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Spatiotemporal transmission of infectious particles in environment: A case study of Covid-19

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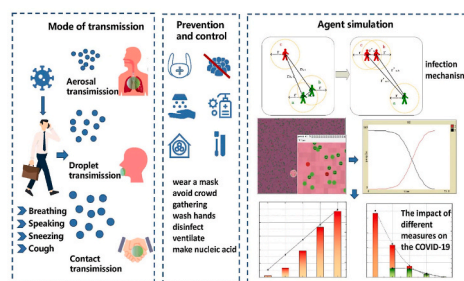
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HIGHLIGHTS

- A novel Spatiotemporal approach based on multi-agent model was proposed.
- Transmission of infectious particles in environment is simulated.
- Various control measures were applied and the influence was measured quantitatively.
- Highlights role of healthcare facilities and population distribution in transmission.

GRAPHICAL ABSTRACT



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ABSTRACT

This study explores the dynamic transmission of infectious particles due to COVID-19 in the environment using a spatiotemporal epidemiological approach. We proposed a novel multi-agent model to simulate the spread of COVID-19 by considering several influencing factors. The model divides the population into susceptible and infected and analyzes the impact of different prevention and control measures, such as limiting the number of people and wearing masks on the spread of COVID-19. The findings suggest that reducing population density and wearing masks can significantly reduce the likelihood of virus transmission. Specifically, the research shows that if the population moves within a fixed range, almost everyone will eventually be infected within 1 h. When the population density is 50%, the infection rate is as high as 96%. If everyone does not wear a mask, nearly 72.33% of the people will be infected after 1 h. However, when people wear masks, the infection rate is consistently lower than when they do not wear masks. Even if only 25% of people wear masks, the infection rate with masks is 27.67% lower than without masks, which is strong evidence of the importance of wearing a mask. As people's daily activities are mostly carried out indoors, and many super-spreading events of the new crown epidemic also originated from indoor gatherings, the research on indoor epidemic prevention and control is essential. This study provides decision-making support for epidemic preventions and controls and the proposed methodology can be used in other regions and future epidemics.

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1. Introduction

In recent decades, infectious diseases have endangered human health and social development (Xia et al., 2023). There are well-known SARS, MERS, Ebola, Zika and recent COVID-19. As monitoring and mitigation of environmental pollutants have been one of the major concerns in recent years (Karimian et al., 2017; Wu et al., 2018; Hojjati-Najafabadi et al., 2023), one of the ultimate usage of epidemiological studies could be to control and mitigate the environmental influence of different disease through considering various factors and scenarios (Mansoorianfar et al., 2022; Vasseghian et al., 2023). Some of the epidemiological studies provide basic dataset for further deep understanding of a phenomenon and its health effect (Chen et al., 2022; Karimian et al., 2023), while others investigate the transmission of an infection and they ways to control it (Hu et al., 2022). Besides, some studies have concentrated on social and psychologic impact of pandemic (Hu et al., 2021). The first case of COVID-19, was reported in December 2019 in Wuhan, China. According to the statistical data of the COVID-19 map released by Johns Hopkins University, as of July 10, 2022, the number of infected people in the world exceeded 555 million, with more than 6.4 million deaths. The COVID-19 epidemic is another public health emergency after SARS in 2003, and it has been identified as a “global pandemic infectious disease” by the World Health Organization (WHO) (Li et al., 2020; Shahin et al., 2022).

COVID-19 is a highly contagious disease that can be spread in various ways. In addition to the standard contact transmission, it is spread by droplets formed when coughing and sneezing (Karia et al., 2020). Aerosol transmission is considered the main route of air transmission. Droplets with viruses are mixed in the air to form aerosols, which can easily lead to infection after inhaling the human body (Tellier et al., 2019; Sohn et al., 2023). Cheng et al. (2020) conducted an epidemiological analysis on patients infected with COVID-19 while wearing masks and not wearing masks and found that wearing masks can effectively control the development of the epidemic. Wang et al. (2020) found that wearing masks at home before primary cases can reduce the probability of secondary transmission.

