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STABILIZING THE SYSTEM IN THE PROBLEM OF EPIDEMIC SPREAD LIMITED TIME OF IMMUNIZATION

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Abstract. A mathematical model of the epidemic development under conditions of limited work of immunization acquired both after recovery and through vaccination is considered. The model is characterized by a nonlinear system of differential equations with some equilibrium position. Based on numerical analysis, it is shown that the state of the system stabilizes after some time and tends to a state that is the equilibrium position not of the original, but of some simplified system. The results obtained have a natural interpretation.

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1 Introduction

Currently, there are hundreds of mathematical models of epidemiology, see, for example, Bailey (1975); Daley & Gani (1999); Brauer & Castillo (2000); Capasso (2008); Vynnycky & White (2010); Martcheva (2015); Brauer et al. (2019). The vast majority of them involve dividing the entire population into compartments of people characterized by a certain state relative to the epidemic. Models differ among themselves in the selected compartments of people, intercompartment transitions and ways of describing these transitions.

When considering an epidemic over a sufficiently long time interval, one should take into account the vaccination of the population, and the vaccinated are usually allocated to a separate compartment, see, for example, Scherer & McLean (2002); Cai et al. (2018); Ghostine et al. (2021); Parolini et al. (2022); Diagne et al. (2021). In Serovajsky et al. (2022), a mathematical model was proposed for the spread of an epidemic under conditions of vaccination with a limited time spent in compartments, which is an extended (by considering vaccination) version of the mathematical model described in Unlu et al. (2020). Overall, it quite plausibly describes the course of the epidemic over a relatively short period of time, but it has several significant drawbacks.

First, the rate of vaccination in this model is assumed to be constant and independent of the course of the epidemic. In fact, the vaccination process is stimulated by a high level of the disease. The second drawback of this model is the assumption that those who have been ill have lifelong immunity, i.e. never get sick again. In a real situation, over time, the immunity of those

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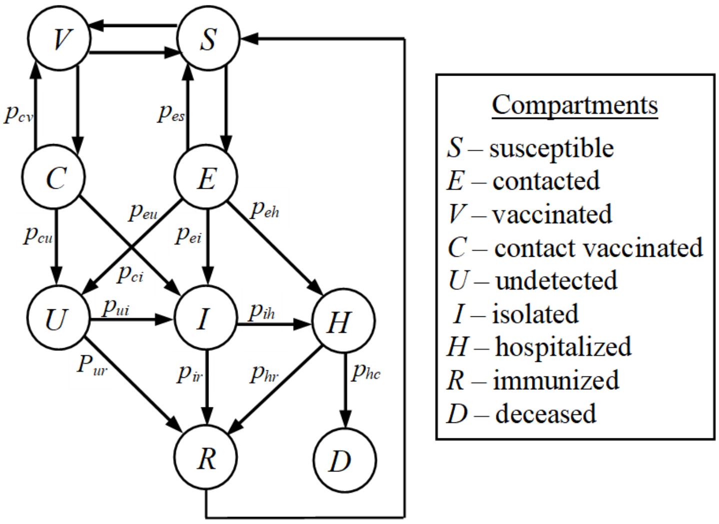

Figure 1: Characteristics of intercompartment transitions

who have been ill decreases. As a result, when considering a system over a sufficiently long-time interval, the possibility of re-infection should be taken into account. Finally, in Serovajsky et al. (2022), the duration of the vaccine is assumed to be unlimited, although in reality the vaccine is valid for a limited time, as a result of which, for more reliable protection of the population, it is desirable to carry out repeated vaccination.

In this paper, we consider a mathematical model in which these shortcomings are eliminated. It is shown that this model has rather interesting properties that are of practical importance.

2 Description of the mathematical model

We consider nine population compartments - susceptible (these include healthy people who may become ill), contact (healthy, who were in contact with sick people), vaccinated (healthy, vaccinated), contact vaccinated (vaccinated, who were in contact with sick people), undetected (infected, in whom the disease has not been officially established; these include patients with an asymptomatic course of the disease, as well as mildly ill patients who have not consulted a doctor), isolated (mildly ill patients undergoing treatment at home); hospitalized (seriously ill, hospitalized); immunized (recovered, immune to the disease) and deceased. In contrast to Serovajsky et al. (2022), here the compartment of recovered patients is replaced by immunized ones, since recovered patients have immunity only for a limited period.

