.4.0.14) which solves the equation (3.4.0.10).*

Remark 3.3 *Obviously, the consequence of this theorem is the fact that we have a unique solution to (3.4.0.10) in the time interval* $[0, \tau]$, *where* $\tau = \min\{\tau_X, \tau_Y^1, \ldots, \tau_Y^d\}$.

Proof. Denote $T = \{\tau_B, \tau_Y^1, ..., \tau_Y^d\}$ and

$$\begin{aligned}
\tau^{(1)} &= \inf\{\tau \in T\}, \\
\tau^{(2)} &= \inf\{\tau \in T : \tau > \tau^{(1)}\}, \\
&\vdots \\
\tau^{(d)} &= \inf\{\tau \in T : \tau > \tau^{(d-1)}\}, \\
\tau^{(d+1)} &= \max\{\max\{\tau \in T\}, \tau^{(d)}\}
\end{aligned}$$

the sequence of stopping times $\tau_B, \tau_Y^1, ..., \tau_Y^d$ ordered from the smallest to the largest one.

First, we prove the uniqueness of a solution to (3.4.0.10) in $[0, \tau^{(1)}]$.

Let $n_0 > a_1 > a_2 > ...$ and $\lim_{n\to\infty} a_n = 0$, denote $D_n = [a_n, n_0]^{d+1}$ and $B_n := \{(x, y) \in [0, n_0]^{d+1} : (\widetilde{x}, \widetilde{y}) \in [0, n_0]^{d+1} : |(x, y) - (\widetilde{x}, \widetilde{y})| < 1/n \Rightarrow (\widetilde{x}, \widetilde{y}) \in B\}$.

Further, construct $\varphi_n^i, \psi_n^i : \mathbb{R}^{d+1} \to \mathbb{R}$ Lipschitz and bounded functions such that

$$\varphi_n^i = \varphi^i \text{ and } \psi_n^i = \psi^i \text{ on } (a_n, n_0] \times [0, n_0]^{i-1} \times (a_n, n_0] \times [0, n_0]^{d-i} \cap B_n, \quad \varphi_n^i \geq 0$$
$$\text{and } \varphi_n^i(x, y) = \psi_n^i(x, y) = 0 \quad \forall (x, y) \in \mathbb{R}^{d+1} : x \in (-\infty, 0] \text{ or } y^i \in (-\infty, 0].$$

The equation

$$\begin{aligned} dX_t &= -\sum_{i=1}^{d} \varphi_n^i(X_t, Y_t)dt + \sum_{i=1}^{d} \psi_n^i(X_t, Y_t)dW_t^i, & X_0 &= x_0, \\ dY_t^i &= \varphi_n^i(X_t, Y_t)dt - \psi_n^i(X_t, Y_t)dW_t^i - \gamma^i Y_t^i dt, & Y_0^i &= y_0^i \end{aligned} \tag{3.4.1.1}$$

has a unique strong solution (X^n, Y^n) as the coefficients $\varphi_n^i(x, y), \psi_n^i(x, y)$ and $\gamma^i y$ are Lipschitz of a linear growth. Denote

$$\lambda_n := \inf\{t \geq 0 : (X_t^n, Y_t^n) \notin D_n \cap B_n\}.$$

Obviously, the solution (X^n, Y^n) to (3.4.1.1) coincides with the solution (X, Y) to (3.4.0.10) in $[0, \lambda_n]$. Observe that $\lambda_n < \infty$ a.s. since $Y_\infty^i = 0$ a.s. by Theorem 3.6 and that the strong uniqueness property of equation (3.4.1.1) implies that

$$(X^{n+1}, Y^{n+1}) = (X^n, Y^n) \text{ on } [0, \lambda_n] \text{ and } \lambda_n < \lambda_{n+1}, \ n \in \mathbb{N}$$

holds outside a P-null set N. Put $\lambda = \sup \lambda_n$ and for each $\omega \in \Omega$ define a continuous function

$$(\widetilde{X}^0(\omega), \widetilde{Y}^0(\omega)) : [0, \lambda(\omega)) \to [0, n_0]^{d+1}$$

by

$$(\widetilde{X}^0(\omega), \widetilde{Y}^0(\omega)) = (X^n(\omega), Y^n(\omega)) \text{ on } [0, \lambda_n(\omega)].$$

