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STOCHASTIC CALCULUS AND ITS APPLICATIONS IN BIOMEDICAL PRACTICE

STOCHASTICKÝ KALKULUS A JEHO APLIKACE V BIOMEDICÍNSKÉ PRAXI

Short version of Ph.D. thesis

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Stochastic process, stochastic differential equation, Brownian motion, Wiener process, matrix equations.

Klíčová slova

Náhodný proces, stochastická diferenciální rovnice, Brownův pohyb, Wienerův proces, maticové rovnice.

Contents

1 Introduction

Theory of stochastic differential equations is used to describe the physical and technical phenomena. We have chosen this topic because randomness is actual issue for the last years. The solution of the stochastic model is a random process. The aim of the study of random phenomena is the construction of a suitable model to understand its working. Knowledge of the model provides to predict the future behavior of the system and making it possible to control and optimize the operation of the corresponding system.

The submitted thesis deals with finding solutions of stochastic differential equations and systems of stochastic differential equations, and determining their stability. The main part of the thesis is based on the theory Stochastic Differential Equations - an introduction with applications by B. Ôksendal [36]. B. Maslowski discusses stochastic equations and stochastic methods in partial differential equations [32]. The book Stochastic bio mathematical models: with applications to neuronal modeling by S. Ditlevsen at al. [9] concerns with noise in living systems. Fundamental knowledge of probability and mathematical statistics is in textbook by M. Navara [35]. The book by X. Mao [28] describes the basic principles and applications of various types of stochastic systems. The book by R. Z. Khasminskii [25] deals with the stochastic stability of differential equations, exact formulas for the Lyapunov exponent, the criteria for the moment and almost sure stability, and for the existence of solutions of stochastic differential equations have been widely used. There are derived conditions for the stability of the mean zero solution stochastic equations with Brownian motion. There is used the Lyapunov method to determine the stability of the solution of the stochastic system. This method for analyzing the behavior of stochastic differential equations provides useful information for the study of stability and its properties for special types of stochastic dynamical systems, allows to specify conditions for the existence of stationary solutions of stochastic differential equations and related problems.

Main results determined the solution and the stability of solutions of differential systems of order 3 and 4. This basic is extended by the stochastic process and there is looked for the solution and the stability of stochastic differential equations and stochastic differential systems (matrix equations). Theoretical results are illustrated on the model of medical practice.

2 Current State

The first English-language text to offer detailed coverage of boundless, stability, and asymptotic behavior of linear and nonlinear differential equations was issued in the 50s of 20th century by R. Bellman [3].

The basic probability theory is introduced in the work Probability through problems [4] of authors M. Capinski and T. J. Zastawniak and in [10] by R. Durrett. Theory of matrices, their applications is described in the following literature [33]- [34], etc.

In the paper [2] authors J. Baštinec and I. Dzahalladova investigate sufficient conditions for stability of solutions of systems of nonlinear differential equations with right-hand side depending on Markov's process and the basic role in proof have Lyapunov functions.

Stochastic differential equations and applications is presented in [22] by A. Friedman, in [23] by J. I. Gikhman and A. V. Skorokhod, in [24] by D. V. Gusak, in [26]- [27] by E. Kolářová and L. Brančík, in [37] by E. Renshaw and in [38] by M. Růžičková at al.

I. Dzhalladova at al. deal with stability for solutions of stochastic systems and stochastic systems with delay in papers [12]- [15]. I. Dzhalladova analyzes optimization of stochastic systems in [11].

J. Diblík at al. investigate in papers [5]- [8] stability and estimation of solutions of differential systems and systems with delay.

2.1 Probability Spaces, Random Variables

Definition 2.1. [36] If Ω is a given set, then a σ-algebra $\mathcal{F}$ on Ω is a family $\mathcal{F}$ of subsets of Ω with the following properties:

(i) $\emptyset \in \mathcal{F}$

(ii) $F \in \mathcal{F} \Rightarrow F^C \in \mathcal{F}$, where $F^C = \Omega \setminus \mathcal{F}$ is the complement of $\mathcal{F}$ in Ω

(iii) $A_1, A_2, \dots \in \mathcal{F} \Rightarrow A := \bigcup\limits_{i=1}^{\infty} A_i \in \mathcal{F}$.

The pair $(\Omega, \mathcal{F})$ is called a measurable space.

Definition 2.2. [36] A probability measure P on a measurable space $(\Omega, \mathcal{F})$ is a function $P : \mathcal{F} \longrightarrow [0, 1]$ such that

(i) $P(\emptyset) = 0, P(\Omega) = 1$.

(ii) if $A_1, A_2, \dots \in \mathcal{F}$ and $\{A_i\}_{i=1}^{\infty}$ is disjoint (i.e. $A_i \cap A_j = \emptyset$ if $i \neq j$) then

$$P\left(\bigcup_{i=1}^{\infty} A_i\right) = \sum_{i=1}^{\infty} P(A_i).$$

The triple $(\Omega, \mathcal{F}, P)$ is called a probability space.

2.2 Brownian Motion

One of the simplest continuous-time stochastic processes is Brownian motion. This was first observed by botanist Robert Brown. He observed that pollen grains suspended in liquid performed an irregular motion. The motion was later explained by the random collisions with the molecules of the liquid. The motion was describe mathematically by Norbert Wiener who used the concept of a stochastic process $W_t(\omega)$, interpreted as the position at time t of the pollen grain ω. Thus, this process is also called Wiener process.

Definition 2.3. The stochastic process B_t is called Brownian motion (or Wiener process) if the process has some basic properties:

(i) $B_0 = 0$

(ii) $B_t - B_s$ has the distribution $N(0, t - s)$ for $t \geq s \geq 0$

(iii) B_t has independent increments, i.e. $B_{t_1},\ B_{t_2} - B_{t_1},\ \ldots,\ B_{t_k} - B_{t_{k-1}}$ are independent for all $0 \leq t_1 < t_2 \cdots < t_k$.

Remark. It holds that

(i) $E\left[B_t\right] = 0$ for $t > 0$.

(ii) $E\left[B_t^2\right] = t$.

Theorem 2.1. *Let B_t be Brownian motion. Then*

$$E\left[B_t B_s\right] = min\left\{t, s\right\}\ \ for\ t \geq 0,\ s \geq 0.$$

Proof. [36], pp. 14.

Definition 2.4. Let $B_i(t), t = 1, 2, \ldots, m$, be a stochastic process. Then $B(t) = (B_1(t), ..., B_m(t))$ denote m-dimensional Brownian motion.

2.3 Itô Formula

Theorem 2.2. *Let X_t be an Itô process given by*

$$dX_t = udt + vdB_t.$$

Let $g(t, x) \in C^2([0, \infty) \times \mathbb{R})$(i.e. g is twice continuously differentiable on $[0, \infty) \times \mathbb{R}$). Then $Y_t = g(t, X_t)$ is again an Itô process, and

$$dY_t = \frac{\partial g}{\partial t}(t, X_t)dt + \frac{\partial g}{\partial x}(t, X_t)dX_t + \frac{1}{2}\frac{\partial^2 g}{\partial^2 x^2}(t, X_t)(dX_t)^2,$$

where $(dX_t)^2 = (dXt) \cdot (dXt)$ is computed according to the rules $dBt \cdot dBt = dt$ and $dt \cdot dt = dt \cdot dBt = dBt \cdot dt = 0$.

Proof. [36], pp. 46.

Theorem 2.3. ***(The Multi-dimensional Itô formula)***
Let

$$dX_t = udt + vdB_t$$

be an n-dimensional Itô process. Let $g(t,x) = (g_1(t,x),\ldots,g_p(t,x))$ *be a* C^2 *map from* $[0,\infty)\times\mathbb{R}^n$ *into* $\mathbb{R}^p$. *Then the process* $Y_t = g(t,X_t)$ *is again an Itô process, whose component number* k, Y_k *is given by*

$$dY_k = \frac{\partial g_k}{\partial t}(t,X)dt + \sum_i \frac{\partial g_k}{\partial x_i}(t,X)dX_i + \frac{1}{2}\sum_{i,j}\frac{\partial^2 g_k}{\partial x_i \partial x_j}(t,X)dX_i dX_j,$$

where $dB_i dB_j = \delta_{i,j}dt, dB_i dt = dtdB_i = 0$, *where* $\delta_{i,j}$ *is the Kronecker delta*

$$\delta_{i,j} = \begin{cases} 1 & i=j, \\ 0 & i \neq j. \end{cases}$$

2.4 Stochastic Differential Equations

Definition 2.5. Let $W_t = (W_1(t),...,W_m(t))$ be m-dimensional Wiener process and $b:[0,T]\times\mathbb{R}^n\to\mathbb{R}^n$, $\sigma:[0,T]\times\mathbb{R}^n\to\mathbb{R}^{n\times m}$ be measurable functions. Then the process $X_t = (X_1(t),...,X_m(t))$, $t\in[0,T]$ is the solution of the stochastic differential equation

$$\frac{\mathrm{d}X_t}{\mathrm{d}t} = b(t,X_t) + \sigma(t,X_t)W_t, \tag{1}$$

$b(t,X_t)\in\mathbb{R},\ \sigma(t,X_t)W_t\in\mathbb{R}$, where W_t is 1-dimensional white noise. Equation (1) can be written as the differential form

$$dX_t = b(t,X_t)\mathrm{d}t + \sigma(t,X_t)\mathrm{d}B_t. \tag{2}$$

We formally replace the white noise W_t by $\frac{\mathrm{d}B_t}{\mathrm{d}t}$ and multiply by $\mathrm{d}t$. After the integration of equation (2) we give the stochastic integral equation

$$X_t = X_0 + \int_0^t b(s,X_s)ds + \int_0^t \sigma(s,X_s)dB_s. \tag{3}$$

2.4.1 Existence and Uniqueness of Solution

Definition 2.6. Let $T>0$ and $b:[0,T]\times\mathbb{R}^n\to\mathbb{R}^n$, $\sigma:[0,T]\times\mathbb{R}^n\to\mathbb{R}^{n\times m}$ be measurable functions satisfying next conditions:

(i) Exist some constant C such that $\mid b(t,x)\mid + \mid \sigma(t,x)\mid \leq C(1+\mid x\mid)$ for $x\in\mathbb{R}^n$, $t\in[0,T]$.

