БИОФИЗИКА

BIOPHYSICS

ДРОБНО-ДИФФЕРЕНЦИАЛЬНАЯ МОДЕЛЬ РАСПРОСТРАНЕНИЯ COVID-19

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Изучается математическая модель распространения пандемии COVID-19, основанная на обыкновенных дифференциальных уравнениях с дробной производной по времени. В модели учитываются восприимчивость населения к заражению, инкубационный период, число контактов между здоровыми и больными людьми, число зараженных, выздоровевших и умерших в определенный период. Для проверки модели в работе проведено сравнение с моделями на основе производной первого порядка по времени, использующими известные данные по итальянскому региону Ломбардия. Результаты позволяют утверждать, что использование математической модели на основе дробной производной по времени посредством данных, таких как восприимчивость населения к заражению, инкубационный период, число зараженных, выздоровевших и умерших в определенный период, поможет органам здравоохранения разработать эффективные меры по борьбе с пандемией. Это особенно возможно, если расширить модель и рассмотреть дифференциальные уравнения в частных производных, описывающих конвекционно-диффузионный процесс с учетом предвидения географического распределения важнейших медицинских ресурсов.

Ключевые слова: COVID-19; SEIRD; дробная производная; дробный метод Адамса.

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FRACTIONAL DIFFERENTIAL MODEL OF THE SPREAD OF COVID-19

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This paper studies a mathematical model of the spread of the COVID-19 pandemic based on ordinary differential equations with a time-fractional derivative. The model takes into account the susceptibility of the population to infection, the incubation period, the number of contacts between healthy and sick people, number of infected, recovered and deceased people in a certain period. To test the model a comparison was made with models obtained with a time derivative of integer orders, with known data for the Italian region of Lombardy. The results suggest that the use of a mathematical model based on a time-fractional derivative with the help of data such as susceptibility of the population to infection, incubation period, number of infected, recovered and deceased people in a certain period, ultimately can help health authorities to develop effective measures against the pandemic. This is especially possible if we expand the model and consider partial differential equations describing the convection-diffusion process, taking into account the prediction of the geographical distribution of the most important medical resources.

Keywords: COVID-19; SEIRD; fractional derivative; fractional Adams method.

Introduction

Throughout its history, humanity has faced challenges such as wars, environmental problems, demographical problems, exhaustion of resources, and other global problems. But these problems were successfully solved due to the development of science and technology and, of course, to an increase in the consumption of Earth's resources. Currently, humanity is going through one of the most difficult periods – the coronavirus pandemic.

Epidemics have repeatedly affected humanity throughout history. It is believed that malaria and tuberculosis devastated ancient Egypt more than 5000 years ago. From 541 to 542 AD, a global pandemic, known as the Justinian Plague, is estimated to have killed 15–25 % of the world's 200 mln population. After the Spanish conquest of Mexico, the local population decreased from about 30 mln in 1519 to just 3 mln 50 years later.

The latest outbreak of the SARS-CoV-2 coronavirus (hereinafter COVID-19) has affected the whole world, which has led to significant damage both in terms of human lives and economic resources. To stop the spread of the disease, governments of different countries have taken different measures, such as quarantine, isolation, and lockdown. The consequences of these measures (both positive and negative) are partly due to the lack of information about the spatiotemporal spread of COVID-19.

It is impossible to conduct an experiment in the current situation, so an important role is assigned to numerical mathematical modelling of the disease spread process. Mathematical modelling is a very promising tool for studying the origin, growth, spread, and extinction of pandemics. Thanks to the construction and analysis of various mathematical models, it becomes possible to predict the dynamics of the epidemic and determine the best measures to fight the epidemic for a specific situation. For example, experts at Imperial College London made a prediction in March, according to which many patients and deaths due to coronavirus infection were waiting for the UK without restrictive measures. Given this prediction, the UK government has changed its policy towards the epidemic and increased the restriction of social activity.

Scientists have discovered that with the help of basic mathematical models researchers can begin to predict the progression of diseases and understand the impact of interventions on the spread of diseases. With the help of more complex models, we can begin to answer questions about the effective allocation of limited resources or the elimination of the consequences of public health interventions, such as closing cafes and banning meetings of large groups of people[1].

Currently, the COVID-19 pandemic is still an open problem for the world. This suggests the relevancy of this work from the point of view of studying various models that are used to describe the development of processes associated with the coronavirus. By studying the virus spread on a mathematical model and analysing the solution, it will be possible to influence the situation and prevent outbreaks. The paper proposes a model and a numerical method for its implementation. In addition, the obtained results are analysed and compared with the available official data.

