The influence of accidental physical contacts between individuals on viral infection

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Abstract. The paper is devoted to the results of numerical modelling of non-stationary effects during the spread of a viral infection in a small group of individuals. We are considering the case of the spread of a viral infection by airborne droplets. Two consecutive stages of infection of the body are considered. At the first stage, virions enter the lungs and as a result of viremia are transported to the affected organs. In the second stage, the virions actively replicate in the affected organs. Random movement of individuals in the group changes the local concentration of virions near the selected individual. The random level of virion concentration may be greater than a certain critical value after which the infection of the selected individual will go into an irreversible stage. The main purpose of our work is to illustrate qualitatively new effects that occur in nonlinear systems in a random environment.

1. Introduction
Due to the ease of spread viral infections pose a great danger for biological communities (see, for example, [1]). A viral infection is dangerous not only for people, but also for animals. For example, African swine fever causes huge losses in agriculture and poses a danger to pig farming in general [2]. Infection occurs as a result of getting microdroplets with virions into the lungs. Once in the blood, virions are transported to biological organs, in which there is an intensive increase in the concentration of the virions. An explosive increase in the concentration of the virions occurs when the initial concentration exceeds a certain critical value [3]. The popular three-stage model of infection of the susceptible - infected - recovered type SIR [4] does not take into account many mechanisms of transmission and development of epidemic. Currently, models that take into account random mechanisms of virion transfer are being developed (see, for example, [5 – 10]). The probability of transmission between members of the population is determined by the frequency of contacts between individuals. Therefore, the directions that take into account the formation of small random clusters of individuals are actively developing (see, for example, [11 – 14]. During the active development of the epidemic, there may be infected individuals in the clusters, which randomly change the concentration of virions in the atmosphere. With a random concentration of virions in the atmosphere, the concentration of the virions in the body may exceed a critical value. In addition, random fluctuations in the virion concentration in the atmosphere lead to a monotonous drift of the virion concentration in the body to a critical value, after which the virions begin to multiply violently. Therefore, restrictive measures to reduce physical contacts between members of the population,
established based on the average values of the virion concentration in the atmosphere, may not be sufficient to prevent the development of the epidemic.

The paper proposes a simple mathematical model of the growth of the virion concentration, taking into account the immune response of the body and the transport of virions from the atmosphere to the area of active reproduction of virions. The study of the influence of virion concentration fluctuations in the atmosphere is carried out on the basis of a numerical solution of a system of stochastic ordinary differential equations. It is shown that in a random environment an explosive increase in the concentration of virions in the body occurs even when an explosion is impossible under deterministic conditions.

2. Reproduction of virions in the body with immune response

2.1. The equation for the concentration of virions

The equation for the concentration of virions \( X(t) \) in the area of its active reproduction has the form

\[
\frac{dX}{dt} = W(X)X \quad X|_{t=0} = X_0
\]

The rate of reproduction \( W(X) \), taking into account the immunity of the body, is modeled as

\[
W(X) = \alpha \left( \frac{X}{X_{cr} + \gamma X} - 1 \right) \left( 1 - \frac{X}{X_{max}} \right)
\]

Here \( \alpha \) is the rate constant of virus degeneration; \( X_{cr} \) is critical concentration of the beginning of active reproduction of virions; \( \gamma \) is the constant of the body's immune response; \( X_{max} \gg X_{cr} \) is the maximum concentration of the virions in the body, after which the individual dies.

We reduce the equation to a dimensionless form. The dimensionless concentrations and time, respectively, have the form \( X^* = X/X_{cr} \), \( X^*_max = X_{max}/X_{cr} \), \( t^* = \alpha t \)

\[
\frac{dX^*}{dt^*} = X^* \left( \frac{X^*}{1 + \gamma X^*} - 1 \right) \left( 1 - \frac{X^*}{X_{max}^*} \right) \quad X^*(0) = X_0^*
\]

This equation has an analytical solution, which in the more general case we will demonstrate later.

2.2. Analysis of the initial virus concentration and immune response

We present the results illustrating the dynamics of changes in the concentration of virions for different initial concentrations and the degree of the body's immune response.

![Figure 1](image1.png)  
Figure 1. Dependence on the initial virion concentration: 1 \( \gamma = 0 \), \( X_0^* = 0.5 \); 2 \( \gamma = 0 \), \( X_0^* = 1.0001 \); 3 \( \gamma = 0 \), \( X_0^* = 0.9999 \); 4 \( \gamma = 0.4 \), \( X_0^* = 1.5 \); 5 \( \gamma = 0.1 \), \( X_0^* = 1.5 \).