(ii) Exist some constant D such that $\mid b(t,x)-b(t,y)\mid + \mid\sigma(t,x)-\sigma(t,y)\mid\leq D\mid x-y\mid)$ for $x,y\in\mathbb{R}^n, t\in[0,T]$.

(iii) Let Z be a random variable which is independent of the σ-algebra $\mathcal{F}_\infty^m$ and $E[\mid Z^2\mid]<\infty$.

Then the stochastic differential equation (3) has a unique t-continuous solution X_t that

$$E\left[\int_0^T \mid X_t \mid^2 \mathrm{d}t\right] < \infty,$$

i.e. the solution is t-continuous for $t \in [0, T]$.

Proof. [36], pp. 65.

2.5 Stability of Stochastic Differential Equations

In the year 1892, A.M. Lyapunov introduced the concept of stability of a dynamic system. Lyapunov developed a method for determining stability without solving the equation, and this method is now known as the Lyapunov direct or second method. To explain the method, let us introduce a few necessary notations. Let K denote the family of all continuous nondecreasing functions $\mu : \mathbb{R}_+ \to \mathbb{R}_+$ such that $\mu(0) = 0$ and $\mu(r) > 0$ if $r > 0$. For $h > 0$, let $S_h = \{x \in \mathbb{R}^n : |x| < h\}$. A continuous function $V(x,t)$ defined on $S_h \times [t_0, \infty)$ is said to be **positive-definite** (in the sense of Lyapunov) if $V(0,t) \equiv 0$ and, for some $\mu \in K$, $V(x,t) \geq \mu(|x|)$ for all $(x,t) \in S_h \times [t_0, \infty)$.

A function $V(x,t)$ is said to be **negative-definite** if $(-V)$ is positive-definite. A continuous non-negative function $V(x,t)$ is said to be **decrescent** (i.e. to have an arbitrarily small upper bound) if for some $\mu \in K$, $V(x,t) \leq \mu(|x|)$ for all $(x,t) \in S_h \times [t_0, \infty)$.

A function $V(x,t)$ defined on $\mathbb{R}^n \times [t_0, \infty)$ is said to be **radially unbounded** if $\lim_{|x|\to\infty} \inf_{t \geq t_0} V(x,t) = \infty$. Let $C^{1,1}(S_h \times [t_0, \infty), \mathbb{R}_+)$ denote the family of all continuous functions $V(x,t)$ from $S_h \times [t_0, \infty)$ to $\mathbb{R}_+$ with continuous first partial derivatives with respect to every component of x and to t. Then $v(t) = V(t, X_t)$ represents a function of t with the derivative

$$\dot{v}(t) = V_t(t, X_t) + V_x(t, X_t)b(t, X_t) = \frac{\partial V}{\partial t}(t, X_t) + \sum_{i=1}^{n} \frac{\partial V}{\partial x_i}(t, X_t)b_i(t, X_t).$$

If $\dot{v}(t) \leq 0$, then $v(t)$ will not increase so the distance of X_t from the equilibrium point measured by $V(t, X_t)$ does not increase. If $\dot{v}(t) < 0$, then $v(t)$ will decrease to zero so the distance will decrease to zero, that is $X_t \to 0$.

Theorem 2.4. ***(Lyapunov theorem)*** *If there exists a positive-definite function $V(x,t) \in C^{1,1}(S_h \times [t_0, \infty), \mathbb{R}_+)$ such that*

$$\dot{V}(x,t) := V_t(t, X_t) + V_x(t, X_t)b(t, X_t) \leq 0$$

for all $(x,t) \in S_h \times [t_0, \infty)$, then the trivial solution is stable. If there exists a positive-definite decrescent function $V(x,t) \in C^{1,1}(S_h \times [t_0, \infty), \mathbb{R}_+)$ such that $\dot{V}(x,t)$ is negative-definite, then the trivial solution is asymptotically stable.

A function $V(x,t)$ that satisfies the stability conditions of Theorem (2.4) is called a Lyapunov function corresponding to the ordinary differential equation. The next text carries over the principles of the Lyapunov stability theory for deterministic systems to stochastic ones.

Definition 2.7. The trivial solution of equation (2) is said to be

(i) stochastically **stable** or **stable in probability** if for every pair of $\epsilon \in (0,1)$ and $r > 0$, there exists $\delta = \delta(\epsilon, r, t_0) > 0$ such that $P\{|x(t, t_0, x_0)| < r\} \geq 1 - \epsilon$ for all $t \geq t_0$, whenever $|x_0| < \delta$. Otherwise, it is said to be stochastically **unstable**.

(ii) stochastically **asymptotically stable** if it is stochastically stable and, moreover, for every $\epsilon \in (0,1)$, there exists $\delta_0 = \delta_0(\epsilon, t_0) > 0$ such that $P\{\lim_{t\to\infty} x(t, t_0, x_0) = 0\} \geq 1 - \epsilon$ whenever $|x_0| < \delta_0$.

(iii) stochastically **asymptotically stable in the large** if it is stochastically stable and, moreover, $P\{\lim_{t\to\infty} x(t, t_0, x_0) = 0\} = 1$ for all $x_0 \in \mathbb{R}^n$.

Suppose one would like to let the initial value be a random variable. It should also be pointed out that when $\sigma^{(x,t)} = 0$, these definitions reduce to the corresponding deterministic ones. We now extend the Lyapunov Theorem (2.4) to the stochastic case. Let $0 < h \leq \infty$. Denote by $C^{2,1}(S_h \times \mathbb{R}_+, \mathbb{R}_+)$ the family of all nonnegative functions $V(x,t)$ defined on $S_h \times \mathbb{R}_+$ such that they are continuously twice differentiable in x and once in t. Define the differential operator L associated with equation (2) by

$$L = \frac{\partial}{\partial t} + \sum_{i=1}^{n} \frac{\partial}{\partial x_i}(t, X_t) b_i(x,t) + \frac{1}{2} \sum_{i,j=1}^{n} \frac{\partial^2}{\partial x_i \partial x_j} \left[\sigma(x,t)\sigma^T(x,t)\right]_{ij}.$$

The inequality $\dot{V}(x,t) \leq 0$ will be replaced by $LV(x,t) \leq 0$ in order to get the stochastic stability assertions.

Theorem 2.5. *If there exists a positive-definite*

*(i) function $V(x,t) \in C^{2,1}(S_h \times [t_0, \infty), \mathbb{R}_+)$ such that $LV(x,t) \leq 0$ for all $(x,t) \in S_h \times [t_0, \infty)$, then the trivial solution of equation (2) is stochastically **stable**.*

*(ii) decrescent function $V(x,t) \in C^{2,1}(S_h \times [t_0, \infty), \mathbb{R}_+)$ such that $LV(x,t)$ is negative-definite, then the trivial solution of equation (2) is stochastically **asymptotically stable**.*

*(iii) decrescent radially unbounded function $V(x,t) \in C^{2,1}(\mathbb{R}^n \times [t_0, \infty), \mathbb{R}_+)$ such that $LV(x,t)$ is negative-definite, then the trivial solution of equation (2) is stochastically **asymptotically stable in the large.***

Proof. [28], pp. 111.

3 Aims of the thesis

The thesis investigates the properties of solutions of stochastic differential equations of the type

$$\mathrm{d}X(t) = AX(t)\mathrm{d}t + G\mathrm{d}B(t),$$

where A and G are matrices.

Furthermore, there is studied the stability investigation of stochastic differential systems of $2, 3$ and 4 order.

The thesis is also focused on systems of stochastic differential equations with delay of the type

$$\mathrm{d}X(t) = AX(t-\tau)\mathrm{d}t + G\mathrm{d}B(t),$$

where A and G are matrices, $\tau \in \mathbb{R}^+$ is constant delay.

In the last phase of the thesis, the acquired knowledge was applied to the biological model. Real biological systems will always be exposed to unexpected environmental influences which may affect system behavior. Therefore, deterministic models need to be extended to models stochastic, which involve complex differences in dynamics. E.g. deterministic model it is not able to control physiological influences such as hormonal changes, blood fluctuations pressure, enzymatic processes, energetic demands, cellular metabolism, or individual characteristics of each individual, such as BMI, genetic equipment, smoking, stress levels, etc.

4 Actual results

4.1 Three-Dimensional Brownian Motion

4.1.1 Solution of Stochastic Differential Equations

Theorem 4.1. *Let*

$$\mathrm{d}X_t = AX_t\mathrm{d}t + G\mathrm{d}B_t \tag{4}$$

be an n-dimensional Itô process, where

$$X_t = \begin{pmatrix} X_1(t) \\ \vdots \\ X_n(t) \end{pmatrix}, A = \begin{pmatrix} a_{11} & \cdots & a_{1n} \\ \vdots & & \vdots \\ a_{m1} & \cdots & a_{mn} \end{pmatrix}, G = \begin{pmatrix} g_{11} & \cdots & g_{1m} \\ \vdots & & \vdots \\ g_{n1} & \cdots & g_{nm} \end{pmatrix}, B_t = \begin{pmatrix} B_1(t) \\ \vdots \\ B_m(t) \end{pmatrix}.$$

Let $f(t,x) = (f_1(t,x), ..., f_p(t,x))$ be a twice continuously differentiable function from $\mathbb{R}^n$ into $\mathbb{R}^p$. Then the process $Y(t) = f(t, X(t))$ is again an Itô process, k, Y_k, is given by

$$\mathrm{d}Y_k = \frac{\partial f_k}{\partial t}(t, X_t)\mathrm{d}t + \sum_i \frac{\partial f_k}{\partial x_i}(t, X_t)(AX_{i,t}\mathrm{d}t + G\mathrm{d}B_{i,t}) + \frac{1}{2}\sum_{i,j}\frac{\partial^2 f_k}{\partial x_i \partial x_j}(t, X_t)(G^2\mathrm{d}B_{i,t}^2),$$

where $\mathrm{d}X_{i,t}\mathrm{d}X_{j,t}$ is computed according to rules of Theorem 2.3.