Figure 1 depicts possible intercompartment transitions. In particular, susceptible individuals leave their compartment either by coming into contact with the sick or by vaccination. The vaccinated may leave their compartment either through contact with patients or at the end of the vaccine's validity period. Over time, contacts will either get sick in one form or another, or not get sick at all. Contact vaccinated individuals either fall ill after some time, becoming undetected or isolated, or revert to the regular vaccinated compartment. Any patient recovers after some time, moving into the immunized compartment, or his illness becomes more severe, and hospitalized may die. The immunized eventually lose their immunity, returning to the susceptible compartment.

So, the model assumes that after some limited time, people from all compartments, except for the susceptible and the deceased, leave their compartment, and everywhere in the future, n_x denotes the time spent in compartment X. When characterizing intercompartment transitions, p_{xy} denotes the proportion of people from compartment X who are passing over time to compartment Y. Naturally, the sum of all the shares of people leaving this compartment will be equal to 1, which for the adopted system of intercompartment transitions, this corresponds to the equalities

$$\begin{aligned} p_{es}+p_{eu}+p_{ei}+p_{eh}&=1,\\ p_{cv}+p_{cu}+p_{ci}&=1,\\ p_{ui}+p_{ur}&=1,\\ p_{ih}+p_{ir}&=1,\\ p_{hr}+p_{hd}&=1. \end{aligned} \tag{1}$$

The number of susceptible in this case decreases due to contacts with patients and vaccination, increases due to the fact that some of the people who have been in contact with patients in the past do not get sick, and also due to the fact that over time, the vaccine expires, and in those who have been ill, the effect of immunity ends. These processes are characterized by the equation

$$\frac{dS(t)}{dt}=-\frac{\kappa_u U(t)+\kappa_i I(t)}{N}S(t)-\frac{v_h H(t)+v_i I(t)}{N}S(t)+p_{es}\frac{E(t)}{n_e}+\frac{R(t)}{n_r}+\frac{V(t)}{n_v}. \tag{2}$$

Here, the rate of decrease of susceptible patients due to contacts with patients (the coefficient before S in the first term on the right side of the equation) is proportional to the number of undetected and isolated patients (hospitalized patients are under medical supervision and are not considered sources of infection). At the same time, the contagiousness coefficient κ_u for undetected exceeds similar ratio κ_i for isolated patients, since it is the unidentified patients that serve as the main source of infection. The division by the number N of the entire population is carried out here for reasons of normalization, as in other models of epidemiology (Bailey, 1975; Daley & Gani, 1999; Brauer & Castillo, 2000; Capasso, 2008; Vynnycky & White, 2010; Martcheva, 2015; Brauer et al., 2019; Scherer & McLean, 2002; Cai et al., 2018; Ghostine et al., 2021; Parolini et al., 2022; Diagne et al., 2021; Serovajsky et al., 2022; Unlu et al., 2020). The rate of decrease in the number of susceptibles due to vaccination (the coefficient in front of S in the second term on the right side of the equation) is proportional to the number of hospitalized and isolated patients, since it is the high level of the disease that stimulates people to be vaccinated, and hospitalized to a greater extent than isolated ones, which corresponds to the ratio between coefficients of proportionality $\nu_i < \nu_h$. Unidentified patients do not affect the rate of vaccination due to the lack of information about them. The last three terms on the right side of the equation characterize the return of susceptible people from other compartments to this compartment. Moreover, the more people in this compartment and the less time people stay in this compartment, the more of them will come to the susceptible compartment per unit of time.

