Influence of delay on epidemic evolution

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Based on the discrete model of the spread of infection in a closed population, the corresponding form of differential equations with delay is found. It is shown that the development of the epidemic is determined by four key parameters: the number of infectious, the average number of dangerous contacts of one infectious person per day, the the probability of infection due to such contact and the average time during which the sick person is able to infect. The decision also depends on the size of the population and the initial number of those infectious agents. The named parameters have a clear meaning and are related to the well-known concept of the reproductive number in the continuous SIR and SEIR models. The conditions for saturation of the epidemic were established by solving the derived differential equations. It is shown that since the infected remain carriers of the virus for a long time, which is characteristic of COVID-19, the solutions proposed here differ significantly from the SIR model.

There are two main kinds of epidemic models: SIS models and SIR (or the extended SIR model - SEIR models). Models of the first kind refer to the pioneering work of [1] and assume that people who have recovered can immediately be infected again. SIR models are built on the assumption that those who have recovered are immune and fall out of the

epidemic for good (see, e.g., [2]). SIS models are used in mathematical epidemiology [3]. An overview is given in [4] (see also references therein). The balance between susceptible and infected members of the population under various conditions of transmission is the subject of research in [5].

The model under consideration, like the SIR ("susceptible-infected-removed") and SEIR("susceptible-exposed-infected-removed") models, assumes immunity for recovered people ([6], [7], and references therein). However, models like SIR and SEIR allow for the possibility of immediate recovery, which is highly questionable for COVID-19 disease. Such a possibility is due to the presence in these models of the time derivative of the number of infectious people dI/dt which is defined by the term -γI (where γ^{-1} is the average duration of disease).

Specificity of the proposed work is that it takes into account some features COVID-19 that follow from the recent discrete epidemic model[8]. Unlike SIR models, the model under consideration for a closed population has three independent parameters. One of them is the average duration of the disease d, understood as the length of time during which the infected person is infected. Another parameter, transmission rate of infection p, is similar to the number of reproducibility $R0$ in SIR models. The parameter p is the product of $p = n_c k$, where n_c is the average number of dangerous contacts per day for one infected person, and k is the average susceptibility of a healthy person to the virus.

We consider here closed populations (country, region, city, etc.), because authorities declare isolation at an early stage of an epidemic. In this case, it is necessary to know the initial state of the population, namely the number of infected people at the beginning of the epidemic According to [8], the discrete equations describing the epidemic day by day (like the official [8] statistics on which we rely) for $l > d$ have the form

$$N_T(l) = N_T(l-1) + N_I(l) n_c \cdot k[1 - N_T(l)/N],$$
$$N_I(l) = N_T(l) - N_T(l-d+1), \tag{1}$$

where $N_I(l)$ is the number of infected people (carriers of the virus capable of infecting) on day l and $N_T(l)$ is the total number of people infected to day l since the beginning of the epidemic. At $l \leq d$ it is assumed that there are no removed (recovered or dead), so $N_I(l) = N_T(l)$. The factor $n_c \cdot k[1 - N_T(l)/N]$ reflects a gradual change in the parameter $p = n_c \cdot k$, since it is assumed impossible to infect the infected as well as the removed.

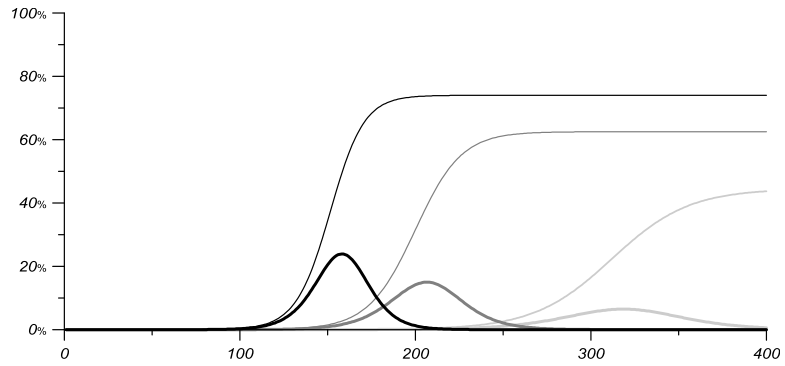

Figure 1: The total number of infections (thin curves) and the current number of infections (bold curves) calculated using the discrete model formula (1) for a free-running epidemic in a limited population as a percentage of its size. Here $p = 0.15$ (black curves), $p = 0.13$ (dark gray curves), $p = 0.11$ (light gray curves); d = 14 days. Axis x is the day after the first infection, axis y is the proportion of affected members of the population.