Proof. Let us substitute $\mathrm{d}X_t = AX_t\mathrm{d}t + G\mathrm{d}B_t$ in equation (4) and use rules of Theorem 2.3, then we get the equivalent expression

$$\begin{aligned} f(t, X_t) &= f(0, X_0) + \int_0^t \left(\frac{\partial f}{\partial s}(s, X_s) + AX_s\frac{\partial f}{\partial x}(s, X_s) + G^2\frac{\partial^2 f}{\partial x^2}(s, X_s)\right)\mathrm{d}s \\ &+ \int_0^t G\frac{\partial f}{\partial x}(s, X_s)\mathrm{d}B_s \end{aligned}$$

Assume that AX_t and G are elementary functions. Using Taylor's theorem we get

$$\begin{aligned} f(t, X_t) &= f(0, X_0) + \sum_j \triangle f(t_j, X_j) = f(0, X_0) + \sum_j \frac{\partial f}{\partial t} \triangle t_j + \sum_j \frac{\partial f}{\partial x} \triangle X_j \\ &+ \frac{1}{2}\sum_j \frac{\partial^2 f}{\partial t^2}(\triangle t_j)^2 + \sum_j \frac{\partial^2 f}{\partial t \partial x}(\triangle t_j)(\triangle X_j) + \frac{1}{2}\sum_j \frac{\partial^2 f}{\partial x^2}(\triangle X_j)^2 + \sum_j R_j, \end{aligned}$$

where $\frac{\partial f}{\partial t}, \frac{\partial f}{\partial x}$, etc. are evaluated at the points $(t_j, X_j), \triangle t_j = t_{j+1} - t_j$, $\triangle X_j = X_{t_{j+1}} - X_{t_j}, \triangle f(t_j, X_j) = f(t_{j+1}, X_{t_{j+1}}) + f(t_j, X_j)$ and $R_j = o(|\triangle t_j|^2 + |\triangle X_j|^2)$ for all j. If $\triangle t_j \to 0$ then

$$\begin{aligned} \sum_j \frac{\partial f}{\partial t} \triangle t_j &= \sum_j \frac{\partial f}{\partial t}(t_j, X_j) \triangle t_j \to \int_0^t \frac{\partial f}{\partial s}(s, X_s)\mathrm{d}s, \\ \sum_j \frac{\partial f}{\partial x} \triangle X_j &= \sum_j \frac{\partial f}{\partial x}(t_j, X_j) \triangle X_j \to \int_0^t \frac{\partial f}{\partial x}(s, X_s)\mathrm{d}X_s. \end{aligned}$$

Moreover, since AX_t and G are elementary we get

$$\begin{aligned}\sum_j \frac{\partial^2 f}{\partial x^2}(\triangle X_j)^2 &= \sum_j \frac{\partial^2 f}{\partial x^2}(A_j X_{t_j})^2(\triangle t_j)^2 + 2\sum_j \frac{\partial^2 f}{\partial x^2} A_j X_{t_j} G_j(\triangle t_j)(\triangle B_j) \\ &+ \sum_j \frac{\partial^2 f}{\partial x^2}(G_j)^2(\triangle B_j)^2.\end{aligned}$$

The first two terms here tend to 0 as $\triangle t_j \to 0$. For example,

$$\mathbb{E}\left[\left(\sum_j \frac{\partial^2 f}{\partial x^2} A_j X_{t_j} G_j(\triangle t_j)(\triangle B_j)\right)^2\right] = \sum_j \mathbb{E}\left[\left(\frac{\partial^2 f}{\partial x^2} A_j X_{t_j} G_j\right)^2\right](\triangle t_j)^3 \to 0.$$

We claim that the last term tends to

$$\int_0^t G^2 \frac{\partial^2 f}{\partial x^2}(s, X_s)\mathrm{d}s \to 0.$$

That completes the proof of the formula (4). □

Corollary 4.2. Suppose the stochastic system (4) with $X_t \neq 0, X_0 = \eta, \eta$ is a constant vector, $B_0 = 0$,

$$\mathrm{d}X_t = AX_t\mathrm{d}t + G\mathrm{d}B_t.$$

First we compute the deterministic part

$$\begin{aligned}\mathrm{d}X_t &= AX_t\mathrm{d}t, \\ X_t &= \mathrm{e}^{At}\eta.\end{aligned}$$

Suppose that $\eta = \phi(t), \phi(t)$ is a function

$$\begin{aligned}X_t &= \mathrm{e}^{At}\phi(t), \\ \mathrm{d}X_t &= \mathrm{e}^{At}\mathrm{d}\phi(t) + \mathrm{e}^{At}A\phi(t), \\ \mathrm{e}^{At}\mathrm{d}\phi(t) + \mathrm{e}^{At}A\phi(t) &= A\mathrm{e}^{At}\phi(t) + G\mathrm{d}B_t, \\ G^{-1}\mathrm{e}^{At}\mathrm{d}\phi(t) &= \mathrm{d}B_t.\end{aligned}$$

At this moment let's solve the right-hand side using Itô formula (5). Choose $X_t \equiv B_t$ and $f(t, X_t) = X_t$. For $Y_t = f(t, B_t) = B_t$ by Itô formula,

$$\begin{aligned}\mathrm{d}Y_t &= 0 + 1 \cdot \mathrm{d}B_t + 0 \cdot \mathrm{d}t, \\ \mathrm{d}B_t &= \mathrm{d}B_t = Bt,\end{aligned}$$

hence

$$G^{-1}\mathrm{e}^{At}\phi(t) = B_t \Rightarrow \phi(t) = G\mathrm{e}^{-At}B_t.$$

Solution of the stochastic system (4) is $X_t = \mathrm{e}^{At}G\mathrm{e}^{-At}B_t$.

4.1.2 Stability of Solution Using Lyapunov Method

The stability of the solution is derived as the same way as it is presented in the following chapter for four-dimensional Brownian motion.

4.2 Four-Dimensional Brownian Motion

4.2.1 Solution of Stochastic Differential Equations

The solution of SDE for multidimensional Brownian motion is described in previous subchapter 4.1.1.

4.2.2 Stability of Solution Using Lyapunov Method

We have a matrix linear stochastic differential equation

$$\mathrm{d}X_t = AX_t\mathrm{d}t + G\mathrm{d}B_t, \tag{5}$$

where $X_t = \begin{pmatrix} X_1(t) \\ X_2(t) \\ X_3(t) \\ X_4(t) \end{pmatrix}, A = \begin{pmatrix} a_{11} & a_{12} & a_{13} & a_{14} \\ a_{21} & a_{22} & a_{23} & a_{24} \\ a_{31} & a_{32} & a_{33} & a_{34} \\ a_{41} & a_{42} & a_{43} & a_{44} \end{pmatrix}, G = \begin{pmatrix} g_{11} & g_{12} & g_{13} & g_{14} \\ g_{21} & g_{22} & g_{23} & g_{24} \\ g_{31} & g_{32} & g_{33} & g_{34} \\ g_{41} & g_{42} & g_{43} & g_{44} \end{pmatrix},$

$B_t = \begin{pmatrix} B_1(t) \\ B_2(t) \\ B_3(t) \\ B_4(t) \end{pmatrix}, a_{ij}, g_{ij}$ for $i, j = 1, 2, 3, 4$ are constants.

Definition 4.1. Lyapunov quadratic function V is given by $V(X_t) = X_t^T Q\, X_t$, where Q is a symmetric positive-definite matrix.

4.2.3 Special Matrix Q

Definition 4.2. Lyapunov quadratic function V is given by $V(X_t) = X_t^T Q\, X_t$, where

$$Q = \begin{pmatrix} q_1 & q_2 & q_3 & q_4 \\ q_2 & q_1 & q_2 & q_3 \\ q_3 & q_2 & q_1 & q_2 \\ q_4 & q_3 & q_2 & q_1 \end{pmatrix}$$

is a symmetric positive-definite matrix, $q_i \in \mathbb{R}, i = 1, 2, 3, 4$. Positive-definite matrix is verified by the Sylvester's criterion. There have to apply these conditions together

$$\begin{aligned} D_1 &= q_1 > 0, \\ D_2 &= q_1^2 - q_2^2 > 0, \\ D_3 &= q_1^3 + 2q_2^2 q_3 - q_1 q_3^2 - 2q_1 q_2^2 > 0, \\ D_4 &= q_1 q_2^3 + q_1 q_2 q_3^2 + q_1^3 q_4 - q_1 q_2^2 q_4 - 2q_1^2 q_2 q_3 - q_1^2 q_2^2 - 2q_2^2 q_3^2 - q_2^3 q_4 + q_2^4 + q_3^4 + 2q_1 q_2^2 q_3 \\ &+ 4q_1 q_2 q_3 q_4 + q_2^2 q_4^2 - 2q_2 q_3^2 q_4 - q_1^2 q_3^2 - q_2^3 q_4 - q_1^2 q_4^2 > 0. \end{aligned}$$