The increase in the number of vaccinated is due to the vaccination of the susceptible and the return to this compartment after some time of those contact vaccinated who did not get sick, and their decrease occurs due to contacts with infection and the expiration of the vaccine. By analogy with formula (2), we obtain the equation

$$\frac{dV(t)}{dt}=\frac{v_h H(t)+v_i I(t)}{N}S(t)+p_{cv}\frac{C(t)}{n_c}-\frac{\kappa_u U(t)+\kappa_i I(t)}{N}V(t)-\frac{V(t)}{n_v}. \tag{3}$$

The change in the number of both contact compartments is growing due to contacts of susceptible and vaccinated with patients, decreases due to the limited time spent in compartments. The result is the equations

$$\frac{dE(t)}{dt}=\frac{\kappa_u U(t)+\kappa_i I(t)}{N}S(t)-\frac{E(t)}{n_e}, \tag{4}$$

$$\frac{dC(t)}{dt}=\frac{\kappa_u U(t)+\kappa_i I(t)}{N}V(t)-\frac{C(t)}{n_e}. \tag{5}$$

The number of undetected increases due to undetected disease of both contact compartments and decreases due to the limited time spent in the compartment, which gives the equation

$$\frac{dU(t)}{dt} = p_{eu}\frac{E(t)}{n_e} + p_{cu}\frac{C(t)}{n_e} - \frac{U(t)}{n_u}. \tag{6}$$

The number of isolated increases due to the disease in isolated form in both contact compartments and the detection of the disease in some of the undetected, and decreases due to the limited time spent in the compartment, which corresponds to the equation

$$\frac{dI(t)}{dt} = p_{ei}\frac{E(t)}{n_e} + p_{ci}\frac{C(t)}{n_c} + p_{ui}\frac{U(t)}{n_u} - \frac{I(t)}{n_i}. \tag{7}$$

The number of hospitalized increases due to the appearance of a severe form of the disease in some of the contacts and the hospitalization of some isolated ones and decreases due to the limited time spent in the compartment, i.e.

$$\frac{dH(t)}{dt} = p_{eh}\frac{E(t)}{n_e} + p_{ih}\frac{I(t)}{n_i} - \frac{H(t)}{n_h}. \tag{8}$$

The number of immunized increases due to the recovery of patients of all categories and decreases as they lose their immunity. The number of deceased increases due to the death of a part of the hospitalized. As a result, we obtain the equations

$$\frac{dR(t)}{dt} = p_{ur}\frac{U(t)}{n_u} + p_{ir}\frac{I(t)}{n_i} + p_{hr}\frac{H(t)}{n_h} - \frac{R(t)}{n_r}, \tag{9}$$

$$\frac{dD(t)}{dt} = p_{hd}\frac{H(t)}{n_h}. \tag{10}$$

Differential equations (2) - (10) with coefficients related by equalities (1) and corresponding initial conditions (all considered functions at the initial moment of time take some non-negative values) constitute the mathematical model of the system being studied.

3 Analysis of the mathematical model

First of all, we note some qualitative properties of the system under consideration.

Theorem 1. *The system has the first integral, which is the sum of all desired functions, and an equilibrium position for which the values of all functions except S and D are equal to zero.*

To prove the first property, it suffices to add equalities (2) - (10) to each other, taking into account conditions (1) and make sure that the sum of the derivatives of all functions will be equal to zero. To prove the second property, all values included in the right-hand sides of differential equations should be equated to zero and the resulting system of algebraic equations should be investigated. In particular, it immediately follows from equation (10) that in equilibrium $H = 0$; then from (8) when E and I are non-negative, it follows that they are also equal to zero, and so on.

The first property means that the size of the entire population (including those who died as a result of the epidemic) does not change over time, which is quite natural, given that we do not take into account here the natural birth and death rates, as well as the contacts of this population with the outside world. This property is common to all models of epidemiology that do not consider the factors given above, see Bailey (1975); Daley & Gani (1999); Brauer & Castillo (2000); Capasso (2008); Vynnycky & White (2010); Martcheva (2015); Brauer et al. (2019); Scherer & McLean (2002); Cai et al. (2018); Ghostine et al. (2021); Parolini et al. (2022); Diagne et al. (2021); Serovajsky et al. (2022); Unlu et al. (2020).