![Figure 2](image2.png)  
Figure 2. Influence of the degree of immune response: 1 \( \gamma = 0.7 \), \( X_0^* = 5 \); 2 \( \gamma = 1 \), \( X_0^* = 5 \).
Figure 1 shows that in the absence of immunity $\gamma = 0$, the initial concentration of virions less than the critical value will decrease (curve 1). When $\gamma = 0$, the initial value $X_0^* = 1$ is the bifurcation point (curves 2 and 3). An increase in the degree of immunity leads to the degeneration of even large initial values of the virion concentration (curves 4 and 5). Figure 2 shows that in the case of absolute immunity $\gamma = 1$, any concentration of virions in the body will degenerate (curves 1 and 2).

3. The concentration of virions in the body taking into account transport from the atmosphere

3.1. Analytical solution of the equation for concentration

The diffusion of virions from the atmosphere into the lungs, the adsorption of virions in the bloodstream and the transport of virions to the affected organs of intensive reproduction occurs during a time of the order of $T_{in}$. Estimating this characteristic time scale $T_{in}$ is a complex microbiological problem. We write down an equation for the concentration of virions in the region of their intensive replication, taking into account the transport of virions from the atmosphere

$$
\frac{dX}{dt} = \alpha X \left( \frac{X}{X_0 + \gamma X} - 1 \right) + \frac{X_{atm}}{T_{in}} \left( 1 - \frac{X}{X_{max}} \right)
$$

Here $X_{atm}$ is the concentration of virions in the atmosphere.

In dimensionless form, the equation for concentration has the form

$$
\frac{dX^*}{dt^*} = \frac{X^*}{1 + \gamma X^*} - 1 + \frac{X_{atm}^*}{T_{in}^*} \left( 1 - \frac{X^*}{X_{max}^*} \right)
$$

Here nondimensional concentration and internal time scale are $X_{atm}^* = X_{atm}/X_{cr}, T_{in}^* = \alpha T_{in}$.

The equation for concentration has an analytical solution in an implicit form. We have the equality

$$(1 - \gamma) X^* \gamma + \frac{X_{atm}^*}{T_{in}^*} (X^* - Z_1^*) (X^* - Z_2^*)$$

The implicit form of the solution has the form

$$
A \ln \left( \frac{X^* - Z_1^*}{X_0^* - Z_1^*} \right) + B \ln \left( \frac{X^* - Z_2^*}{X_0^* - Z_2^*} \right) + C \ln \left( \frac{X_{max}^* - X^*}{X_{max}^* - X_0^*} \right) = \frac{\gamma}{1 - \gamma} X_{max}^* T_{in}^* t^*
$$

Here the coefficients in the solution are equal

$$
A = -\frac{1/\gamma + Z_1}{(Z_2 - Z_1)(Z_1 - X_{max}^*)}, \quad B = \frac{1/\gamma + Z_2}{(Z_2 - Z_1)(Z_2 - X_{max}^*)}, \quad C = \frac{1/\gamma + X_{max}^*}{(X_{max}^* - Z_2)(X_{max}^* - Z_2)}
$$

3.2. Influence of virion flux from the atmosphere

Here we will present the results of the analysis of the dynamics of the growth of the virion concentration in the area of their intensive reproduction at a constant concentration of virions in the atmosphere. All calculations were carried out at $T_{in}^* = 3, X_0^* = 0$.

Figure 3 shows an illustration of the influence of the concentration of virions in the atmosphere on the dynamics of the growth of their concentration in the body. In the absence of immunity, even small constant concentrations of virions in the atmosphere lead to an intensive increase in their concentration (curve 1). An increase in the degree of immunity leads to a constant concentration of virions (curve 2). However, an increase in the concentration of virions in the atmosphere, even with a significant degree of immunity, causes an intensive increase in the concentration of virions in the body (curve 3 and 4). Only with absolute immunity $\gamma = 1$, the concentration of virions in the body reaches a constant value (curve 5).
Figure 3. The effect of constant virion concentration in atmosphere and the degree of immune response: 1 – $\gamma = 0$, $X_{\text{atm}}^* = 0.8$; 2 – $\gamma = 0.2$, $X_{\text{atm}}^* = 0.8$; 3 – $\gamma = 0.2$, $X_{\text{atm}}^* = 1$; 4 – $\gamma = 0.8$, $X_{\text{atm}}^* = 2$; 5 – $\gamma = 1$, $X_{\text{atm}}^* = 2$.