We shall prove that outside another P-null set,

$$\begin{aligned} &\lambda < \infty \Rightarrow \text{ there exists the limit } (\widetilde{X}_{\lambda^-}^0, \widetilde{Y}_{\lambda^-}^0) \in [0, n_0]^{d+1} \text{ such that} \\ &\widetilde{X}_{\lambda^-}^0 = 0 \text{ or } (\widetilde{X}_{\lambda^-}^0, \widetilde{Y}_{\lambda^-}^0) \in \partial B \text{ or } \widetilde{Y}_{\lambda^-}^{0,i} = 0 \text{ for some } i = 1, ..., d. \end{aligned}$$

The existence of the limits $(\widetilde{X}_{\lambda^-}^0, \widetilde{Y}_{\lambda^-}^0)$ is obvious by continuity of $(\widetilde{X}^0, \widetilde{Y}^0)$. Because either $(\widetilde{X}_{\lambda_n}^0, \widetilde{Y}_{\lambda_n}^0) \in \partial B_n$ or $(\widetilde{X}_{\lambda_n}^0, \widetilde{Y}_{\lambda_n}^0) \in \partial D_n$ and $\lambda_n \nearrow \lambda$, we conclude that for some $i = 1, ..., d$, $\widetilde{Y}_{\lambda^-}^{0,i} = 0$ or $(\widetilde{X}_{\lambda^-}^0, \widetilde{Y}_{\lambda^-}^0) \in \partial B$ or $\widetilde{X}_{\lambda^-}^0 = 0$. Therefore $\lambda = \min\{\tau_X, \tau_Y^1, ..., \tau_Y^d\} = \tau^{(1)}$ and $(\widetilde{X}^0, \widetilde{Y}^0)$ is a unique solution to (3.4.0.10) in $[0, \tau^{(1)}]$.

Now, we prove the existence of a unique solution to (3.4.0.10) in $[\tau^{(1)}, \tau^{(2)}]$.

Let $\tau^{(1)} < \infty$. Denote

$$\begin{aligned} A^X &= \{\tau^{(1)} = \tau_B\}, \\ A^i &= \left\{\omega \in \Omega \setminus A^X : \tau_Y^i(\omega) = \tau^{(1)}(\omega)\right\}, \\ \widetilde{A}^i &= A^i \setminus \left(\bigcup_{j \neq i} A_j\right), \\ \widetilde{A}^{i,j} &= \left(A^i \bigcap A^j\right) \setminus \left(\bigcup_{k \neq i, k \neq j} A_k\right), \\ &\vdots \end{aligned}$$

Let $\omega \in A^X$, then we define $(X, Y)^{A^X}$ by

$$\begin{aligned} (X, Y)^{A^x} &= (\widetilde{X}^0, \widetilde{Y}^0) && \text{in} \quad [0, \tau_B], \\ &= (X_{\tau_B}, Y^i_{\tau_B} e^{-\gamma_i (t - \tau_B)}) && \text{in} \quad (\tau_B, \infty). \end{aligned}$$

$(X, Y)^{A^X}$ satisfies (3.4.0.14) and solves (3.4.0.10) in $[0, \infty)$ for almost every $\omega \in A^X$.

Let $\omega \in \widetilde{A}^d$, choose $m \in \mathbb{N}$ and denote

$$C^{d,m} = \left\{\omega \in \widetilde{A}^d : (X_\lambda, Y^1_\lambda, \ldots, Y^{d-1}_\lambda, 0) \in [a_n, n_0]^d \times \mathbb{R} \cap B_m\right\}.$$

Define a random variable

$$\begin{aligned} S = (S_1, ..., S_d) &= (X, Y_1, ..., Y_{d-1})_\lambda && \text{in} \quad C^{d,m}, \\ &= 0 && \text{in} \quad (C^{d,m})^c, \end{aligned}$$

and Lipschitz, bounded functions $\varphi_n^{d,i}$ and $\psi_n^{d,i}$ such that

$$\varphi_n^{d,i}(x, y_1, ..., y_{d-1}) = \varphi_n^i(x, y_1, ..., y_{d-1}, 0), \ \psi_n^{d,i}(x, y_1, ..., y_{d-1}) = \psi_n^i(x, y_1, ..., y_{d-1}, 0)$$

for $i = 1, \ldots, d-1$.