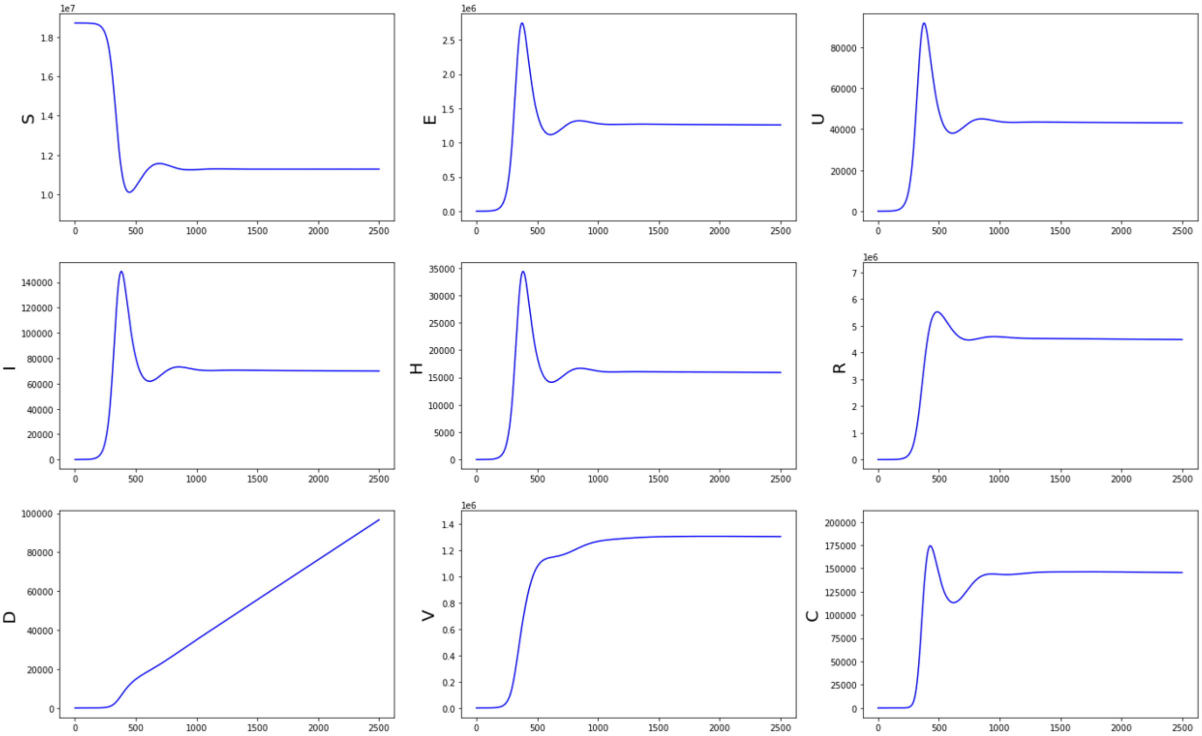

Figure 2: Behavior of the system for "natural" parameter values

According to the second property, only the susceptible and deceased remain in the equilibrium position in the system. The absence of patients indicates that the epidemic is ending. Then the absence of contacts is also inevitable since there will be no contacts with patients. All those who have been ill will eventually lose their immunity. The effect of the vaccine in previously vaccinated people will gradually cease, and there is no incentive for subsequent vaccination due to the absence of cases. Thus, everyone who does not die because of the epidemic will sooner or later move into the category of susceptible.

The calculations were carried out with the following values of the parameters. The total population was assumed to be equal to 18,699,640, which corresponded to the population of Kazakhstan at the time the epidemic began. At the same time, at the initial moment of time, the number of contacts was assumed to be 140, and the rest of the population was classified as susceptible. The number of days spent in compartments took the following values: $n_e = 14$, $n_u = 3$, $n_i = 5$, $n_h = 7$, $n_c = 7$, $n_r = 150$, $n_v = 350$. The contagiousness coefficients were assumed to be equal $\kappa_u = 3.18$, $\kappa_i = 0.171$, while vaccination options $\nu_h = 0.1$, $\nu_i = 0.09$. The following values were chosen for the parameters of intercompartment transitions: $p_{es} = 0.679$, $p_{eu} = 0.154$, $p_{ei} = 0.145$, $p_{eh} = 0.022$, $p_{cv} = 0.9$, $p_{cu} = 0.05$, $p_{ci} = 0.05$, $p_{ui} = 0.03$, $p_{ur} = 0.97$, $p_{ih} = 0.021$, $p_{ir} = 0.979$, $p_{hr} = 0.982$, $p_{hd} = 0.018$. The choice of these parameters is due to expert assessments of specialists, and partially, to the solution of inverse problems for simplified models. The corresponding calculation results are shown in figure 2.

