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Analysis of Dynamic Models of Epidemic

Abstract. *The paper presents and compared the dynamic models of the epidemic. The spreading of epidemic is described by the set of differential equations. Two models presenting different complexity are analyzed and compared. The simplest one recognizes only three classes of individuals (susceptible, infected and recovering). The second one takes into account also the dynamic changes of the diseased individuals, inoculations and quarantine. The results of numerical experiments concerning both models are presented and discussed. The results of analysis have been used in developing the optimization method of identification of the parameter values of the numerical model.*

Streszczenie. *Praca przedstawia modele rozprzestrzeniania się epidemii przy użyciu układu równań różniczkowych. Dwa rozwiązania o różnej złożoności są poddane analizie i porównaniu. Model najprostszy uwzględnia jedynie 3 klasy osobników: zdrowi, ale wrażliwi na zachorowanie, zakażeni (chorzy) oraz klasa osobników, którzy są odporni na zakażenie po przebytej chorobie. W modelu bardziej złożonym rozróżnieniu podlegają osobnicy zakażeni oraz ci, którzy w wyniku zakażenia zachorowali. Uwzględnia się również kwarantannę oraz szczepienia ochronne. Praca przedstawia wyniki symulacji procesu rozprzestrzeniania się ospy w obu modelach. Na podstawie wyników analizy zaproponowano metodę optymalizacyjną identyfikacji parametrów modelu umożliwiającą przewidywanie z góry przebiegu epidemii.(**Analiza dynamicznych modeli rozprzestrzeniania się epidemii**).*

Słowa kluczowe: modelowanie, rozprzestrzenianie się epidemii, procesy dynamiczne, identyfikacja parametrów.
Keywords: modeling, epidemic, dynamic processes, parameter identification.

Introduction

Epidemic is understood as an outbreak of an infectious disease affecting a disproportionately large number of individuals in a population, community or region within a short period of time [1], [2], [7]. The way to examine the possible impact of different control scenarios is to use the proper mathematical models of spreading the epidemics. Such models may be used to answer some very important questions regarding many problems, such as what fraction of the population should be quarantined or vaccinated, how fast the control measures should be implemented, what is the predicted time of the maximum number of infected individuals and many others [1], [3].

The mathematical models should take into account the dynamics of the process; hence the differential or difference equations are applied in mathematical description [8]. The complexity of such models may vary a lot. The simplest models cannot capture the complexity of epidemics and their dynamics. On the other side the complex models are intransparent, more difficult in interpretation and difficult in identification of their parameters.

The first epidemic research limited to studying the number and causes of deaths were investigated in seventeen century. The earliest works of mathematical models describing the process of disease spreading were initiated in eighteen century by Daniel Bernoulli. He created a mathematical model to defend the practice of inoculating against smallpox. He tried to convince the population of the country that universal inoculation would increase the life expectancy. Nowadays, modeling of epidemic spreading is an important direction of research in epidemiology [4], [6], [8].

Fundamental notions of epidemic process

The real nature of the epidemics is purely stochastic with infection treated as an element of chance. However, in its simulation the deterministic dynamic models are mainly used. In these models the individuals forming the population are assigned to different subgroups, each representing a specific stage of the epidemic [2]. The typical classes of individuals used in modeling include:

- susceptibles, the individuals who are susceptible to infection,
- infectious, who are capable of spreading the disease,
- recovering, who are treated as immune to infection in further period of analysis.

All susceptibles are equal at risk of infection and all births are automatically counted as susceptible. The flow of individuals exist between the susceptible and infectious and between infectious and immune.

It is generally assumed that susceptible individuals contract the disease only by getting in contact with the infected. Also, the cured individuals are usually immune to infection. The time constants of the disease spreading depends on the nature of epidemic.

The transition rates from one class to another are mathematically expressed as derivatives, hence the model is fully described by the set of differential equations. In building such model we assume that the population size is differentiable with respect to time and that the epidemic process is deterministic [4], [8].

Simple dynamic model

In the simplest dynamic model we assume the existence of only three classes of individuals: susceptible, infectious and recovering. In further considerations we assume the following assumptions.