Theorem 4.3. *Zero solution of equation* (5) *is stochastically stable if holds* $LV < 0$, *where*

$$\begin{aligned} LV &= 2\left(a_{11}q_1 + a_{21}q_2 + a_{31}q_3 + a_{41}q_4\right) X_1^2(t) + 2\left(a_{12}q_2 + a_{22}q_1 + a_{32}q_2 + a_{42}q_3\right) X_2^2(t) \\ &+ 2\left(a_{13}q_3 + a_{23}q_2 + a_{33}q_1 + a_{43}q_2\right) X_3^2(t) + 2\left(a_{14}q_4 + a_{24}q_3 + a_{34}q_2 + a_{44}q_1\right) X_4^2(t) \\ &+ 2\left(a_{12}q_1 + a_{11}q_2 + a_{22}q_2 + a_{21}q_1 + a_{32}q_3 + a_{31}q_2 + a_{42}q_4 + a_{41}q_3\right) X_1(t)X_2(t) \end{aligned}$$

$$\begin{aligned}
&+\quad 2\left(a_{13}q_1+a_{11}q_3+a_{23}q_2+a_{23}q_1+a_{21}q_2+a_{33}q_3+a_{31}q_1+a_{43}q_4+a_{41}q_2\right)X_1(t)\\
&\times\quad X_3(t)+2\left(a_{14}q_1+a_{11}q_4+a_{24}q_2+a_{21}q_3+a_{34}q_3+a_{31}q_2+a_{44}q_4+a_{41}q_1\right)X_1(t)\\
&\times\quad X_4(t)+2\left(a_{13}q_2+a_{12}q_3+a_{22}q_2+a_{33}q_2+a_{32}q_1+a_{43}q_3+a_{42}q_2\right)X_2(t)X_3(t)\\
&+\quad 2\left(a_{14}q_2+a_{24}q_1+a_{22}q_3+a_{34}q_2+a_{32}q_2+a_{44}q_3+a_{42}q_1\right)X_2(t)X_4(t)+2\left(a_{14}q_3\right.\\
&+\quad \left.a_{24}q_2+a_{23}q_3+a_{34}q_1+a_{33}q_2+a_{44}q_2+a_{43}q_1\right)X_3(t)X_4(t)+q_1\left(g_{11}^2+g_{12}^2+g_{13}^2\right.\\
&+\quad \left.g_{14}^2+g_{21}^2+g_{22}^2+g_{23}^2+g_{24}^2+g_{31}^2+g_{32}^2+g_{33}^2+g_{34}^2+g_{41}^2+g_{42}^2+g_{43}^2+g_{44}^2\right)\\
&+\quad 2q_2\left(g_{11}g_{21}+g_{12}g_{22}+g_{13}g_{23}+g_{14}g_{24}+g_{21}g_{31}+g_{22}g_{32}+g_{23}g_{33}+g_{24}g_{34}\right.\\
&+\quad \left.g_{31}g_{41}+g_{32}g_{42}+g_{33}g_{43}+g_{34}g_{44}\right)+2q_3\left(g_{11}g_{31}+g_{12}g_{32}+g_{13}g_{33}+g_{14}g_{34}\right.\\
&+\quad \left.g_{21}g_{41}+g_{22}g_{42}+g_{23}g_{43}+g_{24}g_{44}\right)+2q_4\left(g_{11}g_{41}+g_{12}g_{42}+g_{13}g_{43}+g_{14}g_{44}\right).
\end{aligned}$$

Proof. After derivation of Lyapunov function of equation (5) we get

$$\mathrm{d}V(X_t)=X_t^TQAX_t\mathrm{d}t+X_t^TQG\mathrm{d}B_t+X_t^TA^T\mathrm{d}tQX_t+\mathrm{d}B_t^TG^TQX_t+\mathrm{d}B_t^TG^TQG\mathrm{d}B_t.$$

In matrix form

$$\begin{aligned}
&\mathrm{d}V\begin{pmatrix}X_1(t)\\X_2(t)\\X_3(t)\\X_4(t)\end{pmatrix}\\
&=\begin{pmatrix}X_1(t)\\X_2(t)\\X_3(t)\\X_4(t)\end{pmatrix}^T\begin{pmatrix}q_1&q_2&q_3&q_4\\q_2&q_1&q_2&q_3\\q_3&q_2&q_1&q_2\\q_4&q_3&q_2&q_1\end{pmatrix}\begin{pmatrix}a_{11}&a_{12}&a_{13}&a_{14}\\a_{21}&a_{22}&a_{23}&a_{24}\\a_{31}&a_{32}&a_{33}&a_{34}\\a_{41}&a_{42}&a_{43}&a_{44}\end{pmatrix}\begin{pmatrix}X_1(t)\\X_2(t)\\X_3(t)\\X_4(t)\end{pmatrix}\mathrm{d}t\\
&+\begin{pmatrix}X_1(t)\\X_2(t)\\X_3(t)\\X_4(t)\end{pmatrix}^T\begin{pmatrix}q_1&q_2&q_3&q_4\\q_2&q_1&q_2&q_3\\q_3&q_2&q_1&q_2\\q_4&q_3&q_2&q_1\end{pmatrix}\begin{pmatrix}g_{11}&g_{12}&g_{13}&g_{14}\\g_{21}&g_{22}&g_{23}&g_{24}\\g_{31}&g_{32}&g_{33}&g_{34}\\g_{41}&g_{42}&g_{43}&g_{44}\end{pmatrix}\begin{pmatrix}\mathrm{d}B_1(t)\\\mathrm{d}B_2(t)\\\mathrm{d}B_3(t)\\\mathrm{d}B_4(t)\end{pmatrix}\\
&+\begin{pmatrix}X_1(t)\\X_2(t)\\X_3(t)\\X_4(t)\end{pmatrix}^T\begin{pmatrix}a_{11}&a_{12}&a_{13}&a_{14}\\a_{21}&a_{22}&a_{23}&a_{24}\\a_{31}&a_{32}&a_{33}&a_{34}\\a_{41}&a_{42}&a_{43}&a_{44}\end{pmatrix}^T\begin{pmatrix}q_1&q_2&q_3&q_4\\q_2&q_1&q_2&q_3\\q_3&q_2&q_1&q_2\\q_4&q_3&q_2&q_1\end{pmatrix}\begin{pmatrix}X_1(t)\\X_2(t)\\X_3(t)\\X_4(t)\end{pmatrix}\mathrm{d}t\\
&+\begin{pmatrix}\mathrm{d}B_1(t)\\\mathrm{d}B_2(t)\\\mathrm{d}B_3(t)\\\mathrm{d}B_4(t)\end{pmatrix}^T\begin{pmatrix}g_{11}&g_{12}&g_{13}&g_{14}\\g_{21}&g_{22}&g_{23}&g_{24}\\g_{31}&g_{32}&g_{33}&g_{34}\\g_{41}&g_{42}&g_{43}&g_{44}\end{pmatrix}^T\begin{pmatrix}q_1&q_2&q_3&q_4\\q_2&q_1&q_2&q_3\\q_3&q_2&q_1&q_2\\q_4&q_3&q_2&q_1\end{pmatrix}\begin{pmatrix}X_1(t)\\X_2(t)\\X_3(t)\\X_4(t)\end{pmatrix}\\
&+\begin{pmatrix}\mathrm{d}B_1(t)\\\mathrm{d}B_2(t)\\\mathrm{d}B_3(t)\end{pmatrix}^T\begin{pmatrix}g_{11}&g_{12}&g_{13}&g_{14}\\g_{21}&g_{22}&g_{23}&g_{24}\\g_{31}&g_{32}&g_{33}&g_{34}\\g_{41}&g_{42}&g_{43}&g_{44}\end{pmatrix}^T\begin{pmatrix}q_1&q_2&q_3&q_4\\q_2&q_1&q_2&q_3\\q_3&q_2&q_1&q_2\\q_4&q_3&q_2&q_1\end{pmatrix}\\
&\times\begin{pmatrix}g_{11}&g_{12}&g_{13}&g_{14}\\g_{21}&g_{22}&g_{23}&g_{24}\\g_{31}&g_{32}&g_{33}&g_{34}\\g_{41}&g_{42}&g_{43}&g_{44}\end{pmatrix}\begin{pmatrix}\mathrm{d}B_1(t)\\\mathrm{d}B_2(t)\\\mathrm{d}B_3(t)\\\mathrm{d}B_4(t)\end{pmatrix}.
\end{aligned}$$