Solutions behave as follows. At first, all functions except S slowly increase while S decreases. Then there is an exponential growth of seven of the considered functions (except for S and D), accompanied by an equally sharp decrease in the function S. At some point in time (approximately at $t = 400$), these functions reach their maximum (and the function S reaches its minimum). After that, damped oscillations of the eight considered functions (except for D) are observed. Starting from some time (approximately at $t = 1000$), the system stabilizes, and the graphs of these functions look like straight lines parallel to the coordinate axis. One gets the impression that the system reaches an equilibrium position, and this situation is typical for the case when the system, which is linearized with respect to the equilibrium state, has 7 negative

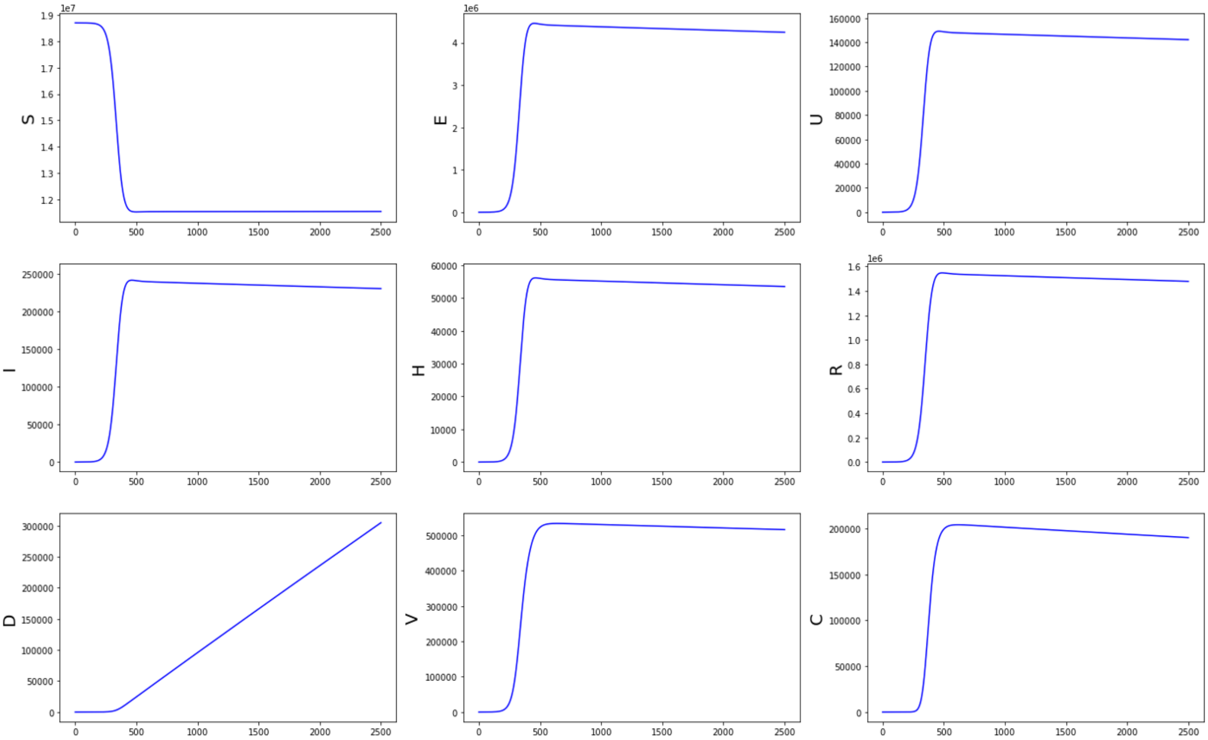

Figure 3: Behavior of the system with reduced parameter values n_r and n_v

eigenvalues and two zero ones.

The result obtained seems paradoxical. First, a qualitatively different behavior of the function D attracts attention, which not only does not reach the equilibrium position, but also grows monotonically, and, judging by the graph, linearly from the moment the system stabilizes. This would be possible if the equation corresponding to this function would have nothing to do with the rest of the system. However, as can be seen from equality (10), the equation for D includes the function H, which is related to the other solutions of the system. Thus, reaching the equilibrium position for the eight considered functions is impossible without a similar behavior of the ninth function. Secondly, it was noted earlier that the system has a first integral, which is the sum of all solutions of the system. As a result, the invariance of the eight considered functions with the monotonous growth of the ninth function is impossible. Thirdly, in accordance with the above theorem, the equilibrium position for the system under consideration is realized only in the case when all values except S and D vanish. At the same time, according to figure 2, the limiting values of all functions turn out to be positive.