The starting population formed ny healthy, but susceptible might be increased by immigration. The assumed immigrant population is equal m, from which αm represents the healthy part and the remaining part $(1\text{-}\alpha)m$ represents infected.

The disease is spread through the contact of the susceptible individual and the infective with the transmission rate *c*. The individuals who contracted the disease and recovered are immune to infection in further stages of process.

Let us denote by x_1 the number of susceptible, x_2 the number of infected and x_3 the number of immune individuals. Additionally, we assume that the immigration rate α of healthy individuals is known. The infection rate c is related to the average time constant of the disease and is also known. The recovery rate v is related to the average time constant of recovery. All of them will be calculated per week. The population m of the immigrants to the considered region of the country will be also referred to the week. Taking into account the given above assumptions we can

write the following system of differential equations describing the process of epidemic spreading

$$\begin{aligned} \frac{dx_1}{dt} &= \alpha m - c x_1 x_2 \\ \frac{dx_2}{dt} &= c x_1 x_2 - \nu x_2 + (1-\alpha) m \\ \frac{dx_3}{dt} &= \nu x_2 \end{aligned} \tag{1}$$

In this model we have assumed the simplest nonlinear interactions between infected and susceptible in the form of product x_1x_2. The typical values of the coefficients related to smallpox taken into account in our experiments were: α=0.9, ν=0.15, transmission parameter c=2.25E-8. The Simulink [5] implementation model of these equations is presented in Figure 1.

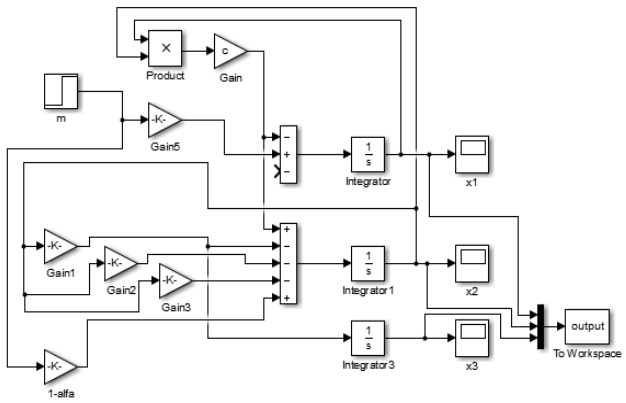

Fig. 1. Simulink model of the epidemic described by equation (1)

Figure 2 illustrates the numerical results of simulation at three different initial conditions of infected: $x_2(0)$=100, $x_2(0)$=1000, $x_2(0)$=10000 and m=2500 individuals per week at the initial population of susceptible equal $x_1(0)$=10000000.

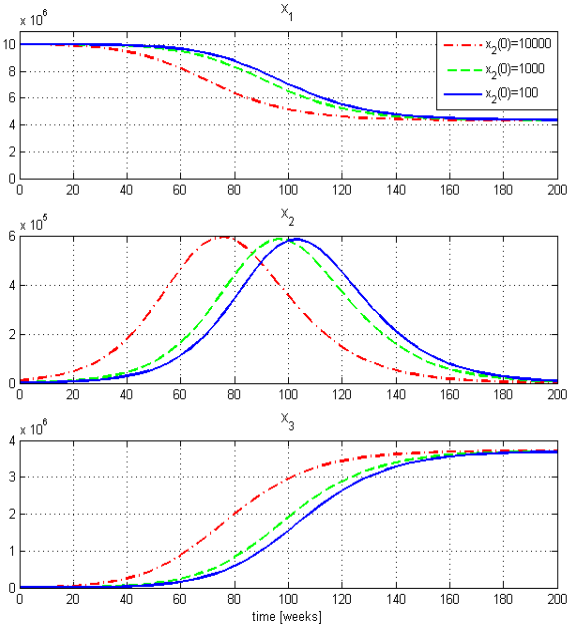

Fig. 2 The change of the population of susceptible, infected and recovered as a function of time

Figure 3 shows the dynamics of the epidemic spreading on the x_1-x_2 plane. We can observe the point corresponding to the highest population of infected (the peak point in epidemic). The maximum number of infected individuals is dependent on their initial values (the higher initial value the larger number of infected). On the other side the peak of infected appears practically at the same number of susceptible individuals.