We get

$$\begin{aligned}
\mathrm{d}V(X_t) &= 2\left(a_{11}q_1 + a_{21}q_2 + a_{31}q_3 + a_{41}q_4\right) X_1^2(t)\mathrm{d}t + 2\left(a_{12}q_2 + a_{22}q_1 + a_{32}q_2 + a_{42}q_3\right) \\
&\times\ X_2^2(t)\mathrm{d}t + 2\left(a_{13}q_3 + a_{23}q_2 + a_{33}q_1 + a_{43}q_2\right) X_3^2(t)\mathrm{d}t + 2\left(a_{14}q_4 + a_{24}q_3 + a_{34}q_2\right. \\
&+\ \left. a_{44}q_1\right) X_4^2(t)\mathrm{d}t + 2\left(a_{12}q_1 + a_{11}q_2 + a_{22}q_2 + a_{21}q_1 + a_{32}q_3 + a_{31}q_2 + a_{42}q_4\right. \\
&+\ \left. a_{41}q_3\right) X_1(t)X_2(t)\mathrm{d}t + 2\left(a_{13}q_1 + a_{11}q_3 + a_{23}q_2 + a_{23}q_1 + a_{21}q_2 + a_{33}q_3 + a_{31}q_1\right. \\
&+\ \left. a_{43}q_4 + a_{41}q_2\right) X_1(t)X_3(t)\mathrm{d}t + 2\left(a_{14}q_1 + a_{11}q_4 + a_{24}q_2 + a_{21}q_3 + a_{34}q_3 + a_{31}q_2\right. \\
&+\ \left. a_{44}q_4 + a_{41}q_1\right) X_1(t)X_4(t)\mathrm{d}t + 2\left(a_{13}q_2 + a_{12}q_3 + a_{22}q_2 + a_{33}q_2 + a_{32}q_1 + a_{43}q_3\right. \\
&+\ \left. a_{42}q_2\right) X_2(t)X_3(t)\mathrm{d}t + 2\left(a_{14}q_2 + a_{24}q_1 + a_{22}q_3 + a_{34}q_2 + a_{32}q_2 + a_{44}q_3\right. \\
&+\ \left. a_{42}q_1\right) X_2(t)X_4(t)\mathrm{d}t + 2\left(a_{14}q_3 + a_{24}q_2 + a_{23}q_3 + a_{34}q_1 + a_{33}q_2 + a_{44}q_2\right. \\
&+\ \left. a_{43}q_1\right) X_3(t)X_4(t)\mathrm{d}t + q_1\left(g_{11}^2 + g_{12}^2 + g_{13}^2 + g_{14}^2 + g_{21}^2 + g_{22}^2 + g_{23}^2 + g_{24}^2 + g_{31}^2\right. \\
&+\ \left. g_{32}^2 + g_{33}^2 + g_{34}^2 + g_{41}^2 + g_{42}^2 + g_{43}^2 + g_{44}^2\right) \mathrm{d}t + 2q_2\left(g_{11}g_{21} + g_{12}g_{22} + g_{13}g_{23}\right. \\
&+\ g_{14}g_{24} + g_{21}g_{31} + g_{22}g_{32} + g_{23}g_{33} + g_{24}g_{34} + g_{31}g_{41} + g_{32}g_{42} + g_{33}g_{43} \\
&+\ \left. g_{34}g_{44}\right) \mathrm{d}t + 2q_3\left(g_{11}g_{31} + g_{12}g_{32} + g_{13}g_{33} + g_{14}g_{34} + g_{21}g_{41} + g_{22}g_{42} + g_{23}g_{43}\right. \\
&+\ \left. g_{24}g_{44}\right) \mathrm{d}t + 2q_4\left(g_{11}g_{41} + g_{12}g_{42} + g_{13}g_{43} + g_{14}g_{44}\right) \mathrm{d}t + 2\left[\left(q_1X_1(t) + q_2X_2(t)\right.\right. \\
&+\ \left. q_3X_3(t) + q_4X_4(t)\right)\left(g_{11}\mathrm{d}B_1(t) + g_{12}\mathrm{d}B_2(t) + g_{13}\mathrm{d}B_3(t) + g_{14}\mathrm{d}B_4(t)\right) \\
&+\ \left(q_2X_1(t) + q_1X_2(t) + q_2X_3(t) + q_3X_4(t)\right)\left(g_{21}\mathrm{d}B_1(t) + g_{22}\mathrm{d}B_2(t) + g_{23}\mathrm{d}B_3(t)\right. \\
&+\ \left. g_{24}\mathrm{d}B_4(t)\right) + \left(q_3X_1(t) + q_2X_2(t) + q_1X_3(t) + q_2X_4(t)\right)\left(g_{31}\mathrm{d}B_1(t) + g_{32}\mathrm{d}B_2(t)\right. \\
&+\ \left. g_{33}\mathrm{d}B_3(t) + g_{34}\mathrm{d}B_4(t)\right) + \left(q_4X_1(t) + q_3X_2(t) + q_2X_3(t) + q_1X_4(t)\right)\left(g_{41}\mathrm{d}B_1(t)\right. \\
&+\ \left.\left. g_{42}\mathrm{d}B_2(t) + g_{43}\mathrm{d}B_3(t) + g_{44}\mathrm{d}B_4(t)\right)\right].
\end{aligned}$$

We apply expectation $\mathbb{E}\left\{\mathrm{d}V(X_t)\right\}$

$$\begin{aligned}
\mathbb{E}\left\{\mathrm{d}V(X_t)\right\} &= 2\left(a_{11}q_1 + a_{21}q_2 + a_{31}q_3 + a_{41}q_4\right) X_1^2(t) + 2\left(a_{12}q_2 + a_{22}q_1 + a_{32}q_2\right. \\
&+\ \left. a_{42}q_3\right) X_2^2(t) + 2\left(a_{13}q_3 + a_{23}q_2 + a_{33}q_1 + a_{43}q_2\right) X_3^2(t) + 2\left(a_{14}q_4\right. \\
&+\ \left. a_{24}q_3 + a_{34}q_2 + a_{44}q_1\right) X_4^2(t) + 2\left(a_{12}q_1 + a_{11}q_2 + a_{22}q_2 + a_{21}q_1\right. \\
&+\ \left. a_{32}q_3 + a_{31}q_2 + a_{42}q_4 + a_{41}q_3\right) X_1(t)X_2(t) + 2\left(a_{13}q_1 + a_{11}q_3 + a_{23}q_2\right. \\
&+\ \left. a_{23}q_1 + a_{21}q_2 + a_{33}q_3 + a_{31}q_1 + a_{43}q_4 + a_{41}q_2\right) X_1(t)X_3(t) + 2\left(a_{14}q_1\right. \\
&+\ \left. a_{11}q_4 + a_{24}q_2 + a_{21}q_3 + a_{34}q_3 + a_{31}q_2 + a_{44}q_4 + a_{41}q_1\right) X_1(t)X_4(t) \\
&+\ 2\left(a_{13}q_2 + a_{12}q_3 + a_{22}q_2 + a_{33}q_2 + a_{32}q_1 + a_{43}q_3 + a_{42}q_2\right) X_2(t)X_3(t) \\
&+\ 2\left(a_{14}q_2 + a_{24}q_1 + a_{22}q_3 + a_{34}q_2 + a_{32}q_2 + a_{44}q_3 + a_{42}q_1\right) X_2(t)X_4(t) \\
&+\ 2\left(a_{14}q_3 + a_{24}q_2 + a_{23}q_3 + a_{34}q_1 + a_{33}q_2 + a_{44}q_2 + a_{43}q_1\right) X_3(t)X_4(t) \\
&+\ q_1\left(g_{11}^2 + g_{12}^2 + g_{13}^2 + g_{14}^2 + g_{21}^2 + g_{22}^2 + g_{23}^2 + g_{24}^2 + g_{31}^2 + g_{32}^2 + g_{33}^2\right. \\
&+\ \left. g_{34}^2 + g_{41}^2 + g_{42}^2 + g_{43}^2 + g_{44}^2\right) + 2q_2\left(g_{11}g_{21} + g_{12}g_{22} + g_{13}g_{23} + g_{14}g_{24}\right. \\
&+\ \left. g_{21}g_{31} + g_{22}g_{32} + g_{23}g_{33} + g_{24}g_{34} + g_{31}g_{41} + g_{32}g_{42} + g_{33}g_{43} + g_{34}g_{44}\right) \\
&+\ 2q_3\left(g_{11}g_{31} + g_{12}g_{32} + g_{13}g_{33} + g_{14}g_{34} + g_{21}g_{41} + g_{22}g_{42} + g_{23}g_{43}\right. \\
&+\ \left. g_{24}g_{44}\right) + 2q_4\left(g_{11}g_{41} + g_{12}g_{42} + g_{13}g_{43} + g_{14}g_{44}\right) = LV\mathrm{d}t.
\end{aligned}$$

For $Q = I$, where I is a unit matrix, we get

$$\begin{aligned}
LV &= 2a_{11}X_1^2(t) + 2a_{22}X_2^2(t) + 2a_{33}X_3^2(t) + 2a_{44}X_4^2(t) + 2\left(a_{12} + a_{21}\right) X_1(t)X_2(t) \\
&+\ 2\left(a_{13} + a_{23} + a_{31}\right) X_1(t)X_3(t) + 2\left(a_{14} + a_{41}\right) X_1(t)X_4(t) + 2a_{32}X_2(t)X_3(t)
\end{aligned}$$

$$
\begin{aligned}
&+\quad 2\left(a_{24}+a_{42}\right)X_2(t)X_4(t)+2\left(a_{34}+a_{43}\right)X_3(t)X_4(t)+\left(g_{11}^2+g_{12}^2+g_{13}^2+g_{14}^2\right.\\
&+\quad \left.g_{21}^2+g_{22}^2+g_{23}^2+g_{24}^2+g_{31}^2+g_{32}^2+g_{33}^2+g_{34}^2+g_{41}^2+g_{42}^2+g_{43}^2+g_{44}^2\right).
\end{aligned}
$$

□

Now we can find conditions of a stability system. The system will be stable if the Lyapunov function LV is negative definite, so

$$
\begin{aligned}
&\quad 2a_{11}X_1^2(t)+2a_{22}X_2^2(t)+2a_{33}X_3^2(t)+2a_{44}X_4^2(t)+2\left(a_{12}+a_{21}\right)X_1(t)X_2(t)\\
&+\quad 2\left(a_{13}+a_{23}+a_{31}\right)X_1(t)X_3(t)+2\left(a_{14}+a_{41}\right)X_1(t)X_4(t)+2a_{32}X_2(t)X_3(t)\\
&+\quad 2\left(a_{24}+a_{42}\right)X_2(t)X_4(t)+2\left(a_{34}+a_{43}\right)X_3(t)X_4(t)+\|G\|^2\le 0.
\end{aligned}
$$

Remark: Because $\|G\|^2 \geq 0$, therefore the matrix A must be sufficiently negative, to obtain a negative definite function. We will demonstrate that the matrix A must be more dominant than the matrix G for the stability of the stochastic system,

$$\|A\| \gg \|G\|.$$

Corollary 4.4. We consider matrices A and G in the form

$$A=\begin{pmatrix} a & 0 & 0 & 0\\ 0 & a & 0 & 0\\ 0 & 0 & a & 0\\ 0 & 0 & 0 & a\end{pmatrix}, G=\begin{pmatrix} \frac{a}{10} & 0 & 0 & 0\\ 0 & \frac{a}{10} & 0 & 0\\ 0 & 0 & \frac{a}{10} & 0\\ 0 & 0 & 0 & \frac{a}{10}\end{pmatrix}.$$

The matrix A will be negative definite under following conditions:

$$
\begin{aligned}
&D_1 = a<0,\\
&D_2 = a^2>0,\ D_2 \text{ follows from } D_1,\\
&D_3 = a^3<0 \Leftrightarrow a<0\wedge a^2>0, D_3 \text{ follows from } D_1, D_2,\\
&D_4 = a^4>0 \Leftrightarrow a^2>0,\ D_4 \text{ follows from } D_2.
\end{aligned}
$$

First of all, we will find the solution of the differential system A. We find eigenvalues of matrix A as the solution of the characteristic equation

$$\begin{vmatrix} a-\lambda & 0 & 0 & 0\\ 0 & a-\lambda & 0 & 0\\ 0 & 0 & a-\lambda & 0\\ 0 & 0 & 0 & a-\lambda\end{vmatrix}=0,$$

$$(a-\lambda)^4=0 \Rightarrow \lambda_{1,2,3,4}=a.$$

Then $X_1(t)=\mathrm{e}^{at}, X_2(t)=t\mathrm{e}^{at}, X_3(t)=t^2\mathrm{e}^{at}, X_4(t)=t^3\mathrm{e}^{at}$. The general solution is given by a linear combination $X_t = C_1X_1(t)+C_2X_2(t)+C_3X_3(t)+C_4X_4(t)$ with arbitrary constants C_1, C_2, C_3, C_4, so $X_t = C_1\mathrm{e}^{at}+C_2t\mathrm{e}^{at}+C_3t^2\mathrm{e}^{at}+C_4t^3\mathrm{e}^{at}, t\in\mathbb{R}$, and because $a<0$, then this solution is stable.