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[1]*Christian Ya.* How to model a pandemic [Electronic resource] // The Conversation. 2020. URL: https://theconversation.com/how-to-model-a-pandemic-134187 (date of access: 05.08.2021).

At the moment, there are many different works devoted to this problem, for example [1–3]. The basic model of virus spread is the SIR (susceptible – infected – removed) model, in which the rate of pandemic growth depends on the number of infected carriers and the number of individuals not yet infected [4]. People who have not yet had the disease are marked as susceptible. It is assumed that every person is born susceptible and capable of being infected. Those who are able to transmit disease to susceptible people are infected. The third group is called the removed class. These are people who have suffered an illness, recovered, and now are immune to it, or those who have died. The removed people contribute no longer to the spread of the disease. This model is described by a simple system of three differential equations:

$$\frac{dS}{dt} = -\beta r S(t) \frac{I(t)}{N},$$

$$\frac{dI}{dt} = \beta r S(t) \frac{I(t)}{N} - \gamma I(t),$$

$$\frac{dR}{dt} = \gamma I(t),$$

where S, I, R are the number of people susceptible to the disease, infected and removed people, respectively; r is the number of contacts per unit of time; β is the probability of transmission of the disease during contact; γ is the recovery rate; $N = S + I + R$ is the total number of people.

The SIR model illustrates the importance of social isolation for infected people. By staying at home until full recovery, you effectively transfer yourself from an infected class directly to a removed class without spreading the virus. This simple action can reduce the scale of the outbreak, reducing the possibility of transmitting the disease to susceptible people.

But it is possible to improve this model if we consider the human demography for diseases when the time frame of the dynamics of the disease is comparable to the human demography. There are many ways to model human demography: a constant level of immigration, constant indicators of fertility and mortality per capita, a mortality rate depending on density, mortality from diseases. Then the SIR model can be represented in a different form:

$$\frac{dS}{dt} = \Lambda - \beta r S(t) \frac{I(t)}{N} - \mu S(t),$$

$$\frac{dI}{dt} = \beta r S(t) \frac{I(t)}{N} - (\gamma + \mu) I(t),$$

$$\frac{dR}{dt} = \gamma I(t) - \mu R(t),$$

where Λ is the fertility rate; μ is the mortality rate.

A simple SIR model is not enough to cover the subtleties of many outbreaks of infectious diseases. For example, it doesn't consider the phenomenon of delayed processes in time that characterises COVID-19, when a certain time passes from the moment of infection to the moment of active manifestation of the virus, after which a person becomes an open spreader of infection, called the incubation period. Then this model can be complicated by adding another group of people who have the disease in the incubation period (exposed). In this case, the SEIR (susceptible – exposed – infected – removed) model [5] is described by a system of four equations:

$$\frac{dS}{dt} = \Lambda - \beta r S(t) \frac{I(t)}{N} - \mu S(t),$$

$$\frac{dE}{dt} = \beta r S(t) \frac{I(t)}{N} - (\sigma + \mu) E(t),$$

$$\frac{dI}{dt} = \sigma E(t) - (\gamma + \mu) I(t),$$

$$\frac{dR}{dt} = \gamma I(t) - \mu R(t),$$

where E is the number of people who have the disease in the incubation period; σ is the inverse incubation period of the disease; $N = S + E + I + R$.

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The SEIR model reflects the behaviour of the infection more accurately, but it is impossible to estimate the total number of people who died from the disease (and, accordingly, the scale of the epidemic) with its help. In this case, we can consider the SEIRD (susceptible – exposed – infected – recovered – deceased) model [6], described by a system of five differential equations:

$$\frac{dS}{dt} = \Lambda - \beta r S(t) \frac{I(t)}{N} - \mu S(t),$$

$$\frac{dE}{dt} = \beta r S(t) \frac{I(t)}{N} - (\mu + \sigma) E(t),$$

$$\frac{dI}{dt} = \sigma E(t) - (\gamma + \mu) I(t),$$

$$\frac{dR}{dt} = \gamma (1 - \mu_C(t)) I(t) - \mu R(t),$$

$$\frac{dD}{dt} = \gamma \mu_C(t) I(t),$$

where D is population loss due to the disease; $\mu_C(t) \sim e^{-\xi t}$ is a death rete due to COVID-19; $N(t) = S(t) + E(t) + I(t) + R(t)$.
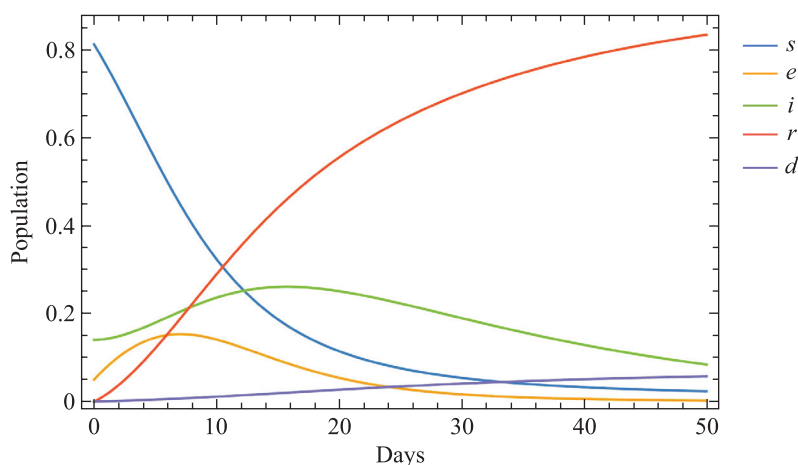

Fig. 1. Evolution of SEIRD model

The numerical solution of SEIRD model with parameters described below is presented on fig. 1. We can observe that this model (like SIR, SEIR) predicts a larger number of infections than are presented in official statistics. This may be since not all people pass the COVID-19 detection test, but this does not explain the sharpness of the peaks and the very rapid attenuation of the number of people exposed to infection. To eliminate this problem, we propose to use differential operators of fractional orders in the model.

Theoretical basis

Following [1] consider the model described by a system of differential equations in fractional derivatives:

$$\partial_{0,t}^{\alpha_1} s(x, t) = \lambda n - \left(1 - \frac{A}{n}\right) \beta_i s i - \left(1 - \frac{A}{n}\right) \beta_e s e - \mu s + \nabla \cdot (n v_s \nabla s),$$

$$\partial_{0,t}^{\alpha_2} e(x, t) = \left(1 - \frac{A}{n}\right) \beta_i s i + \left(1 - \frac{A}{n}\right) \beta_e s e - (\sigma + \varphi_e + \mu) e + \nabla \cdot (n v_e \nabla e),$$

$$\partial_{0,t}^{\alpha_3} i(x, t) = \sigma e - (\varphi_d + \varphi_r + \mu) i + \nabla \cdot (n v_i \nabla i), \qquad (1)$$

$$\partial_{0,t}^{\alpha_4} r(x, t) = \varphi_r i + \varphi_e e - \mu r + \nabla \cdot (n v_r \nabla r),$$

$$\partial_{0,t}^{\alpha_5} d(x, t) = \varphi_d i,$$

where $s(x, t)$ is the number of healthy people susceptible to the disease; $e(x, t)$ is the number of infected people having the disease in the incubation period; $i(x, t)$ is the number of infected people; $r(x, t)$ is the number of people who are no longer susceptible to the disease; $d(x, t)$ is the number of deceased people; $n = s + e + i + r$ is the entire population. These functions are normalised for the entire population of the country. Further λ is the birth rate, σ is the inverse of the incubation period of the disease, φ_r is the recovery rate, φ_e is the asymptomatic recovery rate, φ_d is the mortality rate among patients, β_e is the asymptomatic contact rate, β_i is the contact rate with symptoms, μ is the mortality rate without the COVID-19, A is a parameter that accounts the distribution of resources and is intended for modelling the trends of outbreaks in large populations, and v_s, v_e, v_i, v_r are parameters of the diffusion of various population groups, which we take as zero, since this paper does not consider the spatial spread of infection. In this model a Gerasimov – Caputo time-fractional derivative operator of order α $(0 < \alpha < 1)$ is used:

$$\partial_{0,t}^{\alpha} u(x, t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t \frac{u'_\tau(x, \tau) d\tau}{(t-\tau)^\alpha}.$$