Excluding $N_I(l)$ we obtain a nonlinear equation for $N_T(l)$

$$N_T(l) = N_T(l-1) + \{N_T(l) - N_T(l-d+1)\}n_c \cdot k[1 - \frac{N_T(l)}{N}], \tag{2}$$

Figure 1 shows the curves according to equations (1). For the calculations, we used the initial condition $N_I(l = 1) = N_T(l = 1) = 1 + n_c k$. As follows from Fig. 1, the theory describes the level of onset of collective immunity depending on characteristic parameters. It can be rigorously shown that accounting for special quarantine measures is reduced to replacing in equations (1), (2) $n_c k \to n_l \cdot k$, where the number n_l reflects the change in the average daily number of dangerous contacts due to the adoption or withdrawal of protective measures.

In equation (2), we can go from discrete time l, to continuous time. To do this, we denote $t = \Delta t(l-1)$, where Δt is a unit of time equal to one day, and put $N_T(l) = x(t)N$, $N_T(l) - NT(l-1) = x'(t)N$. Then equation (2) is rewritten as

$$x'(t) = p[x(t) - \theta(t-T)x(t-T)][1 - x(t)], \tag{3}$$

where $\theta(t)$ is a Heaviside step function, and $T = d - 1$. Here it is assumed that time is still measured in days, i.e., $\Delta t = 1$, otherwise the coefficient p must be renormalized. At the initial stage of the epidemic $0 \le t \le T$, the equation (3) has the form

$$x'(t) = px(t)[1 - x(t)], \tag{4}$$

and its solution is

$$x_0(t) = \frac{\epsilon e^{pt}}{\epsilon e^{pt} - \epsilon + 1}, \tag{5}$$

where $x(0) = \epsilon$ is determined by the initial fraction of virus carriers in the population that can infect. The solution (5) is an initial function for equation (3), that is, $x(t) = x_0(t)$ at $0 \le t \le T$.

There are two stationary solutions to equation (5), namely, an unstable solution $x_0(t) = 0$ and a stable solution $x_0(t) = 1$, which is the limit $x_0(t)$ (5) at the point $t \to \infty$. On the contrary, the differential equation with delay (3) has an arbitrary stationary solution $x(t) = C$ for $t > T$ $(0 \le C \le 1)$. Obviously, for a long time, any solution to equation (3) tends to some stationary stable saturation value, as shown in Figure 1.

The minimum saturation value can be estimated by linearizing the equation (3) near an arbitrary stationary solution $x(t) = C$. Let $x(t) = C + \delta x(t)$, then the linearized equation is $\delta x'(t) = p(1 - C)[\delta x(t) - \delta x(tT)]$. Assuming that $\delta x(t) = \exp(\lambda t/T)$, we arrive at the characteristic equation

$$\lambda + (e^{-\lambda} - 1)Tp(1 - C) = 0. \tag{6}$$

One of the roots of this equation is $\lambda = 0$. The other valid root of equation (6) is negative $\lambda < 0$ if $Tp(1 - C) < 1$. In other words, the stationary solution $x(t) = C$ is stable if

$$C > \begin{cases} 0, & Tp \le 1 \\ 1 - \dfrac{1}{Tp}, & Tp > 1 \end{cases} \tag{7}$$

Consequently, the saturation value $x_\infty(p) = \lim_{t\to\infty} x(t)$ must exceed the value given by equation (7). Figure 2 shows the dependence of the asymptotic value of the solution of Eq. (3) on pT calculated for two values of the initial perturbation, $\epsilon = 10^{-6}$ (curve 1) and $\epsilon = 5 \cdot 10^{-2}$ (curve 2). If $pT < 1$, there is no significant increase in epidemics. For large values of pT, the saturation level is always greater than the value given by equation (7), and tends to unity at $pT \gg 1$. For sufficiently small values of $\epsilon \ll 1$, the function $x_\infty(p)$ tends to a universal curve independent of the initial perturbation (e.g., curve 1 in Fig. 2). However, the time required to reach the saturation value depends on the initial perturbation.