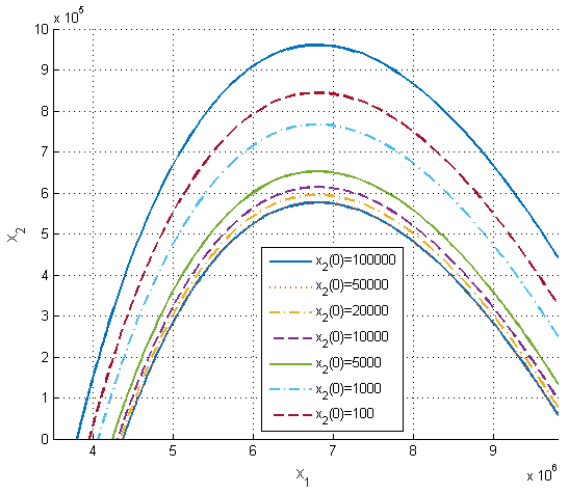

Fig. 3. The illustration of the epidemic spreading on the x-y plane at various initial conditions of infected

Complex dynamic model

In the epidemic processes we can observe more complex mechanisms. Disease may not appear at a time the host is infected. Hence the incubation period should be also included in the model. The host infected with pathogen is infectious after a period of latency. The infected host may experience immune period, but is still a carrier and capable of transmitting disease to others. The infectious period is a duration of time within which the host is able to transmit the disease to other individuals. Some infected may be also isolated from the population (quarantine). If vaccine exists, the individuals receiving the vaccine pass automatically from susceptible to recovered individuals.

In more complex model of epidemics we have made the following assumptions.

- Initial population consists entirely of susceptible individuals, who may contract the disease through contact with sick as in the simplest epidemic model.
- The infection may be introduced by immigration from outside, a fraction of which is sick.
- Outbreak of epidemic disease is recognized after a specific period of time immediately followed by a cassation of immigration.
- After recognizing existence of epidemic, part of the susceptible individuals is inoculated with a vaccine making them immune to this particular disease.
- Starting at the time inoculation begins, a portion of sick or become sick later are separated from the general population by quarantine.
- Sick individuals either recover and become immune to the disease, or die.

As a result of these assumptions the following classes of individuals have been introduced:

$x_1=x_1(t)$ – population of susceptible individuals at time t
$x_2=x_2(t)$ – population of infected individuals at time t
$x_3=x_3(t)$ – population of immune individuals at time t
$x_4=x_4(t)$ – population of diseased individuals at time t
$x_5=x_5(t)$ – number of sick individuals quarantined from the whole population at time t
$s=s(t)$ – the total number of infected individuals
m – rate of immigration at time t
n – rate of inoculations of susceptibles at time t

Figure 4 illustrates the general transition diagram among the introduced classes of individuals: immigrants, susceptibles, infected, immune, quarantined and diseased.

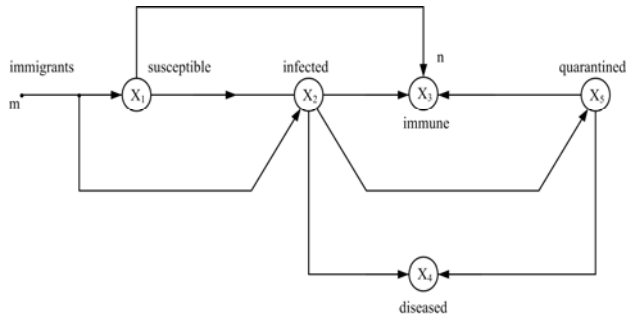

Fig. 4. The transition diagram representing flow of signals among five classes of individuals

The above assumptions have resulted in the following system of differential equation of the model [4], [7].