At this moment, we find stability of solution of the stochastic system. We determine stability of solution for $Q=I$

$$\mathrm{d}V(X_t) \;=\; 2\left(aX_1^2(t)+aX_2^2(t)+aX_3^2(t)+aX_4^2(t)+\frac{a^2}{50}\right)\mathrm{d}t+\frac{a}{5}X_1(t)\mathrm{d}B_1(t)$$

$$+ \quad \frac{a}{5}X_2(t)\mathrm{d}B_2(t) + \frac{a}{5}X_3(t)\mathrm{d}B_3(t) + \frac{a}{5}X_4(t)\mathrm{d}B_4(t).$$

$$\mathbb{E}\left\{\mathrm{d}V(X_t)\right\} = 2\left(aX_1^2(t) + aX_2^2(t) + aX_3^2(t) + aX_4^2(t) + \frac{a^2}{50}\right)\mathrm{d}t = LV\mathrm{d}t.$$

If holds the inequality $LV \leq 0$, thus $a\left\|X(t)\right\|^2 \leq -\frac{a^2}{50}$,
for $X_t = C_1\mathrm{e}^{at} + C_2t\mathrm{e}^{at} + C_3t^2\mathrm{e}^{at} + C_4t^3\mathrm{e}^{at}, t \in \mathbb{R}$, then the system is stochastic stable.

Corollary 4.5. We consider matrices A and G in the form

$$A = \begin{pmatrix} a_1 & 1 & 1 & 1 \\ 0 & a_2 & 1 & 1 \\ 0 & 0 & a_3 & 1 \\ 0 & 0 & 0 & a_4 \end{pmatrix}, G = \begin{pmatrix} \frac{a_1}{10} & 1 & 1 & 1 \\ 0 & \frac{a_2}{10} & 1 & 1 \\ 0 & 0 & \frac{a_3}{10} & 1 \\ 0 & 0 & 0 & \frac{a_4}{10} \end{pmatrix}.$$

where $a_i \neq a_j$ for $i \neq j; i,j = 1,2,3,4$. The matrix A will be negative definite with following conditions:

$$\begin{aligned} &D_1 = a_1 < 0, \\ &D_2 = a_1a_2 > 0 \Leftrightarrow a_2 < 0,\ D_2 \text{ follows from } D_1, \\ &D_3 = a_1a_2a_3 < 0 \Leftrightarrow a_3 < 0, D_3 \text{ follows from } D_2, \\ &D_4 = a_1a_2a_3a_4 > 0 \Leftrightarrow a_4 < 0,\ D_4 \text{ follows from } D_3. \end{aligned}$$

First of all we find solution of the differential system A. We find eigenvalues of matrix A as the solution of the characteristic equation

$$\begin{vmatrix} a_1 - \lambda & 1 & 1 & 1 \\ 0 & a_2 - \lambda & 1 & 1 \\ 0 & 0 & a_3 - \lambda & 1 \\ 0 & 0 & 0 & a_4 - \lambda \end{vmatrix} = 0,$$

$$(a_1 - \lambda)(a_2 - \lambda)(a_3 - \lambda)(a_4 - \lambda) = 0.$$

According to previous example the general solution with arbitrary constants C_1, C_2, C_3, C_4 is given by $X_t = C_1\mathrm{e}^{a_1t} + C_2\mathrm{e}^{a_2t} + C_3\mathrm{e}^{a_3t} + C_4\mathrm{e}^{a_4t}, t \in \mathbb{R}$.

We can write for a general matrix H

$$H = \begin{pmatrix} a_1 & \alpha & \beta & \gamma \\ 0 & a_2 & \delta & \epsilon \\ 0 & 0 & a_3 & \kappa \\ 0 & 0 & 0 & a_4 \end{pmatrix},$$

where $\alpha, \beta, \gamma, \delta, \epsilon, \kappa \in \mathbb{R}$, the general solution is

$$X_t = C_1\mathrm{e}^{a_1t} + C_2\mathrm{e}^{a_2t} + C_3\mathrm{e}^{a_3t} + C_4\mathrm{e}^{a_4t}, t \in \mathbb{R},$$

where C_1, C_2, C_3, C_4 are constants.
We find stability of solution of the stochastic system. We determine stability of solution for $Q = I$.

$$\mathrm{d}V(X_t) \quad = \quad 2\left(3 + a_1X_1^2(t) + a_2X_2^2(t) + a_3X_3^2(t) + a_4X_4^2(t) + X_1(t)X_2(t) + 2X_1(t)X_3(t)\right.$$

$$
\begin{aligned}
&+ \quad X_1(t)X_4(t) + X_2(t)X_4(t) + X_3(t)X_4(t) + \frac{a_1^2+a_2^2+a_3^2+a_4^2}{200}\Bigg) \mathrm{d}t \\
&+ \quad 2X_1(t)\left(\frac{a_1}{10}\mathrm{d}B_1(t) + \mathrm{d}B_2(t) + \mathrm{d}B_3(t) + \mathrm{d}B_4(t)\right) + 2X_4(t)\frac{a_4}{10}\mathrm{d}B_4(t) \\
&+ \quad 2X_2(t)\left(\frac{a_2}{10}\mathrm{d}B_2(t) + \mathrm{d}B_3(t) + \mathrm{d}B_4(t)\right) + 2X_3(t)\left(\frac{a_3}{10}\mathrm{d}B_3(t) + \mathrm{d}B_4(t)\right).
\end{aligned}
$$

$$
\begin{aligned}
\mathbb{E}\left\{\mathrm{d}V(X_t)\right\} &= 2\big(3 + a_1X_1^2(t) + a_2X_2^2(t) + a_3X_3^2(t) + a_4X_4^2(t) + X_1(t)X_2(t) + 2X_1(t) \\
&\times \quad X_3(t) + X_1(t)X_4(t) + X_2(t)X_4(t) + X_3(t)X_4(t) + \frac{a_1^2+a_2^2+a_3^2+a_4^2}{200}\Bigg) \mathrm{d}t \\
&= LV\mathrm{d}t.
\end{aligned}
$$

If holds the inequality $LV \le 0$, thus

$$
\begin{aligned}
& a_1X_1^2(t) + a_2X_2^2(t) + a_3X_3^2(t) + a_4X_4^2(t) + X_1(t)X_2(t) + 2X_1(t)X_3(t) \\
+ \quad & X_1(t)X_4(t) + X_2(t)X_4(t) + X_3(t)X_4(t) \le -\frac{a_1^2+a_2^2+a_3^2+a_4^2}{100} - 6,
\end{aligned}
$$

for $X_t = C_1\mathrm{e}^{a_1t} + C_2\mathrm{e}^{a_2t} + C_3\mathrm{e}^{a_3t} + C_4\mathrm{e}^{a_4t}, t \in \mathbb{R}$, then the system is stochastic stable.

Corollary 4.6. We consider symmetric matrices A and G in the form

$$
A = \begin{pmatrix} a_1 & 0 & 0 & a_2 \\ 0 & a_1 & a_2 & 0 \\ 0 & a_2 & a_1 & 0 \\ a_2 & 0 & 0 & a_1 \end{pmatrix}, G = \begin{pmatrix} \frac{a_1}{10} & 0 & 0 & \frac{a_2}{10} \\ 0 & \frac{a_1}{10} & \frac{a_2}{10} & 0 \\ 0 & \frac{a_2}{10} & \frac{a_1}{10} & 0 \\ \frac{a_2}{10} & 0 & 0 & \frac{a_1}{10} \end{pmatrix}.
$$

The matrix A will be negative definite with following conditions:

$$
\begin{aligned}
&D_1 = a_1 < 0, \\
&D_2 = a_1^2 > 0, \ D_2 \ \text{ follows from } \ D_1, \\
&D_3 = a_1^3 - a_1a_2^2 < 0 \Leftrightarrow a_1 < 0 \wedge a_1^2 - a_2^2 > 0 \Rightarrow |a_2| < |a_1|. \\
&D_4 = a_1^4 - 2a_1^2a_2^2 + a_2^4 > 0 \Leftrightarrow (a_1^2 - a_2^2)^2 > 0, \ D_4 \ \text{ holds for arbitrary } \ |a_1| \neq |a_2|.
\end{aligned}
$$

Based on these conditions, follows $a_1 < 0$ and $|a_2| < |a_1|$. We find solution of the differential system A. We find eigenvalues of matrix A as the solution of the characteristic equation

$$
\begin{vmatrix} a_1-\lambda & 0 & 0 & a_2 \\ 0 & a_1-\lambda & a_2 & 0 \\ 0 & a_2 & a_1-\lambda & 0 \\ a_2 & 0 & 0 & a_1-\lambda \end{vmatrix} = 0,
$$

$$
\begin{aligned}
[(a_1-\lambda)^2 - a_2^2]^2 &= 0, \\
|a_1 - \lambda| &= |a_2|.
\end{aligned}
$$

Then we get

$$
\text{for } \ a_2 > 0 \ \text{ is } \ X_{1,2}(t) = (1,1)^T\mathrm{e}^{(-a_1+a_2)t},
$$

$$\begin{aligned}
&\text{for} \quad a_2 < 0 \quad \text{is} \quad X_{1,2}(t) = (-1,1)^T \mathrm{e}^{(-a_1+a_2)t},\\
&\text{for} \quad a_2 < 0 \quad \text{is} \quad X_{3,4}(t) = (1,1)^T \mathrm{e}^{(-a_1-a_2)t},\\
&\text{for} \quad a_2 > 0 \quad \text{is} \quad X_{3,4}(t) = (1,-1)^T \mathrm{e}^{(-a_1-a_2)t}.
\end{aligned}$$