It seems that the behavior of the system shown in figure 2 doesn't illustrate the system getting the equilibrium position, but something else. To verify this, let's change the values of the system parameters. Namely, we significantly (by an order of magnitude) reduce the number of days spent in the immunized and vaccinated compartments, assuming $n_r = 15$, $n_v = 35$. These values have no practical significance (loss of immunity in half a month after recovery and termination of the vaccine a month after its administration are completely unrealistic). However, in this case, we are interested in the qualitative behavior of the system, in principle. The results of the calculations are shown in figure 3.

As we can see, the behavior of all functions in figures 2 and 3 did not change significantly. We observe the slow growth of the seven considered functions at the initial stage of the process (with a slow decrease in the function S) again. Then the processes accelerate, and growth becomes exponential, after which these functions reach their maximum (and S - minimum), and at about the same time as the last time. After that, the system also stabilizes (although clearly faster than in figure 2), and the graphs of all functions look like straight lines. As before, the function D since the stabilization of the system is represented as linearly increasing. However, the fundamental difference is that in this case the indicated seven functions are decreasing, and there are no contradictions with the theorem given earlier. Indeed, such behavior of the system (decrease of seven functions, the increase of one of them and the practical invariance of the function S) does not contradict the properties of the first integral of the system, and it can be expected that the decreasing seven functions tend to zero with an unlimited increase in time, which corresponds to the true state of equilibrium of the system. As a result, it can be expected that in figure 2, these seven functions are also decreasing, but the rate of their decrease is so small that it is practically impossible to visually detect this decrease in the estimated time.

However, the question arises what kind of effect we observe in figure 2? What state does the system under consideration enter by the moment of its stabilization? Let us return to the consideration of equation (10), which describes the behavior of the function D, the number of deaths as a result of the epidemic. On the right side of this equality is a non-negative value, initially zero, and subsequently positive. As a result, this function turns out to be monotonically increasing, which is observed in the graphs. However, at the initial moment of time, it is equal to zero, while the function S (the number of susceptible) has the order of 10^7 (the order of the size of the entire population). The growth rate of the D function is equal to the value of the H function (the number of hospitalized, in fact, seriously ill patients), multiplied by the p_{hd} coefficient (mortality rate). However, at the initial stage of the epidemic, there are almost no hospitalized, and even during the peak of the epidemic, this value is on the order of 10^4, which is a fraction of a percent of the total population for the selected set of parameters. In addition, the mortality rate is significantly less than one. Thus, the growth rate of the function D turns out to be extremely small. Accordingly, the system behaves for a long time as if the ninth differential equation does not exist at all. Thus, the growth rate of the function D turns out to be extremely small. As a result, this function has practically no effect on the behavior of the system as a whole over a sufficiently long time interval.

It is natural to ask what happens if we consider the system (1) - (9), i.e. if we exclude equation (10) from consideration altogether? To do this, it is enough to define $p_{hd} = 0$. Then, by the last of equalities (1), we have $p_{hr} = 1$. This means zero deaths from the epidemic, i.e. all those who are sick will recover over time. Note that the system of differential equations (1) - (9) also has a first integral equal to the sum of all (now eight) available functions. How about the equilibrium position? We recall that the justification of the equality to zero in the equilibrium position of seven functions from the system (1) - (10) began with equating the right side of equality (10) to zero, which gave us $H = 0$. After that, with the involvement of other equations, similar results were established for six more functions. In the absence of equation (10), it is impossible to carry out similar reasoning, and the equilibrium position will change significantly. Figure 4 shows the results of calculations for the considered system with zero mortality, while keeping all other parameters unchanged.