Let $n > m$ and define

$$\begin{aligned}
X^n_{\tau^{(1)}+h} =& S_1 - \sum_{i=1}^{d-1} \int_{\tau^{(1)}}^{\tau^{(1)}+h} \varphi_n^{d,i}(X_t^n, Y_t^{n,1}, ..., Y_t^{n,d-1})dt \\
&+ \sum_{i=1}^{d} \int_{\tau^{(1)}}^{\tau^{(1)}+h} \psi_n^{d,i}(X_t^n, Y_t^{n,1}, ..., Y_t^{n,d-1})dW_t^i \\
Y^{n,1}_{\tau^{(1)}+h} =& S_2 + \int_{\tau^{(1)}}^{\tau^{(1)}+h} \varphi_n^{d,1}(X_t^n, Y_t^{n,1}, ..., Y_t^{n,d-1}) \\
&- \gamma^1 Y_t^{n,1}dt - \int_{\tau^{(1)}}^{\tau^{(1)}+h} \psi_n^{d,1}(X_t^n, Y_t^{n,1}, ..., Y_t^{n,d-1})dW_t^1 \\
&\vdots \\
Y^{n,d-1}_{\tau^{(1)}+h} =& S_d + \int_{\tau^{(1)}}^{\tau^{(1)}+h} \varphi_n^{d,d-1}(X_t^n, Y_t^{n,1}, ..., Y_t^{n,d-1}) \\
&- \gamma^{d-1} Y_t^{n,d-1}dt - \int_{\tau^{(1)}}^{\tau^{(1)}+h} \psi_n^{d,d-1}(X_t^n, Y_t^{n,1}, ..., Y_t^{n,d-1})dW_t^{d-1}.
\end{aligned}$$

Then, $(X^n_{\tau^{(1)}+t}, Y^{n,1}_{\tau^{(1)}+t}, ..., Y^{n,d-1}_{\tau^{(1)}+t})$ must coincide a.s. with the strong unique solution $(\widehat{X}_t^n, \widehat{Y}_t^{n,1}, ..., \widehat{Y}_t^{n,d-1})$ to

$$\begin{aligned}
dX_t &= -\sum_{i=1}^{d-1} \varphi_n^{d,i}(X_t, Y_t^1, ..., Y_t^{d-1})dt + \sum_{i=1}^{d-1} \psi_n^{d,i}(X_t, Y_t^1, ..., Y_t^{d-1})d\widehat{W}_t^i, \\
dY_t^1 &= \varphi_n^{d,1}(X_t, Y_t^1, ..., Y_t^{d-1})dt - \psi_n^{d,1}(X_t, Y_t^1, ..., Y_t^{d-1})d\widehat{W}_t^i - \gamma^1 Y_t^1 dt, \\
&\vdots \\
dY_t^{d-1} &= \varphi_n^{d,d-1}(X_t, Y_t^1, ..., Y_t^{d-1})dt - \psi_n^{d,d-1}(X_t, Y_t^1, ..., Y_t^{d-1})d\widehat{W}_t^i - \gamma^{d-1} Y_t^{d-1} dt,
\end{aligned} \tag{3.4.1.2}$$

with initial conditions $X_0 = S_1$, $Y_0^1 = S_2, \ldots$, $Y_0^{d-1} = S_d$, where $\widehat{W}_t = W_{\tau^{(1)}+t} - W_{\tau^{(1)}}$, therefore $(X^n, Y^{n,1}, ..., Y^{n,d-1})$ is uniquely determined in $[\tau^{(1)}, \infty)$.

In the same way as above, we can define the process $(\widetilde{X}_t, \widetilde{Y}_t^1, ..., \widetilde{Y}_t^{d-1})$ in $[\tau^{(1)}, \lambda^1)$, so that it coincides with process $(X_t^n, Y_t^{n,1}, ..., Y_t^{n,d-1})$ in time interval $[\tau^{(1)}, \lambda_n^1]$ and has a limit $(\widetilde{X}, \widetilde{Y}^1, ..., \widetilde{Y}^{d-1})_{\lambda^1_-}$. The stopping times λ_n^1 and λ^1 are defined by

$$\begin{aligned}
&\lambda_n^1 := \inf\{t \geq \tau^{(1)} : (X_t^n, Y_t^{n,1}, ..., Y^{n,d-1}, 0) \notin [a_n, n_0]^d \times \mathbb{R} \cap B_n\}, \\
&\lambda^1 := \sup \lambda_n^1.
\end{aligned}$$