$$
\begin{aligned}
\frac{dx_1}{dt} &= -cx_1x_2 + \alpha m - n \\
\frac{dx_2}{dt} &= cx_1x_2 - a_{24}x_2 - a_{23}x_2 - a_{25}x_2 + (1-\alpha)m \\
\frac{dx_3}{dt} &= a_{23}x_2 + a_{53}x_5 + n \\
\frac{dx_4}{dt} &= a_{24}x_2 + a_{54}x_5 \\
\frac{dx_5}{dt} &= \begin{cases} 0 & 0 \le t \le t_0 \\ a_{25}x_2 - a_{53}x_5 - a_{54}x_5 & else \end{cases} \\
\frac{ds}{dt} &= (1-\alpha)m + cx_1x_2
\end{aligned}
\tag{2}
$$

The coefficient a_{23} represents the ratio of the population of infected people becoming immune, a_{24} – the ratio of infected who are sick, a_{25} the quarantine ratio among infected, a_{53} the immune ratio among quarantined, a_{54} the ratio of sick people among the quarantined.

The Simulink diagram implementing the above system of differential equations is presented in Figure 5. In the numerical experiments we have assumed the typical data corresponding to the smallpox [4].

The values of model parameters were as follows [8]: a_{23}=0.1 per week, a_{24}=0.003 per week, a_{25}=0.05 per week, a_{53}=0.1 per week, a_{54}=0.003 per week, α=0.9, c=2.25E-8 per people/week. The following initial values of the investigated variables have been assumed in the simulations: $x_1(0)$=10000000, $x_2(0)$=100, 1000 and 10000, $x_3(0)$=0, $x_4(0)$=0, $x_5(0)$=0.

The population of the immigration per week, taken in experiments was equal 2500 people. We have considered the influence of the inoculation on the process of epidemic spreading. Few cases are investigated: no inoculation $n(0)$=0 and $n(0)$= 5000, 10000 and 15000 inoculations per week, starting after a period of t_0 (in experiment this period was equal 8 weeks).

Figure 6 presents the time changes of 6 mentioned classes of populations at three initial conditions of $x_2(0)$ when no inoculations have been introduced. We can see, that the initial number of infected plays an important role in spreading the epidemic. The larger is this number the quicker progress of the epidemic spreading. However, the interesting point is that in all cases of initial conditions the epidemic ends at similar number of susceptible, who were not infected.

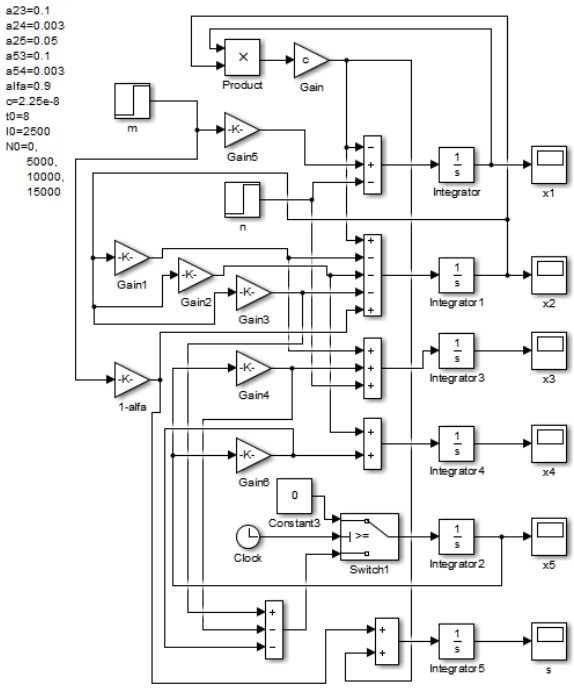

Fig. 5. The Simulink diagram implementing the complex model of epidemic described by eq. (2)