The model (fig. 2) takes into account asymptomatic transmission of infection, which is considered a key factor in the COVID-19 pandemic [7]. The first and second equations from the model (1) show that exposed asymptomatic patients can transmit COVID-19 to susceptible people with a contact rate of β_e. This is consistent with recent studies suggesting that patients can transmit COVID-19 almost immediately after infection [7]. In addition, the third and fourth equations from the model (1) include the infected patients who do not develop symptoms and who move directly to the recovered population. It is also assumed that recovered patients are immune therefore there is not any reverse flow from the equation for r to the equation for s [8].
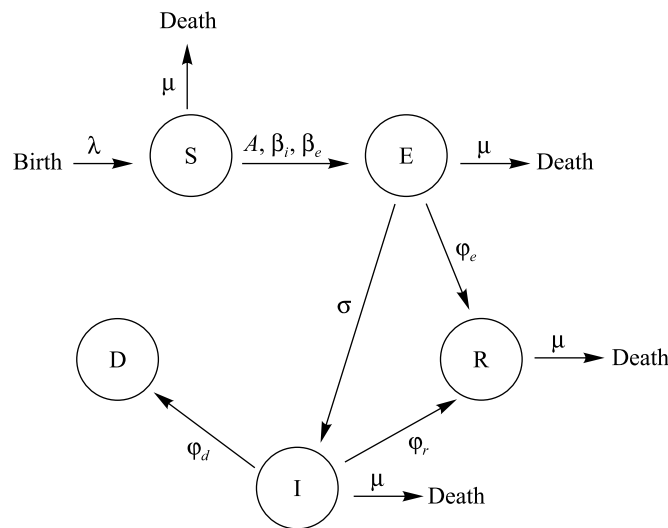

Fig. 2. A block diagram describing the dynamics
between subgroups of people in the model (1)

Since there is quite detailed data on the development of infection for the Italian region of Lombardy, we took the coefficients for our model from there. We assume $\sigma = \frac{1}{7}$ days^{-1}, $\varphi_r = \frac{1}{24}$ days^{-1}, $\varphi_d = \frac{1}{160}$ days^{-1}, and $\varphi_e = \frac{1}{6}$ days^{-1}. These values are based on the data available in the literature on mortality, incubation period and recovery time of infected and asymptomatic patients [7]. In addition, we do not consider the birth rate or mortality without COVID-19 (that is, we set $\lambda = 0$ and $\mu = 0$ accordingly). The time scale in our simulations is days. Based on the results of parameter calibration, we initially set $\beta_i = \beta_e = 3.3 \cdot 10^{-4}$ people$^{-1} \cdot$ days^{-1}.

Given the uncertainty in the currently available COVID-19 data, we believe that an assessment of the parameters aimed at matching the dynamics of all parts of the model is impractical. Since not every member of the population is tested for infection, and asymptomatic cases are known to exist in possibly large numbers, we think that the available data on cases of infection may lead to an unrealistic adjustment of the parameters. Conversely, the data presented for COVID-19 deaths provide greater reliability for calibrating the model parameters. Therefore, we strive for a quantitative agreement in the subgroup of the deceased $d(t)$ and a qualitative agreement for the remaining model subgroups $s(t)$, $e(t)$, $i(t)$, $r(t)$.

When developing the numerical method, it was taken into account that with fractional differential equations are interrelated with first-order differential equations, and therefore we combine the fractional-order algorithm and the classical method. The results of the work allow us to give recommendations on the choice of these two algorithms, indicating the need for both methods to be based on very similar principles of construction. Therefore, the Adams approach was chosen.

Consider a system of differential equations with Caputo fractional derivative:

$$\partial_{0, t}^{\alpha} \mathbf{u}(t) = \mathbf{f}(t, \mathbf{u}),$$

where $\mathbf{u} = (u_1, \ldots, u_n)^T$ and $\mathbf{f} = (f_1, \ldots, f_n)^T$, $f_i = f_i(t, u_1, \ldots, u_n)$, are unknown and given functions, respectively. On the interval $[0, T]$, we construct a grid $\omega_\tau = \left\{ t_j = j\tau, \ j = \overline{0, j_{\max}}, \ \tau = \dfrac{T}{j_{\max}} \right\}$. Let $\mathbf{u}_j$ be an approximate solution at the node t_j. The numerical solution is obtained by predictor-corrector scheme [9; 10]:

$$\mathbf{u}_{j+1}^{*} = \mathbf{u}_0 + \frac{\tau^\alpha}{\Gamma(\alpha + 1)} \sum_{k=0}^{j} g_{k, j+1} \mathbf{f}(t_j, \mathbf{u}_j),$$

$$\mathbf{u}_{j+1} = \mathbf{u}_0 + \frac{\tau^\alpha}{\Gamma(\alpha + 2)} \sum_{k=0}^{j} q_{k, j+1} \mathbf{f}(t_k, \mathbf{u}_k) + q_{j+1, j+1} \mathbf{f}(t_{j+1}, \mathbf{u}_{j+1}^{*}),$$