Denote

$$\begin{aligned}(X,Y)^m(\omega) &= (\widetilde{X}^0,\widetilde{Y}^0)_t(\omega) && \text{in} \quad [0,\tau^{(1)}]\\ &= (\widetilde{X},\widetilde{Y}^1,...,\widetilde{Y}^{d-1},0)_t(\omega) && \text{in} \quad [\tau^{(1)},\lambda^1],\end{aligned}$$

$\omega \in C^{d,m}$, then $(X,Y)^m$ solves (3.4.0.10) and satisfies (3.4.0.14) for almost every $\omega \in C^{d,m}$ in $[0,\lambda^1]$. Let $l > m$, then $(X,Y)^m(\omega) = (X,Y)^l(\omega)$ for almost every $\omega \in C^{d,m}$ and moreover $\lim\limits_{m\to\infty} P(C^{d,m}) = P(\widetilde{A}^d)$, hence there exists a process $(X,Y)^{\widetilde{A}^d}$ such that $(X,Y)^{\widetilde{A}^d} = (X,Y)^m \ \forall\omega \in C^{d,m}$ and $\forall m \in \mathbb{N}$, therefore $(X,Y)^{\widetilde{A}^d}$ solves (3.4.0.10) and satisfies (3.4.0.14) for almost every $\omega \in \widetilde{A}^d$ on $[0,\lambda^1]$.

Use the same procedure to construct the processes $(X,Y)^{\widetilde{A}^i}$, $(X,Y)^{\widetilde{A}^{i,j}}$,..., and define a process $(\widetilde{X}^1,\widetilde{Y}^1)$ by

$$\begin{aligned}(\widetilde{X}^1,\widetilde{Y}^1)(\omega) &= (X,Y)^{A^X}(\omega) && \omega \in A^X,\\ &= (X,Y)^{\widetilde{A}^i}(\omega) && \omega \in \widetilde{A}^i,\\ &= (X,Y)^{\widetilde{A}^{i,j}}(\omega) && \omega \in \widetilde{A}^{i,j},\\ &\vdots\end{aligned}$$

$(\widetilde{X}^1,\widetilde{Y}^1)$ is a solution to (3.4.0.10) in $[0,\lambda^1]$ which satisfies (3.4.0.14). The uniqueness of such a process follows from the construction. As before, it is possible to show that $\lambda^1 = \tau^{(2)}$.

If $P\{\lambda^1 < \infty\} > 0$, use the same procedure again to construct the process $(\widetilde{X}^2,\widetilde{Y}^2)$ which solves the equation (3.4.0.10) on $[0,\lambda^2)$ and satisfies (3.4.0.14). Repeating the same procedure, we get a process (X,Y) which solves (3.4.0.10) in $[0,\infty)$ and satisfies (3.4.0.14).

□

The last theorem presents conditions which guarantee that each solution (X,Y) to (3.4.0.10) is absorbed by the barrier $\{y_i = 0\}$. It means, that after the first time when the i-th pathogen strain is removed, no one can be infected by this pathogen and the pathogen can not be restored.

Theorem 3.9 *Let φ^i and ψ^i $i = 1,...,d$ satisfy (3.4.0.11), (3.4.0.12) and suppose that there exists $\varepsilon > 0$ such that $\varphi^i(x,y) \le \gamma^i y^i \ \forall (x,y) \in [0,n_0]^{d+1}$ such that $y^i \in [0,\varepsilon]$. Then any arbitrary solution (X,Y) to (3.4.0.10) satisfies that $Y_t^i = 0$ for all $t \ge \tau_Y^i$ almost surely.*

Proof. Note that

$$M_t^i := -I_{[\tau_Y^i<\infty]} \int_{\tau_Y}^{t+\tau_Y} \psi^i(X_s,Y_s)dW_s^i$$

is a continuous $\mathcal{F}_{\tau_Y^i+t}$-local martingale and

$$Y^i_{t+\tau^i_Y} = I_{[\tau^i_Y<\infty]} \int_{\tau^i_Y}^{t+\tau^i_Y} \varphi^i(X_s, Y_s) - \gamma^i Y^i_s ds + M^i_t, \quad t \geq 0,$$

a continuous $\mathcal{F}_{\tau_Y^i+t}$-semimartingale. Denoting

$$\tau^i_\delta := \inf\{t \geq 0 : Y^i_{t+\tau^i_Y} \geq \delta\}, \quad \delta > 0,$$