Comparing Figures 2 and 4, it can be noted that the behavior of the eight considered functions is practically the same, and only the ninth function, which characterizes the number of deaths and increased earlier, now remains equal to zero. Clearly, the zero-mortality state of the system enters its own equilibrium position. At first, the state of the original system (1) - (10) also enters it, since the ninth function has practically no effect on the system for quite a long time. Distinguishing sufficiently small neighborhood of this state occurs much earlier than the ninth function increases to some significant value. However, the monotonically increasing function D begins to make a noticeable impact (moreover, increasing as it grows) on the behavior of the system over time (but not very soon). And since the system has the indicated first integral, this will inevitably lead to a decrease in the totality of all other functions. As a result, the original system gradually reaches its own equilibrium position, characterized by the equality to zero of the seven considered functions. This is exactly the picture we see on figure 3. Significantly reducing the parameters n_r and n_v, we have significantly accelerated all processes, since now

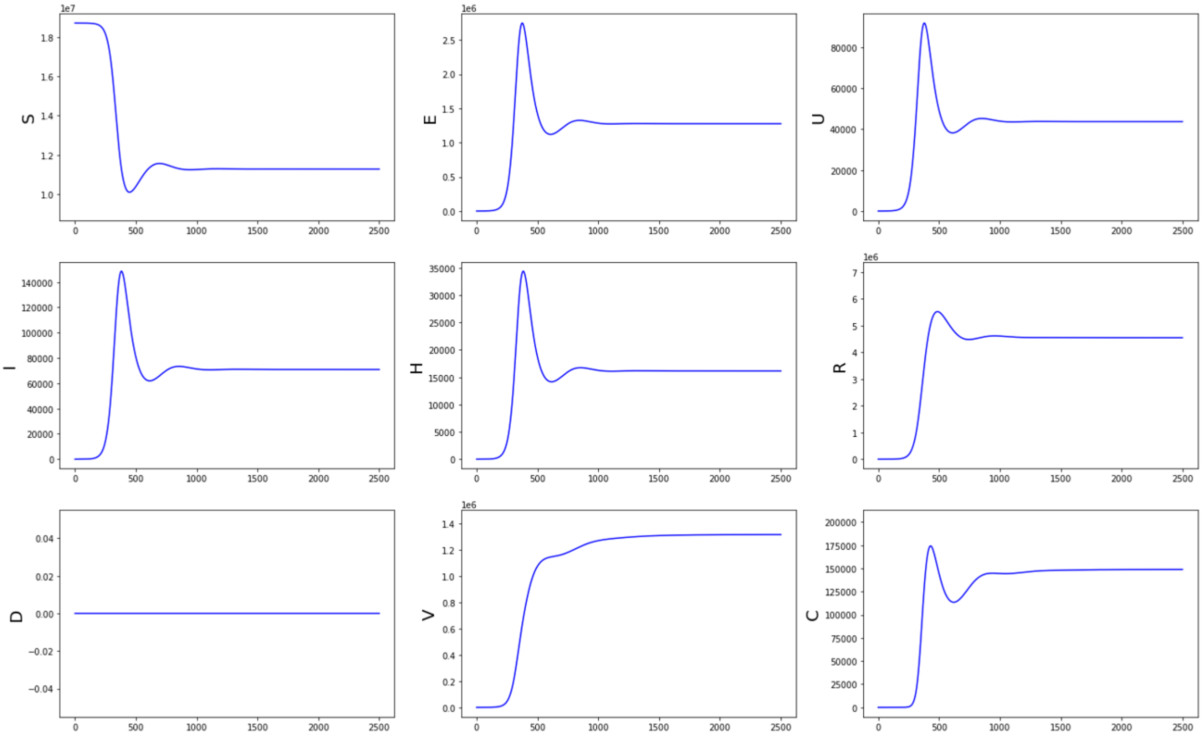

Figure 4: Behavior of the system at zero mortality

those who have been ill and vaccinated lose their immunity much earlier and can get sick. On figure 2, the behavior of the system remains essentially the same, only events develop much more slowly.

It is interesting that the found "approximate position of equilibrium" has a deep practical meaning. After a turbulent course (in our case, after about three years), the epidemic stabilizes at a relatively low level. Someone will still get sick, and someone will die, i.e. the epidemic will remain. This is the property of ordinary epidemics. It is also extremely important that the phenomenon under consideration can be an object of qualitative and quantitative analysis, since the stabilization of system (1) - (10) corresponds to the equilibrium position of the simplified system (1) - (9) with zero mortality. The results obtained can be used to predict the development of the epidemic over a sufficiently long time interval.

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