Examples of epidemic growth calculated using the proposed model (3) and the SIR model (see, for example, [7]) are shown in Fig. 2. For a sufficiently small initial perturbation ϵ, the SIR model predicts about twice the saturation time.

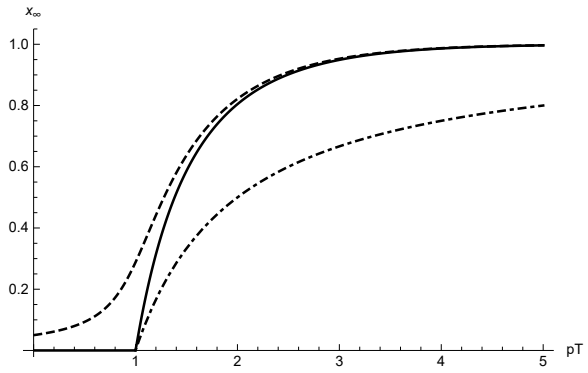

Figure 2: Dependence of the saturation level of the epidemic x_∞ on pT. Curve 1 — $\epsilon = 10^{-6}$, curve 2 — $\epsilon = 5 \cdot 10^{-2}$, curve 3 is given by equation (7).

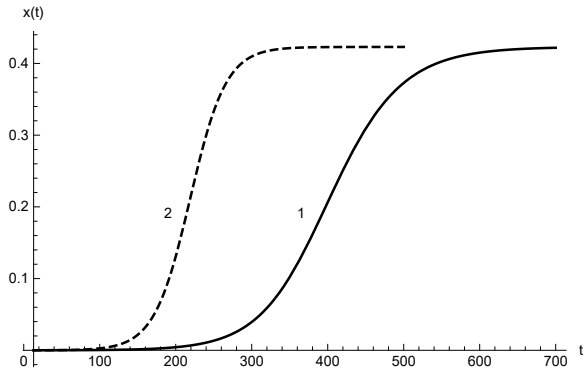

Figure 3: Comparison of two models. Curve 1 is calculated according to the SIR model (see, for example, [7]), curve 2 is a delayed equation (3). Selected parameters $\epsilon = 10^{-5}$, $p = 0,1$, $T = 13$.

As already mentioned, there are an infinite number of stationary states of equation with delay (3). On the contrary, there is only one root of equation $F(x_1) = 0$, which can be written as $x_1(\epsilon, pT) = 1 + W\left(-pTe^{-pT(\epsilon+1)}\right)/(pT)$, where $W(z)$ is the Lambert function (see, e.g., [10]). It is easy to check that the stationary state is stable, i.e. $F'(x_1) > 0$. It was found numerically that, for a sufficiently small value of the initial perturbation $\epsilon \ll 1$, the saturation levels given by both models are practically equal.

To describe the real course of the epidemic, we need to better know the characteristics of COVID-19. In view of this, here, instead of a SIR-type model based on ordinary differential equations, the delayed differential equation is obtained that takes into account the duration of the COVID-19 disease.

Here we restrict ourselves to closed populations (country, region, city, etc.). Of course, there is a constant exchange between populations. However, at an early stage of the epidemic, the authorities use restrictive measures to reduce such flows to a minimum. Pre-quarantine cross-border transmission cannot be accurately calculated. This initial stage of the epidemic can named a free-flowing epidemic. The impact of the flow of people between regions on the epidemic is a separate task that can be considered, in particular, using the model proposed here.

A significant novelty of the obtained results is also the assessment of the effects of quarantine measures through an "external impact function" on the epidemic n_l $(p(l))$. The role of the various quarantine measures and the quantification of their impact is still unclear and debated. Nevertheless, the model under consideration makes it possible to find this function at the beginning of an epidemic by back-calculating [8] from the available discrete statistics [9]. In this way, it is possible to estimate the impact of quarantine measures for individual regions and countries in general, since the dates and rules of administrative restrictions are known.

We also show and investigate the emergence of collective immunity under quarantine conditions. This is a property of the deterministic model with the delay process of transition from the subset of carriers V to the subset of cured individuals R, which is not present in the known SIR and SEIR models and their modifications. This delay is a characteristic feature of COVID-19. It has been shown that this type of collective immunity can be maintained at a relatively low level. The theory presented can describe the entire epidemic process, including the new waves of COVID-19 infections currently observed and the periodic change in the balance between quarantine measures and reduction of quarantine restrictions.

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