we define an $\mathcal{F}_{\tau_Y^i+t}$-stopping time and by $M^i_{t\wedge\tau^i_\delta}$ an $\mathcal{F}_{\tau_Y^i+t}$-local martingale. It follows that for arbitrary $0 < \delta \leq \varepsilon$

$$M^i_{t\wedge\tau^i_\delta} = Y^i_{t\wedge\tau^i_\delta+\tau^i_Y} - I_{[\tau^i_Y<\infty]} \int_{\tau^i_Y}^{t\wedge\tau^i_\delta+\tau^i_Y} \varphi^i(X_s, Y_s) - \gamma^i Y^i_s ds \geq 0$$

is a nonnegative $\mathcal{F}_{\tau_Y^i+t}$-local martingale, hence a nonnegative $\mathcal{F}_{\tau_Y^i+t}$-supermartingale. Therefore

$$Y^i_{t\wedge\tau^i_\delta+\tau^i_Y} = Y^i_{\tau^i_Y} = 0, \quad t \geq 0,$$

holds almost surely for arbitrary $0 < \delta \leq \varepsilon$. Especially, the implication

$$\tau^i_Y < \infty, \quad \tau_\delta < \infty \quad \Rightarrow \quad Y^i_{\tau^i_\delta+\tau^i_Y} = 0$$

is true outside a P-null set. It follows that $P[\tau^i_Y < \infty, \tau^i_\delta < \infty] = 0$ for all $0 < \delta \leq \varepsilon$, hence the process Y^i is absorbed by $\{y^i = 0\}$.

□

3.4.2 Examples

In this section, we illustrate different behavior of a solution to (3.4.0.10) in dependence on choice of φ^i and ψ^i and the applications of the results from the previous section.

For simplicity, we choose $B = (0, \infty) \times \mathbb{R}^d$, hence $\tau_B = \tau_X$ and the process (X, Y) is absorbed by the natural barrier if and only if it is absorbed by the barrier $\{x = 0\} \cup \{y^1 = 0\} \cup ... \cup \{y^d = 0\}$. In Example 3.2, Example 3.3 and Example 3.4, we choose $d = 1$, therefore for simplicity of notation, we write ϑ, ψ, γ, Y and y_0 instead of ϑ^1, ψ^1, γ^1, Y^1 and y^1_0.

Example 3.2 *Consider the deterministic equation*

$$dX_t = -\gamma Y_t^+ I_{[X_t>0]} dt, \quad \mathrm{d}Y_t = \gamma Y_t^+ I_{[X_t>0]} dt - \gamma Y_t dt, \tag{3.4.2.1}$$

with $x_0 = y_0 = \gamma = 1$. This is the equation (3.4.0.10) with $\varphi(x,y) = \gamma y^+ I_{(0,\infty)}(x)$ and $\psi(x,y) = 0$, i.e. φ and ψ satisfy (3.4.0.11) and (3.4.0.12). A solution is found easily as

$$X_t = (1-t)^+, \quad Y_t = e^{-(t-1)^+}, \tag{3.4.2.2}$$

with $\tau_X = 1$ and $\tau_Y = +\infty$. Because $\varphi(x,y) \leq \gamma y$ for all $x \in [0, n_0]$ it follows by Lemma 3.5 and Theorem 3.9 that any solution to (3.4.2.1) is a nonnegative process absorbed by natural barrier. Theorem 3.8 further yields that (3.4.2.2) is a unique solution to (3.4.2.1) as φ and ψ are locally Lipschitz maps on $(0, n_0]^2$.

Example 3.3 *Consider the equation*

$$dX_t = I_{[X_t>0, Y_t>0]} dW_t, \quad dY_t = -\gamma Y dt - I_{[X_t>0, Y_t>0]} dW_t, \tag{3.4.2.3}$$

with $x_0 > y_0 > 0$, i.e. $\varphi(x,y) = 0$ and $\psi(x,y) = I_{(0,\infty)^2}(x,y)$. Using Theorem 3.8 together with Theorem 3.9 we get that equation (3.4.2.3) has a unique solution which is absorbed by the natural barrier $\{x = 0\} \cup \{y = 0\}$.