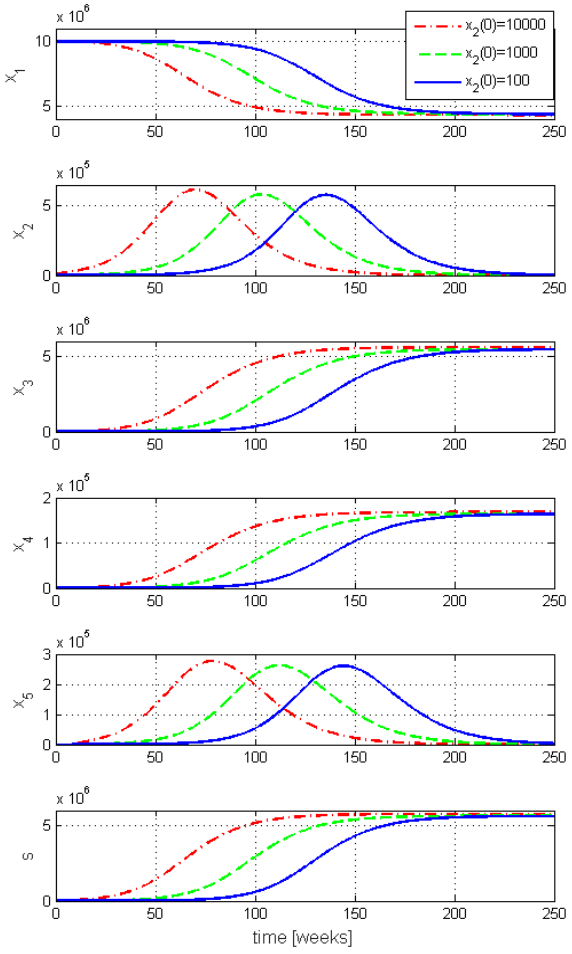

Fig. 6. The process of spreading the epidemic at different initial population of infected and no inoculations

In the next step the influence of the inoculations has been investigated and the corresponding curves presenting the process of spreading the epidemic as a function of

inoculations are studied. Figure 7 depicts the results corresponding to different rates of inoculations per week: $n(0)$=0, 1000, 10000 and 15000 and for constant initial population of infected equal 1000. They show the reduced number of infected and sick individuals after inoculation. The higher is the number of inoculated the higher its influence on the epidemic process. The peak number of sick people has been reduced more than twice after introducing the limited inoculations (15000 per week) in the population of 10000000.

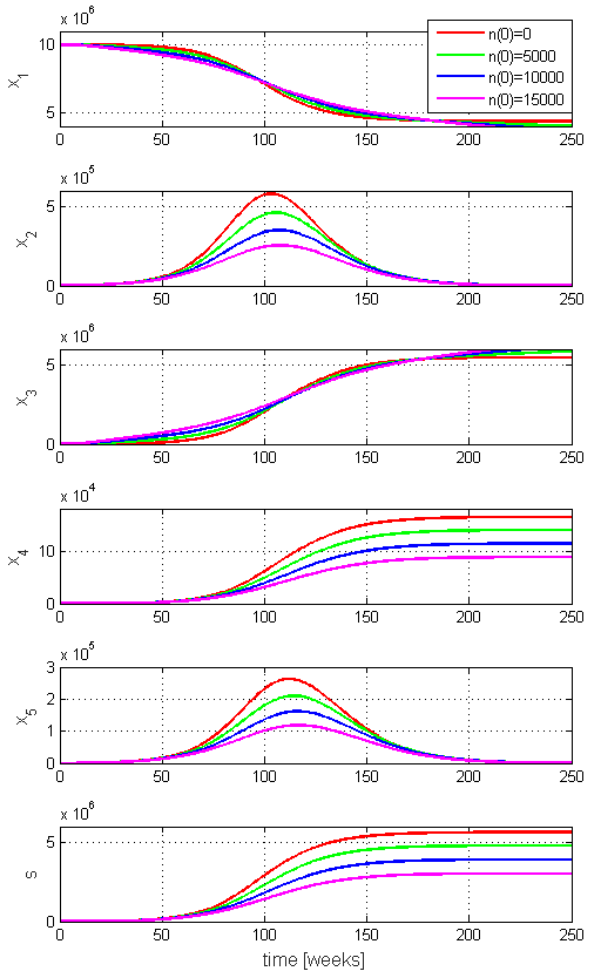

Fig. 7. The process of spreading the epidemic at different initial number of infected and different number of inoculations per week $n(0)$=0, 5000, 10000 and 15000