(2)

where

$$g_{k, j+1} = (j - k + 1)^\alpha - (j - k)^\alpha,$$

$$q_{k, j+1} = \begin{cases} j^{\alpha+1} - (j - \alpha)(j + 1)^\alpha, & k = 0, \\ (j - k + 2)^{\alpha+1} - 2(j - k + 1)^{\alpha+1} + (j - k)^{\alpha+1}, & 1 \le k \le j, \\ 1, & k = j + 1. \end{cases}$$

To apply the algorithm at each step, according to the formula (2), the predictor $\mathbf{u}_{j+1}^{*}$ is being calculated first, then the value $\mathbf{f}(t_{j+1}, \mathbf{u}_{j+1}^{*})$ for determination of the corrector $\mathbf{u}_{j+1}$ considered to be an approximate solution at the next time layer. This scheme is very useful and effective for the numerical solution of fractional differential equations.

Results and discussion

The numerical solution of the system (1) is presented on fig. 3–7. All computations were performed in the *Wolfram Mathematica*. The graphs show the distribution over time of the number of people from a certain group at different orders of the fractional derivative in a mathematical model. It can be seen from the graphs that the smaller the order of the fractional derivative is, the faster the curves come out on horizontal straight parallel axes, i. e. the stationarity of the process is established what in general does not mean that the number of, for example, infected people will not grow, just the growth rate will not be so high.

Taking into account the official data from Italy (fig. 8), and comparing them with the results obtained, we were convinced that our model is consistent with the published statistics in Italy. As it can be seen all processes, in fact, do not have obvious peaks that were characteristic of the differential model with derivatives of integer orders, and with the characteristic features of the fractional derivative (memory) they reach the stationary state faster with time. All the data was provided by the Johns Hopkins University, who made the data available for educational and academic research purposes.

Thus, we can conclude that the model proposed in this paper correctly describes the general trends in the spread of the disease. However, we do not claim its absolute accuracy, for several reasons:

1) a limited number of tests conducted for the presence of COVID-19;

2) the percentage of people who have suffered the disease asymptomatically is not taken into account, because they can be detected only after testing for antibodies;

3) the COVID-19 virus has not yet been fully studied and many parameters cannot be set absolutely accurately;

4) spatial trends in the spread of the disease are not taken into account.
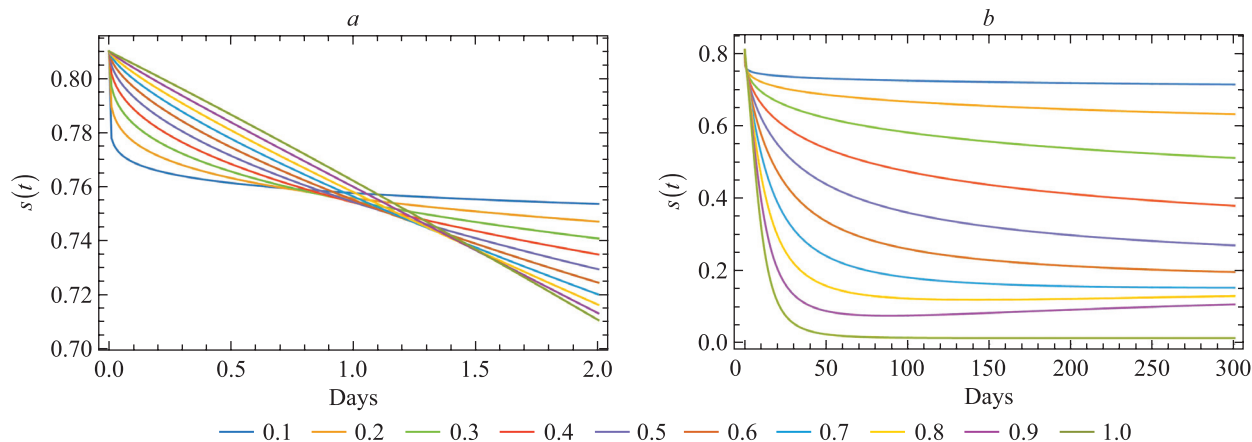
But we will leave these details for future research.