Because $X_t = x_0 + W_{t\wedge\tau}$ and $Y_t = y_0 - \gamma \int_0^t Y_s \,\mathrm{d}s - W_{t\wedge\tau} \leq y_0 - W_{t\wedge\tau}$ almost surely then $\tau_X = \inf\{\tau_Y \geq t \geq 0 : W_t = -x_0\}$ and $\tau \leq \tau_{(-x_0,y_0)}$ where $\tau_{(-x_0,y_0)} := \inf\{t \geq 0 : W_t \notin (-x_0, y_0)\}$, hence $\tau < \infty$ almost surely (see Proposition 7.3, p. 14, in [11]).

It remains to prove that $P[\tau_X < \infty] > 0$ and $P[\tau_Y < \infty] > 0$. First define $\tau_{\check{y}} := \inf\{t \geq 0 : W_t = y_0 - \gamma n_0 t\}$ and note that $\tau_Y \geq \tau_{\check{y}}$. Obviously, $\tau_X \wedge \tau_{\check{y}} \leq \frac{1}{\gamma}$, hence (see p. 295 in [3])

$$\begin{aligned} P[\tau_X < \infty] &\geq P\left[\tau_X \leq \frac{1}{\gamma}\right] \geq P\left[\tau_{\check{y}} > \frac{1}{\gamma}\right] \\ &= \int_{\frac{1}{\gamma}}^{\infty} \frac{y_0}{\sqrt{2\pi} t^{\frac{3}{2}}} \exp\left\{-\frac{(y_0 - \gamma n_0 t)^2}{2t}\right\} \mathrm{d}t > 0 \end{aligned}$$

holds. On the other hand, if we denote $\tau_{y_0} = \inf\{t \geq 0 : W_t = y_0\}$, then $P[\tau_Y < \tau_X] \geq P[\tau_{y_0} \leq \tau_X] = \frac{x_0}{n_0} > 0$ (see again Proposition 7.3, p. 14, in [11]), therefore $P[\tau_Y < \infty] \geq \frac{x_0}{n_0} > 0$.

Example 3.4 *In Example 5.6 in [18], Štěpán compared two stochastic versions of Kermack-McKendrick model, where the diffusion coefficient is equal to the trend coefficient (the first model) or the diffusion coefficient is chosen as the square root of the trend coefficient (the second model). The models are given by*

$$\begin{aligned} dX_t &= -\beta X_t Y_t dt + \beta X_t Y_t dW_t, \\ dY_t &= +\beta X_t Y_t dt - \gamma Y_t - \beta X_t Y_t dW_t, \end{aligned} \tag{3.4.2.4}$$

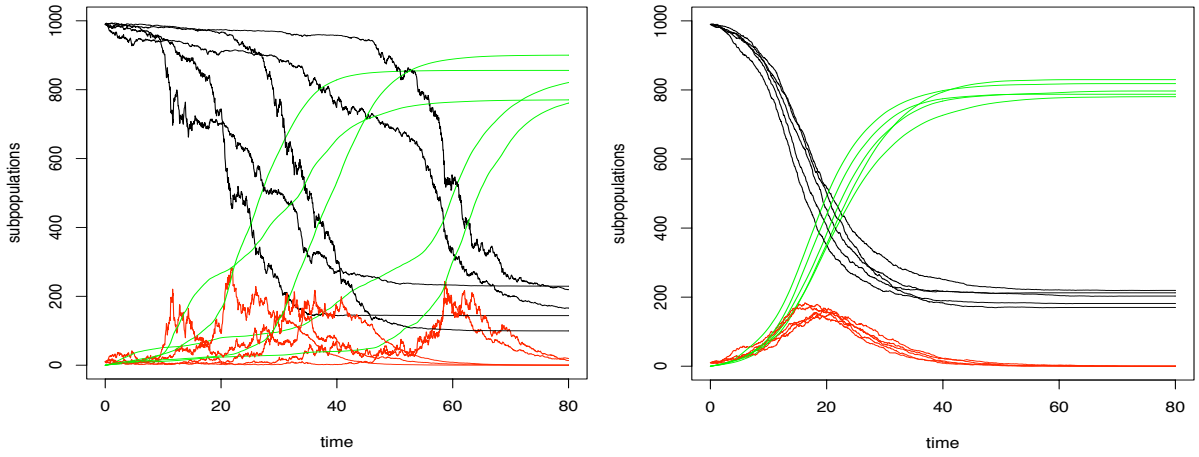

Figure 3.7:
Five simulation of $(X_t, Y_t, \gamma \int_0^t Y_s ds)$, where (X_t, Y_t) is a solution to (3.4.2.4) (left) and (3.4.2.5) (right). The black line is used for susceptibles, the red line for infectives and the green one for removals.