The general solution for constants C_1, C_2, C_3, C_4 is given by a linear combination $X_t = C_1X_1(t)+C_2X_2(t)+C_3X_3(t)+C_4X_4(t)$. We find stability of solution of the stochastic system. We determine stability of solution for $Q = I$.

$$\begin{aligned}
\mathrm{d}V(X_t) &= 2\left[a_1(X_1^2(t)+X_2^2(t)+X_3^2(t)+X_4^2(t)) + a_2(X_1(t)X_3(t)+2X_1(t)X_4(t)\right.\\
&+ \left. X_2(t)X_3(t)) + \frac{a_1^2}{50} + \frac{a_2^2}{50}\right]\mathrm{d}t + 2X_1(t)\left(\frac{a_1}{10}\mathrm{d}B_1(t) + \frac{a_2}{10}\mathrm{d}B_4(t)\right)\\
&+ 2X_2(t)\left(\frac{a_1}{10}\mathrm{d}B_2(t) + \frac{a_2}{10}\mathrm{d}B_3(t)\right) + 2X_3(t)\left(\frac{a_2}{10}\mathrm{d}B_2(t) + \frac{a_1}{10}\mathrm{d}B_3(t)\right)\\
&+ 2X_4(t)\left(\frac{a_2}{10}\mathrm{d}B_1(t) + \frac{a_1}{10}\mathrm{d}B_4(t)\right).
\end{aligned}$$

$$\begin{aligned}
\mathbb{E}\left\{\mathrm{d}V(X_t)\right\} &= 2\left[a_1(X_1^2(t)+X_2^2(t)+X_3^2(t)+X_4^2(t)) + a_2(X_1(t)X_3(t)\right.\\
&+ \left. 2X_1(t)X_4(t) + X_2(t)X_3(t)) + \frac{a_1^2}{50} + \frac{a_2^2}{50}\right]\mathrm{d}t = LV\mathrm{d}t.
\end{aligned}$$

If holds the inequality $LV \le 0$, thus

$$a_1\left\|X(t)\right\|^2 + a_2(X_1(t)X_3(t) + 2X_1(t)X_4(t) + X_2(t)X_3(t)) \le -\frac{a_1^2+a_2^2}{50},$$

for $X_t = C_1X_1(t) + C_2X_2(t) + C_3X_3(t) + C_4X_4(t), t \in \mathbb{R}$, then the system is stochastic stable.

Corollary 4.7. If we use in the equation (5) a general matrix A, then we do not receive any usable results with using this method. There were chosen the types of matrices used in medicine.

4.3 Immune System Response to Infection

The oldest documented use of immunological methods dates to the 10th century in China, where it was used to inhale dried smallpox scabs to protect against smallpox. This method was improved at the end of the 18th century by English physician Edward Jenner $(1749-1823)$, when the cow smallpox virus was used to vaccinate against smallpox and the fundamentals of vaccination were laid.

Within this thesis, a stochastic differential system based on a Marchuk model is investigated. The available literature related to the Marchuk mathematical model of infectious disease and immune response is presented in [1], [16]- [21], [29]- [31]. The mathematical model takes the form of a system of differential equations with a delayed argument and with Brownian motion.

4.3.1 Antigen Dynamics

Dynamics of antigens and their elimination by reaction with antibodies is described by

$$\mathrm{d}V(t) = (\beta - \gamma F(t))V(t)\mathrm{d}t + \vartheta(V(t) - V(0))\mathrm{d}B(t),$$

where $V(t)$ is the amount of antigens in time t, $F(t)$ is the amount of antibodies in time t, $\beta > 0$ is the antigen reproduction rate, $\gamma > 0$ is the antigen neutralization in case antigen-antibody meeting, $B(t)$ is a Brownian motion.

4.3.2 Plasma Cell Dynamics

Plasma cells are a type of white blood cells that produce antibodies. The amount of plasma cells is described by the equation

$$\mathrm{d}C(t) = \alpha F(t-\tau)V(t-\tau)\mathrm{d}t - \mu_C(C(t) - C(0))\mathrm{d}t + \vartheta(C(t) - C(0))\mathrm{d}B(t),$$

where $C(t)$ is the amount of plasma cells in time t, τ is the delay of plasma cell forming, $\alpha > 0$ is the immune system reactivity, $C(0)$ is the amount of plasma cells in a healthy organism, μ_C indicates plasma cell lifetime, and $B(t)$ is a Brownian motion.

4.3.3 Antibody Dynamics

Antibodies are proteins that react with antigens, destroy them and are described by

$$\mathrm{d}F(t) = \rho C(t)\mathrm{d}t - \mu_F F(t)\mathrm{d}t - \eta\gamma V(t)F(t)\mathrm{d}t + \vartheta[C(t) - C(0) + F(t) - F(0)]\mathrm{d}B(t),$$

where ρ is the antibody formation rate, μ_F is the antibody lifetime coefficient, η is the rate of antibodies necessary to neutralize one antigen, and $B(t)$ is a Brownian motion.

4.3.4 Relative Characteristics of the Affected Organ

Relative organ damage is described by the equation

$$\mathrm{d}m(t) = \sigma V(t)\mathrm{d}t - \mu_m m(t)\mathrm{d}t,$$

where $m(t)$ characterizes the rate of damage caused in the infected organism, $\sigma > 0$ is damage to the body directly proportional to the amount of antigens, μ_m is the coefficient of natural regeneration of an organism.

4.3.5 Simulation of the Sub Clinical Form

There must be met the condition of stability $\beta < \gamma F(0)$. We simulate the sub clinical disease for an antigen reproduction rate $\beta = 0.2$, initial dose of antigens $V(0) = 0.01$ and $\vartheta = 0.2$, see Figure 1.

The immune response is sufficiently strong and all antigens that have been reached into the organism are destroyed by antibodies present in the organism (without the production of new ones). The speed of antigen reproduction is too small as compared with the neutralization of antigens by antibodies. This state corresponds to the gentle course, the immune system meets with this course commonly. The infected person does not observe any symptoms, the disease is hidden and quickly disappears.

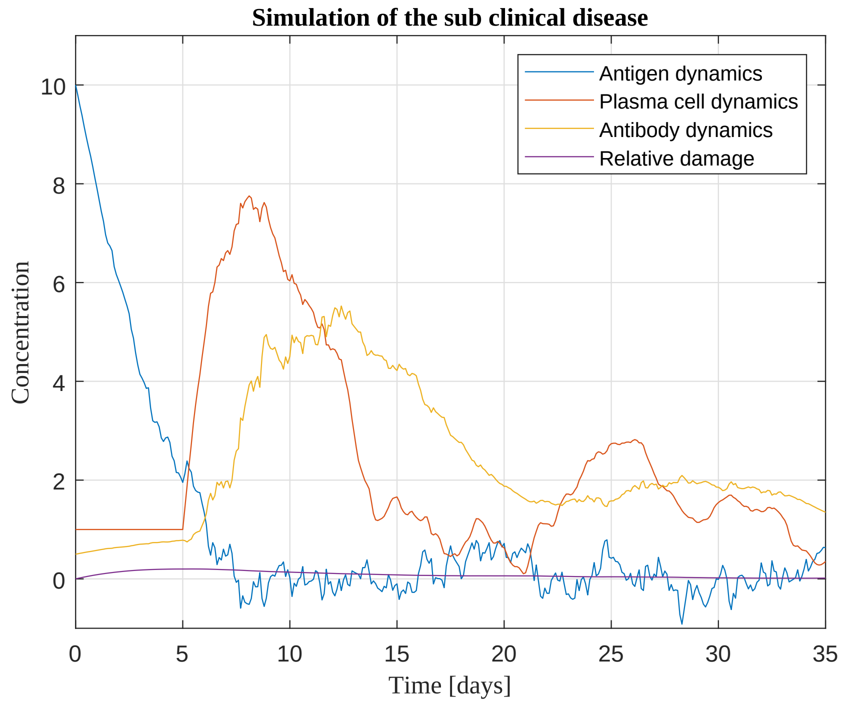

Figure 1: Sub clinical form. [own source]

4.3.6 Simulation of the Acute Form

The initial amount of antigen $V(0)$ meets the inequality

$$0 \leq V(0) \leq \frac{\mu_F(\gamma F(0) - \beta)}{\beta\eta\gamma} = V_{IB},$$

where V_{IB} is called an immunological barrier. We simulate the acute form for an antigen reproduction rate $\beta = 0.6$, initial dose of antigens $V(0) = 0.01$ and $\vartheta = 0.2$, see Figure 2.

The organism is infected by the initial amount of pathogens $V(0) < V_{IB}$, the disease does not develop, the number of antigens converges over time to 0 and the affected organ is restored and the organism is cured.

4.3.7 Simulation of the Chronic Form

The solution is asymptotic stable for $\alpha \to \infty$, for the following inequalities $\mu_C \leq 1$ and

$$0 < \beta - \gamma F(0) < \left(\tau + \frac{1}{\mu_C + \mu_F}\right)^{-1}.$$

We simulate the chronic form of disease for an antigen reproduction rate $\beta = 0.95$, initial dose of antigens $V(0) = 0.00001$ and $\vartheta = 0.15$, see Figure 3.

After the sharp initial antigen growth, most of them is exterminated. However, after a while, the disease is returned and the antigen population converges to an equilibrium state by inhibited oscillations.