Fig. 3. Evolution of the number of people susceptible to the disease
over time for different orders of the fractional derivative:
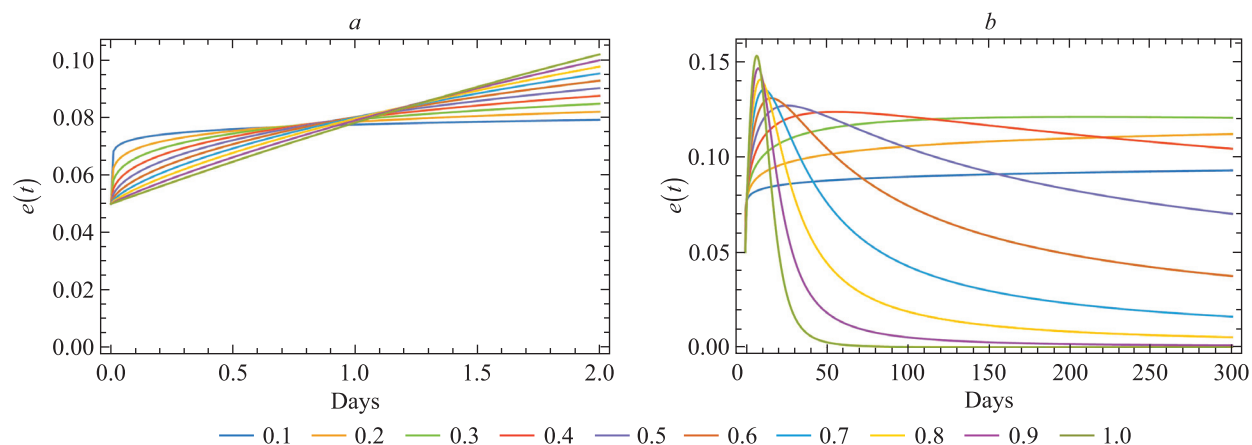*a* – 2 days dynamics; *b* – 300 days dynamics

Fig. 4. Evolution of the number of exposed people over time
for different orders of fractional derivative:
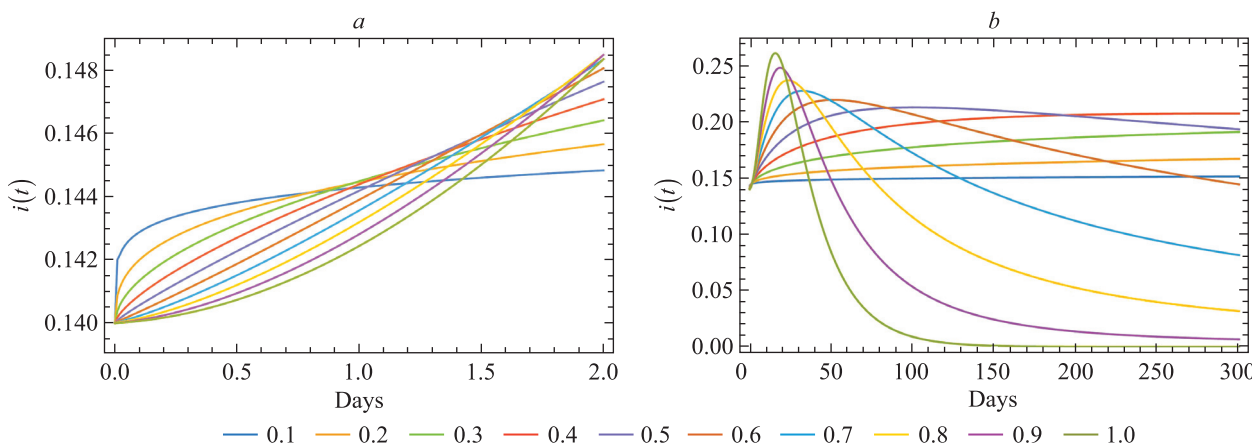*a* – 2 days dynamics; *b* – 300 days dynamics