and

$$\begin{aligned} dX_t &= -\beta X_t^+ Y_t^+ dt + \sqrt{\beta X_t^+ Y_t^+} dW_t \\ dY_t &= +\beta X_t^+ Y_t^+ dt - \gamma Y_t - \sqrt{\beta X_t^+ Y_t^+} dW_t. \end{aligned} \tag{3.4.2.5}$$

The model given by (3.4.2.5) was presented in more general form in Section 3.2. Both of these models may be called "a natural stochastic version of Kermack-McKendrick model", but while for the equation (3.4.2.4) we get $\tau_X = \tau_Y = \infty$ a.s., for the equation (3.4.2.5), we know only $P[\tau_X = \infty] > 0$. We can also see in Figure 3.7, that the choice of diffusion coefficient in (3.4.2.5) does not change the behavior of the model dramatically, on the other hand, the choice in (3.4.2.4) provides much more rugged paths.

Example 3.5 *Consider the equation*

$$\begin{aligned} dX_t &= -\beta X_t^+ Y_t^{1,+} dt + Y_t^{1,+} I_{[X_t>0]} dW_t^1 + I_{[X_t>0, Y_t^2>0]} dW_t^2, & x_0 > 0, \\ dY_t^1 &= \beta X_t^+ Y_t^{1,+} dt - \gamma^1 Y_t^1 + Y_t^{1,+} I_{[X_t>0]} dW_t^1, & y_0^1 > 0, \\ dY_t^2 &= -\gamma^2 Y_t^2 dt - I_{[X_t>0, Y_t^2>0]} dW_t^2, & y_0^2 > 0, \end{aligned} \tag{3.4.2.6}$$

with $\beta > 0$, i.e. $\varphi^1(x, y^1, y^2) = \beta x y^1 I_{[x>0, y^1>0]}$, $\psi^1(x, y^1, y^2) = y^1 I_{[x>0, y^1>0]}$, $\varphi^2(x, y^1, y^2) = 0$ and $\psi^2(x, y^1, y^2) = I_{[x>0, y^2>0]}$. Using Theorem 3.8, we get that the equation (3.4.2.6) has a unique solution which is absorbed by the natural barrier. Let (X_t, Y_t^1, Y_t^2) is a solution to (3.4.2.6), then

$$Y_t^1 = y_0^1 + \int_0^t (\beta X_s - \gamma^1) Y_s^1 ds + \int_0^t Y_s^1 dW_s^1$$

for all $t \in [0, \tau_X \wedge \tau_Y^1]$*, and therefore by Itô formula*

$$Y_t^1 = y_0^1 \exp\left\{\int_0^t \beta X_s - \gamma^1 - \frac{1}{2} ds - W_t^1\right\} > 0, \quad \forall t \in [0, \tau_X \wedge \tau_Y^1],$$

which together with Lemma 3.7 imply $\tau_Y^1 = \infty$ *almost surely. Using Theorem 3.9 for* Y_t^2*, we get* $Y_t^2 = 0$ *for all* $t \geq \tau_Y^2$ *a.s and by Lemma 3.5,* $X_t = 0$ *for all* $t \geq \tau_X$*, hence* (X_t, Y_t^1, Y_t^2) *is absorbed by the natural barrier, therefore the equation (3.4.2.6) has a unique solution. If we denote* $\tau_{W^2, y_0^2} := \inf\{t \geq 0 : W_t^2 = y_0^2\}$*, then* $\min\{\tau_X, \tau_Y^2\} \leq \tau_{W^2, y_0^2} < \infty$ *almost surely.*

More informations about this model with $d = 1$ and $B = (0, \infty) \times \mathbb{R}$ including further interesting examples can be found in [18].

Chapter 4

Conclusion

In this work, we presented the differential equation which describes Kermack-McKendrick model with vaccination, we studied properties of the solution to this DE and showed a formula for computing the number of removals at infinity, and the way how to find the maximum of infectives. In the numerical part, we compared different strategies of vaccination and determined the optimal vaccination strategy for a given penalization function.

In the second part, four stochastic models driven by stochastic differential equation were presented.