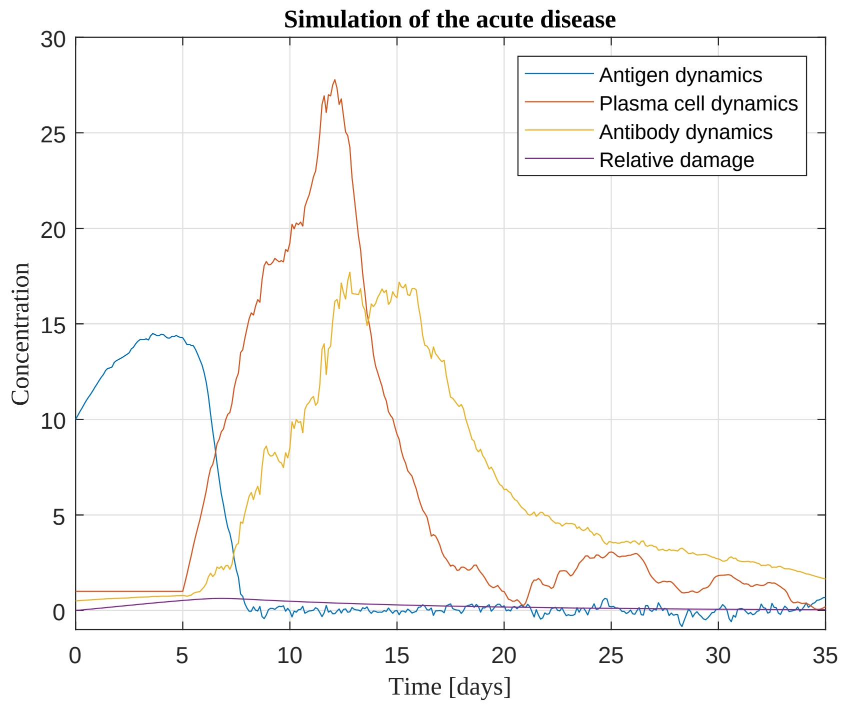

Figure 2: Acute form. [own source]

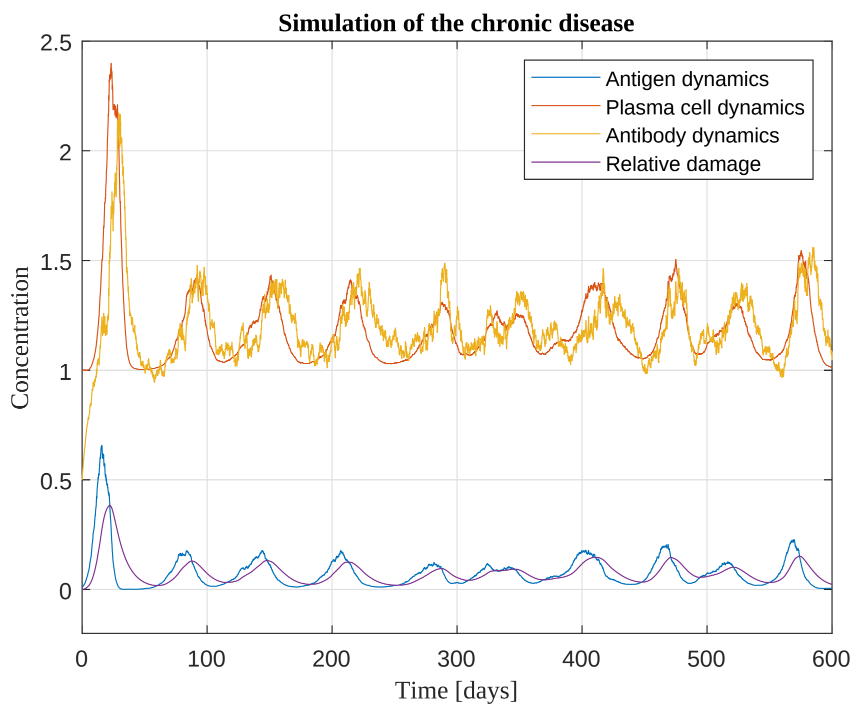

Figure 3: Chronic form. [own source]

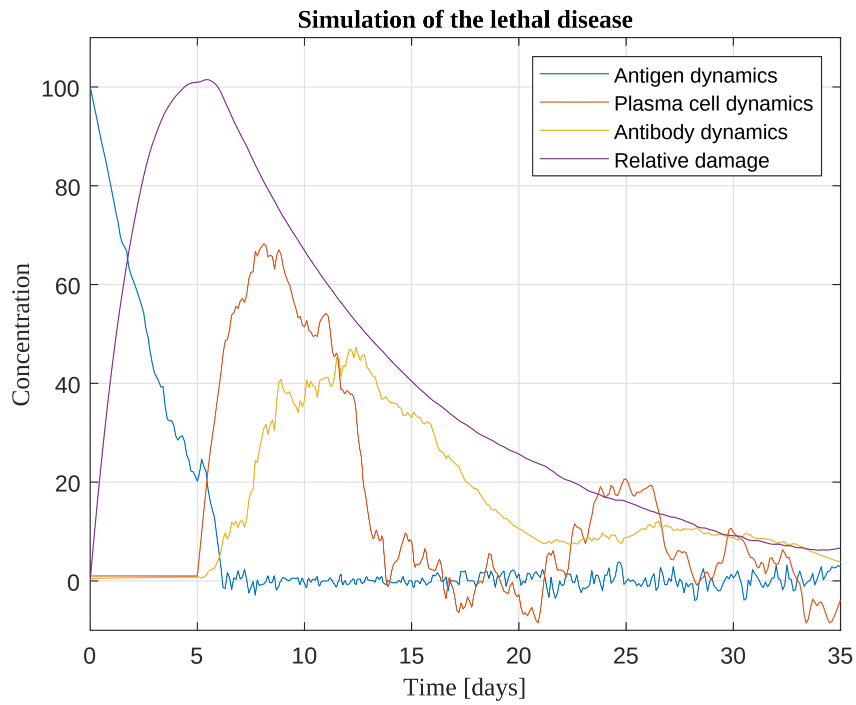

Figure 4: Lethal form. [own source]

4.3.8 Simulation of the Lethal Form

At last, we get to the course of diseases ending lethally. The organism (organ) failure may be caused by too high initial dose of antigens, too high growth speed of antigens or lower antibody production. In this short version of thesis, we present only the first case.

The first case, we simulate the lethal form of disease for an antigen reproduction rate $\beta = 0.2$, initial dose of antigens $V(0) = 0.1$ and $\vartheta = 0.2$, see Figure 4.

The organism is exposed to too high the initial dose of antigens $V(0)$, while the initial level of antibodies $F(0)$ and plasma cells $C(0)$ in the body is small compared to the antigen's dose. Antigens are not promptly removed from the organism and the immune system delay leads to organism failure.

5 Conclusion

Mathematical modeling is a discipline which deals with the mathematical description of phenomena around us. If we want the model to be as faithfully as possible, we need to improve it. And it is the precise moment of stochastic modeling which can approach the reality with a certain probability by extending the deterministic system to a random process.

The basis of understanding the stochastic structure is to be well acquainted with the basic concepts, including Brownian motion, which was first observed at the beginning of the 19th century as a random movement of pollen grains in water. At the beginning of the 20th century the essence of this phenomenon was elucidated by Albert Einstein, based on kinetic theory of matter. Since then, stochastic theory has experienced unprecedented development, especially in the last 60 years, and today we are able to describe a random process using stochastic differential equations based on Itô integral.

Based on the theory of stochastic differential equations and systems, a solution of the stochastic equation with Brownian motion was found. A solution of stochastic modeling can be found in four positions. If the system after deviation depending on the initial conditions converge to its original position, we say that the system is stable. If the system after deviation converges to a different equilibrium position, then we say that the system is stochastically stable. However, there may also be situation when the system after deviation does not return or remain in a deviation position. Then we say that the system is unstable. The main part of the thesis was therefore not only the search for a suitable solution of the stochastic equation or the stochastic system, but also the search for a general formula for determining the stability of the solution of the given stochastic equations or systems of the orders 3 and 4. It is necessary to state that it is possible to study systems of orders higher than 4, but it is mainly a programming issue.

Stochasticity is unavoidable when considering biological systems and processes, both at the macro scale with populations surviving in rapidly and unpredictably changing environments, but also and especially at the molecular level, where entropic considerations can have significant implications. Not only must systems be robust but some systems actually rely upon Brownian motions in order to operate efficiently. Therefore, the final part of the thesis is devoted to the application of the stochastic process to the biomedical model. There is simulated the immune system's response to infection. The deterministic model was extended about Brownian motion and four types of immune response reactions were observed (sub clinical, acute, chronic and lethal form). The subject of another study may be a simulation of a delayed model for the body's immune response to the use of drugs, which takes time to manifest. An interesting topic of another study may also be the hyper-toxic form of the viral disease and its associated epidemic.

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There are selected from a total of 13 author's publications:

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Languages

Czech, English, Slovak, Russian - basic

Abstract

In the presented dissertation is defined the stochastic differential equation and its basic properties are listed. Stochastic differential equations are used to describe physical phenomena, which are also influenced by random effects. Solution of the stochastic model is a random process. Objective of the analysis of random processes is the construction of an appropriate model, which allows understanding the mechanisms. On their basis observed data are generated. Knowledge of the model also allows forecasting the future and it is possible to control and optimize the activity of the applicable system. In this dissertation is at first defined probability space and Wiener process. On this basis is defined the stochastic differential equation and the basic properties are indicated. The final part contains biology model illustrating the use of the stochastic differential equations in practice.

Abstrakt

V předložené práci je definována stochastická diferenciální rovnice a jsou uvedeny její základní vlastnosti. Stochastické diferenciální rovnice se používají k popisu fyzikálních jevů, které jsou ovlivněny i náhodnými vlivy. Řešením stochastického modelu je náhodný proces. Cílem analýzy náhodných procesů je konstrukce vhodného modelu, který umožní porozumět mechanismům, na jejichž základech jsou generována sledovaná data. Znalost modelu také umožňuje předvídání budoucnosti a je tak možné kontrolovat a optimalizovat činnost daného systému. V práci je nejdříve definován pravděpodobnostní prostor a Wienerův proces. Na tomto základě je definována stochastická diferenciální rovnice a jsou uvedeny její základní vlastnosti. Závěrečná část práce obsahuje biologický model ilustrující použití stochastických diferenciálních rovnic v praxi.