Fig. 5. Evolution of the number of infected people over time
for different orders of the fractional derivative:
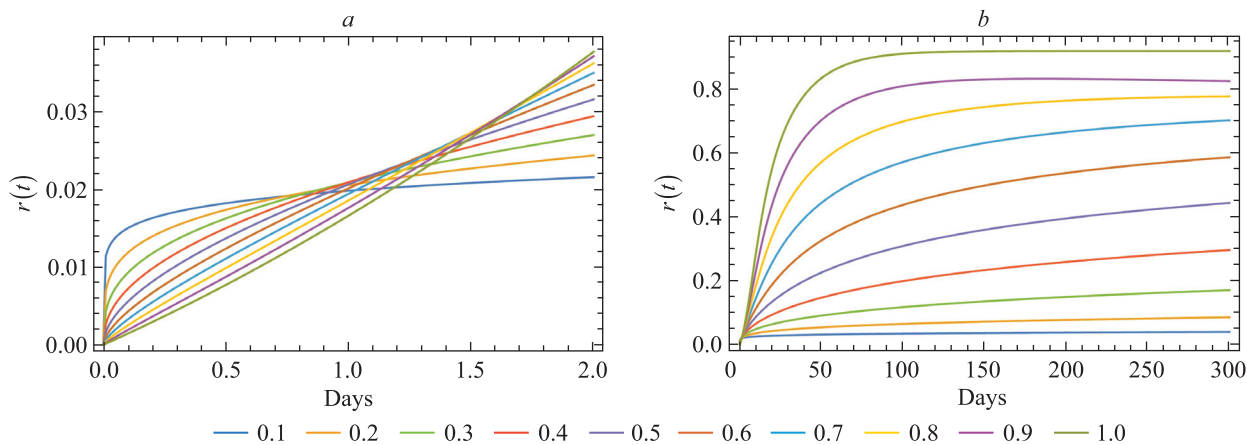*a* – 2 days dynamics; *b* – 300 days dynamics

Fig. 6. Evolution of the number of recovered people over time
for different orders of the fractional derivative:
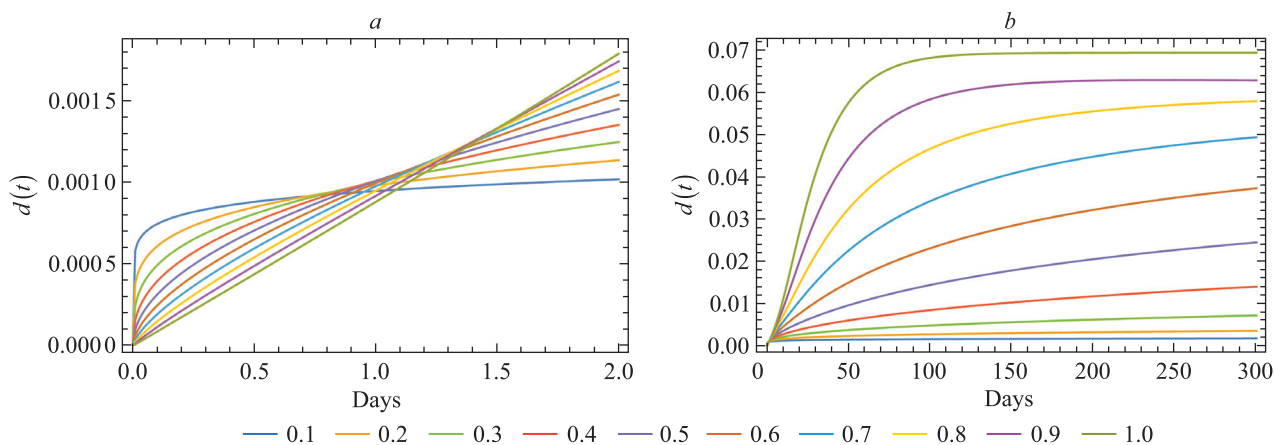*a* – 2 days dynamics; *b* – 300 days dynamics

Fig. 7. Evolution of the number of deceased people over time
for different orders of the fractional derivative:
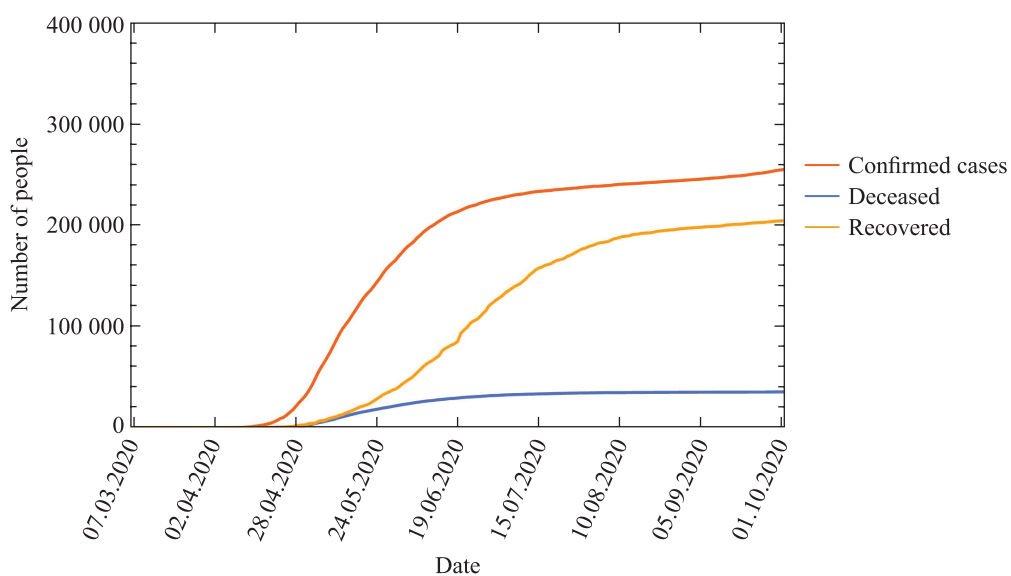*a* – 2 days dynamics; *b* – 300 days dynamics