The first one is a model with migration for which we suggested such a generalization which allowed us to model epidemics with nonzero incubation time, and proved the theorem about the existence and uniqueness of a solution to the SDE associated with the model.

We suggested three stochastic versions of a model with vaccination, and discussed their respective merits. Their behavior is compared by means of a numerical study, a procedure to exhibit the optimal vaccination strategy is proposed.

We also studied the SDE which provided a model with multiple pathogens and prove the theorem about the existence and uniqueness of the solution to this equation.

The last part introduced the SDE for modeling the general epidemics. Its properties are studied, the conditions for the coefficients of the equation are formulated to ensure the natural behavior of epidemics. We presented the sufficient conditions for having an absorbed solution and finally the theory presented is illustrated by several examples.

The thesis provides a complex frame for the epidemics modeling using the differential and stochastic differential equations, including vaccination, migration of population and epidemics with multiple pathogens. Nevertheless, there remains a few unanswered questions.

Therefore, we conclude our study by a list of open problems:

- We presented a numerical search for the optimal vaccination strategy, an analytical treatment of the problem is still missing.
- As far as the stochastic models are concerned we still have the problem how to establish Z_∞, $E[X_t]$, $E[Y_t]$ and $E[Z_t]$ for a given time $t > 0$.
- The final interesting and important problem is to determine the existence and uniqueness of a solution to the partial differential equation (3.4.0.16) and to solve the equation.

Bibliography

[1] Allen L.J.S., Kirupaharan N. (2005) *Asymptotic Dynamics of Deterministic and Stochastic Epidemic Model with Multiple Pathogens*. International Journal of Numerical Analysis and Modeling **3(2)**, 329-344.

[2] Amann H. (1990) *Ordinary Differential Equations: An Introduction to Nonlinear Analysis*. Walter de Gruyter, Berlin.

[3] Borodin A.N., Salminen P. (2002) *Handbook of Brownian Motion-Facts and Formulae*. Birkhäuser Verlag, Basel.

[4] Daley D.J., Gani J. (1999) *Epidemic Modelling; An Introduction*. Cambridge University Press, Cambridge.

[5] Dupačová J., Hurt J., Štěpán J. (2002) *Stochastic modeling in economics and finance*. Kluwer Academic Publishers, Dordrecht.

[6] Harville D.A. (1997) *Matrix Algebra from a Statistician's perspective*. Springer-Verlag, New York.

[7] Kallenberg O. (2002) *Foundations of modern probability, second edition*. Springer-Verlag, New York.

[8] Kannan D., Lakshmikantham V. (2002) *Handbook of Stochastic analysis and applications*. Marcel Dekker, Inc., New York.

[9] Kermack W.O., McKendrick A.G. (1927) *A contribution to the mathematical theory of epidemics*. Proc. Roy. Soc. London A **115**, 700-721.

[10] Øksendal B. (2007) *Stochastic Differential Equations: An Introduction with Applications, sixth edition*. Springer-Verlag, Berlin-Heilderberg.

[11] Rogers L.C.G., Williams D. (1994) *Diffusions, Markov processes and martingales, volume 1 - Foundations*. Cambridge University Press, Cambridge.

[12] Rogers L.C.G., Williams D. (1994) *Diffusions, Markov processes and martingales, volume 2 - Itô Calculus*. Cambridge University Press, Cambridge.

[13] Staněk J. (2006) *Stochastická verze klasického modelu vývoje epidemie*. Proceedings of ROBUST 06 conference (eds. Antoch J., Dohnal G.), JČMF, 297-303.

[14] Staněk J. (2006) *Stochastic Epidemic models*. Proceedings of WDS'06 conference (eds. Šafránková J., Pavlů J.), Matfyzpress, 82-87.

[15] Staněk J. (2008) *Kermack-McKendrick Epidemics Vaccinated*. Kybernetika **44**, 705-714.

[16] Staněk J. (2009) *Stochastický model vývoje epidemie s vakcinací*. Proceedings of ROBUST 08 conference (eds. Antoch J., Dohnal G.), JČMF, accepted.

[17] Štěpán J., Hlubinka D. (2007) *Kermack-McKendrick epidemics model revisited*. Kybernetika **43**, 395-414.

[18] Štěpán J., Staněk J. (2009) *Absorption in Stochastic Epidemics*. Kybernetika **45**, accepted.

[19] Štěpán J. *Private communication.*