Identification of model parameters

The results of analysis of the epidemic process enable making the identification of the parameters of its mathematical model. This task has been solved by applying the optimization method, minimizing the discrepancy betwen the results of the model and the real process. The optimization problem might have many local solutions due to the nonlinearity of the model (multimodal optimization problem). The genetic algorithm, which is able to find global minimum, was used in the solution of this task. In further experiments both epidemic models were considered. The objective function subject to the minimization was defined in the first model on the basis of x_1 (susceptible), x_2 (infected) and x_3 (immune) individuals in the following way

$$\min_{\alpha,c,v} E = \frac{1}{2}\sum_{n=1}^{p}\sum_{i=1}^{3}\left(x_i(n) - d_i(n)\right)^2 \tag{3}$$

The index n denotes the number of measured time points (n=1, 2, ..., p) of the curve. The respective destination values of the real process were denoted by $d_i(n)$. In the experiements we have generated them using the known model of epidemy of the following parameter values: α=0.9, c=2.25e-08, v=0.15 and different initial conditions of the process.

The genetic algorithm was applied with the following parameters: population 30, no of generations 50, crossover coefficient 0.85, mutation coefficient 0.02, roulette wheel used in selecting the parents for future generations. The optimized parameters are composed of two variables: α, v and c. On the basis of practical experience it is possible to set the feasible parameter ranges for both optimized variables. The specified parameter values have fallen within their respective bounds as shown below

$$\begin{aligned} 0.5 &\le \alpha \le 1 \\ 10^{-5} &\le c \le 5\cdot 10^{-5} \\ 0.05 &\le v \le 0.3 \end{aligned}$$

The typical run of the genetic algorithm is well characterized by the change of the objective function in the succeeding generations as presented in Figure 8. The best objective functions corresponding to individual and the mean value of all chromosomes are demonstrated.

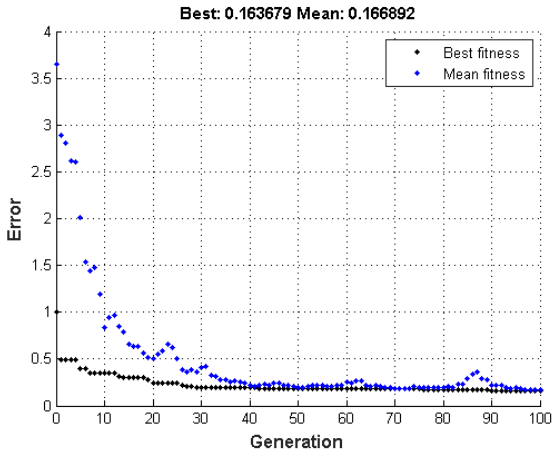

Fig. 8. The change of the objective function as a function of generations (the best individual and mean objective function of the population)

As a result of application of the genetic algorithm we have got the following estimated values of the optimized parameters of the model: α=0.892, c=2.192e-08 and v=0.148. They are in good agreement with the real values.

Figure 9 presents the results of the genetic optimization procedure in reconstruction of the time curves. The actual curves $x_1(t)$, $x_2(t)$ and $x_3(t)$ representing the model are very close to their destinations. The errors (the difference between the estimated and destination values of all curves) are presented in the bottom of the appropriate figures. In the most time regions their values are very small with respect to their destinations (below 2%). The average percentage error calculated for all curves and points of time related to their appropriate destinations was also very small (below 1%).

The next experiments have been done for the complex model described by system of equations (2). The optimized parameters are now: a_{23}, a_{24}, a_{25}, a_{53}, a_{54}, α *and* c. The genetic algorithm was applied once again and the objective function under minimization was defined in the same way as in the previous experiment, however, this time all five variables x_1 (susceptible), x_2 (infected), x_3 (immune), x_4 (diseased) and x_5 (sick quarantined) individuals have been taken into account.