4. Explosive growth of the virion concentration in a random atmosphere

4.1. Direct numerical simulation

Taking into account fluctuations in the concentration of virions in the atmosphere, the equation for their concentration in the region of intensive reproduction has the form

$$\frac{dX^*}{dt} = \left[ X^* \left( \frac{X^*}{1 + \gamma X^*} - 1 \right) + \frac{\langle X_{\text{atm}}^* \rangle + x_{\text{atm}}^*}{T_{\text{in}}^*} \right] \left( 1 - \frac{X^*}{X_{\text{max}}^*} \right) - \langle x_{\text{atm}}^* \rangle = 0$$

Here, the angle brackets $\langle \cdots \rangle$ indicate the averaging over an ensemble of random realizations; $\langle x_{\text{atm}}^* \rangle$ is the average concentration of virions in the atmosphere, $X_{\text{atm}}^* = \langle x_{\text{atm}}^* \rangle + x_{\text{atm}}^*$; $x_{\text{atm}}^*$ is fluctuations in the concentration of virions in the atmosphere.

We model the fluctuations of the virion concentration in the atmosphere as a solution of a stochastic ordinary differential equation

$$\frac{dx_{\text{atm}}^*}{dt} = \frac{1}{T_{\text{atm}}^*} \left( \eta_{\text{atm}}^* - x_{\text{atm}}^* \right)$$

Here $T_{\text{atm}}^*$ is a time scale of fluctuations in the concentration of virions in the atmosphere, which depends on the characteristics of physical contacts of individuals in the group; $\eta_{\text{atm}}^*$ is random delta-correlated Gaussian process (white noise)

$$\langle \eta_{\text{atm}}^*(t) \eta_{\text{atm}}^*(t') \rangle = \langle \eta_{\text{atm}}^* \rangle \delta(t - t')$$

The solution of the equation for fluctuations generates color noise with an autocorrelation function that exponentially decays in time. The system of equations for the actual concentration in the body and fluctuations of concentration in the atmosphere was integrated numerically by the simple Euler-Maruyama method [15].

4.2. Calculation results

We will present the results of calculations of the random process of concentration fluctuations in the body for two scenarios.

In the first case, we will illustrate the possibility of an explosive increase in the concentration of virions in the body, when in a deterministic situation a static concentration of virions in the body is realized. Secondly, the case of the influence of virion concentration fluctuations in the atmosphere for the explosive growth of virions in a deterministic situation will be considered.

Figure 4 illustrates an example of an explosive increase in the concentration of virions in the body. In a stationary concentration of virions in the atmosphere, immunity leads to the achievement of a constant concentration value in the body. Under the same conditions, accidental contacts cause an explosive increase in concentration in an initially healthy body. For a stationary concentration of
virions in the atmosphere, the immune system reduces virions concentration in the body to a constant value. Fluctuations in the concentration of virions in the atmosphere eventually lead to the crisis development of infection.

Figure 5 shows that in the case of a crisis development of infection at a constant concentration in the atmosphere, fluctuations in the concentration of virions lead to a significantly earlier onset of the crisis.

Direct numerical simulation of the growth of virions in the body at a random concentration of virions in the atmosphere indicates a qualitative difference in the behavior of a nonlinear system in a random environment.

5. Main conclusions
The considered model belongs to the class of deterministic nonlinear systems of explosive type. The influence of random fluctuations of parameters leads to a qualitatively different behavior of such systems compared to a deterministic situation. In a random environment, an explosion can occur even with averaged values of parameters, at which loss of stability is impossible in a deterministic system.

A mathematical model of the growth of the virus concentration in the body is presented, taking into account random contacts between infected individuals:

✓ A model of virions transport from the lungs of an individual to the organs of intensive growth of the virion concentration is proposed.
✓ A model of the growth of the virion concentration in the area of intensive replication is proposed, taking into account the immune response of the body.
✓ The analysis of the influence of the initial concentration of the virion in the body, the degree of immunity and the constant concentration of the virion in the atmosphere on the dynamics of changes in the concentration of the virion in the body is carried out.
✓ It is shown that fluctuations in the concentration of the virion in the atmosphere always contribute to an earlier onset of a crisis with an explosive character of virion replication in the body.

6. References
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