Fig. 8. Official data for Italy from 07.03.2020 to 01.10.2020
according to the Johns Hopkins Coronavirus Resource Center

Conclusions

The problem of the spread of COVID-19 infection is still relevant for the whole world. This paper and others in this direction are intended to provide proof of the importance of using systems of differential equations with fractional orders derivatives. With the help of fractional operators previous morbidity can be taken into account, which allows us to obtain much more accurate results than with a derivatives of integer orders.

Our model was implemented numerically using the Adams – Bashford algorithm. There is a good qualitative agreement of the computational experiment with reality, which indicates a fairly accurate representation of the overall dynamics of the outbreak. However, there are still ways to improve our model, such as, for example, adding a diffusion operator and considering the spatial spread of the virus, which is supposed to be considered in our further research.

References

1. Viguerie A, Lorenzo G, Auricchio F, Baroli D, Hughes ThJR, Patton A, et al. Simulating the spread of COVID-19 *via* a spatially-resolved susceptible – exposed – infected – recovered – deceased (SEIRD) model with heterogeneous diffusion. *Applied Mathematics Letters*. 2021;111:106617. DOI: 10.1016/j.aml.2020.106617.

2. Liu M, Cao J, Liang J, Chen M. *Epidemic-logistics modeling: a new perspective on operations research.* Singapore: Springer; 2020. 287 p.

3. Kucharski AJ, Russell TW, Diamond C, Yang Liu, Edmunds J, Funk S, et al. Early dynamics of transmission and control of COVID-19: a mathematical modelling study. *Lancet Infectious Diseases*. 2020;20(5):553–558. DOI: 10.1016/S1473-3099(20)30144-4.

4. Cooper I, Mondal A, Antonopoulos CG. A SIR model assumption for the spread of COVID-19 in different communities. *Chaos, Solitons and Fractals*. 2020;139:110057. DOI: 10.1016/j.chaos.2020.110057.

5. Chitnis N. Introduction to SEIR models. In: *Swiss Tropical and Public Health Institute. Workshop on mathematical models of climate variability, environmental change and infectious diseases; 2017 May 8; Trieste, Italy* [Internet]. Basel: Swiss TPH; 2017 [cited 2021 March 5]. [about 38 p.]. Available from: http://indico.ictp.it/event/7960/session/3/contribution/19/material/slides/0.pdf.

6. Ala'raj M, Majdalawieh M, Nizamuddi N. Modelling and forecasting of COVID-19 using a hybrid dynamic model based on SEIRD with ARIMA corrections. *Infectious Disease Modelling*. 2021;6:98–111. DOI: 10.1016/j.idm.2020.11.007.

7. Giordano G, Blanchini F, Bruno R, Colaneri P, Di Filippo A, Angela Di Matteo, et al. Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy. *Nature Medicine*. 2020;26:855–860. DOI: 10.1038/s41591-020-0883-7.

8. Lan Lan, Dan Xu, Guangming Ye, Chen Xia, Shaokang Wang, Yirong Li, et al. Positive RT-PCR test results in patients recovered from COVID-19. *JAMA*. 2020;323(15):1502–1503. DOI: 10.1001/jama.2020.2783.

9. Changpin Lia, Chunxing Tao. On the fractional Adams method. *Computers & Mathematics with Applications*. 2009;58(8): 1573–1588. DOI: 10.1016/j.camwa.2009.07.050.

10. Owolabi KM, Atangana A. *Numerical methods for fractional differentiation*. Singapore: Springer; 2019. 328 p. (Springer series in computational mathematics; volume 54). DOI: 10.1007/978-981-15-0098-5.