(4) $$\min E = \frac{1}{2}\sum_{n=1}^{p}\sum_{i=1}^{5}\left(x_i(n)-d_i(n)\right)^2$$

The destination values for all variables have been generated by using the mathematical model presented in the previous chapter with known parameters of the epidemy (the same as these used in analysis). The following lower (L) and upper (U) limits for the optimized parameters α, v, c, a_{23}, a_{24}, a_{25}, a_{53} and a_{54} have been assumed:

L=[0.5 0.05 1e-8 0.01 0.0001 0.01 0.01 0.0001]
U=[1 0.2 5e-8 0.5 0.05 0.5 0.5 0.2]

As a result of application of the genetic algorithm we have obtained the following estimated values of the parameters of the process model: α=0.994, v=0.170, c=2.389e-08, a_{23}=0.109, a_{24}=0.0034, a_{25}=0.055, a_{53}=0.101, a_{54}=0.0028. They are well compatible with their real values used in generating the destinations, providing good fit to the appropriate destinations.

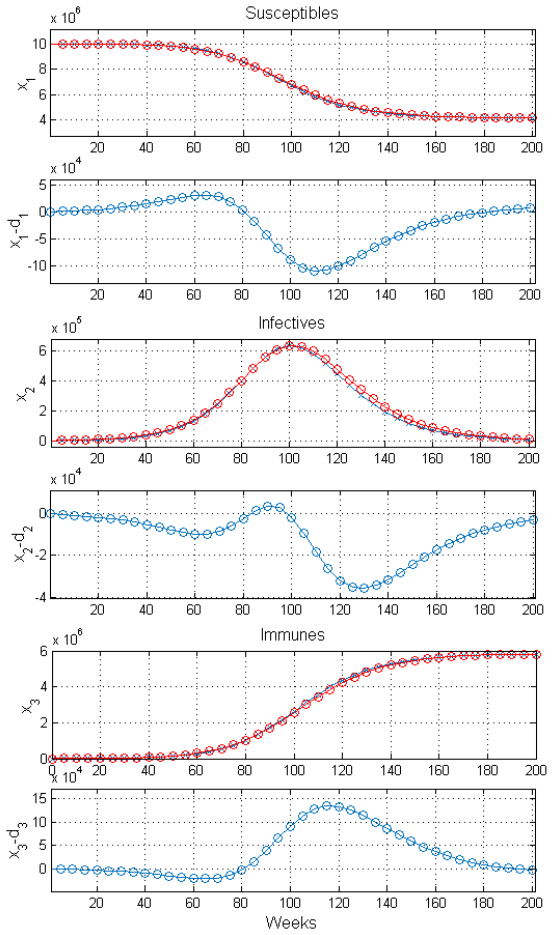

Fig. 9. The real (red color) and the estimations of x_1, x_2 and x_3 (represented by blue color) made by the model in the epidemic process and their appropriate errors of estimation (the changes within time of analyzed epidemic process)

The curves representing the obtained changes of all optimized variables (from x_1 to x_5) are in good agreement with the corresponding destinations. Table 1 presents the mean percentage discrepancy between corresponding estimated and destination curves within the analyzed time span, used in an optimization process. It was defined on the basis of norms as following

(5) $$\varepsilon_i = \frac{\|\mathbf{x}_i - \mathbf{d}_i\|}{\|\mathbf{d}_i\|}\cdot 100\%$$

for i=1, 2, 3, 4 and 5, where $\boldsymbol{x}_i$ and $\boldsymbol{d}_i$ represent estimated and destination values, respectively, of i-th variable gathered in the form of vectors.

Table 1. The mean percentage discrepancy between the corresponding estimated and destination curves for all types of individuals

ε_1	ε_2	ε_3	ε_4	ε_5	ε_{mean}
0.82%	0.88%	1.30%	1.28%	4.14%	3.27%

The total mean percentage error ε_{mean} (the average of the mean errors between the estimated and destination values for all types of individuals) assumes also small value (below 4%).

Conclusions

The paper has presented the study concerning modeling of epidemic. Two differential models of epidemic spreading have been analyzed: the simplest one recognizing only three classes of individuals (susceptible, infected and recovering) and more complex one, taking into account also the diseased individuals and quarantined. The results of numerical simulation of both models have been presented and compared.

The obtained results create the basic step for the inverse problem, in which on the basis of the observed dynamics of the epidemic the identification of the parameters used in the model is done. This task was solved by the genetic algorithm. The results obtained for the simple and complex models are very encouraging and prove their usefulness in identification of parameters of the epidemic models. They might be used in predicting the details of epidemic process in the future.

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