Since the outbreak of COVID-19, scholars have conducted research focusing on the development trend of the SARS-Cov-2 virus and COVID-19. At present, relevant studies mainly focus on etiology (Joob and Wiwanitkit, 2021), epidemiology (Salmi, 2022), transmission dynamics (Gomes and Serra, 2021; Nepomuceno et al., 2022), epidemic prediction, and epidemic prevention strategies (Assaf et al., 2020; Tiwari et al., 2020). Among them, the growth forecast of the epidemic situation and the evaluation and analysis of epidemic prevention policies are mainly studied by constructing corresponding models. Statistical modeling helps researchers to obtain the mechanism of propagation of different phenomena and the essential factors in the formation and transmission process and construct hypothetical environments that cannot be analyzed in different natural scenes through hypothetical experiments (Karimian et al., 2020; Fang et al., 2022). Chen et al. (2021) analyzed the spatial and temporal distribution characteristics of COVID-19 in the Chinese mainland and the influencing factors using statistical techniques, correlation analysis, and GIS representation. In addition, the prevalence of COVID-19 under different control intensities was simulated by the improved SIR model. Wu et al. (2020) calculated the possible infection risks from Wuhan to other cities in China and from China to other countries by using the location data and official aviation guide data and predicted that some countries might face a COVID-19 pandemic in the first half of 2020. Jia et al. (2020) used mobile phone signaling data in Wuhan during the Spring Festival travel rush in 2020. They established a spatiotemporal risk source model based on human mobility, which verified the influence of population mobility on the spatiotemporal distribution of different cities on the Chinese mainland. The model can also identify areas with a high risk of transmission in the early stage. Kissler et al. (2020) analyzed the seasonal, immune, and cross-immune characteristics of some coronaviruses like COVID-19 and

predicted the transmission dynamics of COVID-19 in the United States within five years. They projected that SARS-CoV-2 can proliferate at any time of year and if an immunity to SARS-CoV-2 is permanent, the virus could disappear for 5 or more years after causing a major outbreak. These mentioned models predict and simulate the transmission in macro or meso levels. They are suitable for explaining the spread law of epidemics in a large area (province or country), but they cannot provide accurate simulation conditions for indoor environments. However, to accurately simulate the transmission dynamics, and identify the infection process through the interaction between members, it is essential to analyze the influencing factors microscopically, especially in small groups or indoor environments, such as in about 40-square-meter classroom.

Agent model uses various agents to simulate the spread of infectious particle, the infection rate, and the influence of the epidemic in the corresponding location. Therefore, this technique can predict the epidemic situation and evaluate different controlling measures. A multi-agent system is a distributed intelligent system composed of several simple agents that can cooperate to complete global or local activities and use related technologies. In a multi-agent system, we can define multiple agent types and set multiple or single agent to complete an activity in a specific area at a specific time, which is called local activity. In addition, it is also possible to set up multi-agents to be active in the whole area, and called it global.

The multi-agent system has autonomy, flexibility, and expansibility, which is conducive to modeling and analyzing the spread of COVID-19 in different scenarios. Micro-individual models can directly show the spread process of the epidemic situation in a small-scale space, predict the spread of the epidemic in different places in the city, and provide the basis for accurate and real-time prevention and control in the city (Ronchi and Lovreglio, 2020).

Aiming at the spread of COVID-19 at the microscopic scale, based on the multi-agent modeling method, this paper uses the NetLogo platform to design and build a simulation model of COVID-19 prevention and control. The spatiotemporal transmission process of the COVID-19 epidemic in the process of crowd movement in an indoor environment is simulated. Moreover, the transmission mechanism of COVID-19 is investigated, in detail, including the transmission mode of COVID-19 and the key factors affecting the spread of the epidemic. Among these factors, the biological factors of susceptible people, such as the interaction between individual autoimmune systems or viruses, are the internal factors. In addition, among the external factors, natural environmental factors and non-drug interventions are also considered. Furthermore, by simulating and analyzing the influence of different prevention and control measures on the epidemic situation, this paper depicts the spread process of the epidemic situation on small scale (classrooms, buses, living rooms) that provides more detail about spread of the infectious particles. Also, it puts forward reasonable suggestions for preventing the epidemic situation from spreading, which helps to reach sustainable environment (Karimian et al., 2013).

2. Methods

2.1. Mechanisms of the spread of the COVID-19 virus

2.1.1. Model of transmission

The novel coronavirus spreads very fast, mainly because there are many mucosal cells in our lips, nasal cavity, and mouth. The mucosal cells contain novel coronavirus receptor-binding enzymes (Zhong et al., 2020). After the virus enters the human body, it releases RNA in single strands. RNA constantly replicates and generates different viral protein structures with ribosomes. At the same time, it will be secreted outside the cell to continuously infect new cells, which is the virus transmission process after entering the human body. The above is the transmission process of the virus after entering the human body (Yesudhas et al., 2021). When an infected person coughs and sneezes, a large amount of

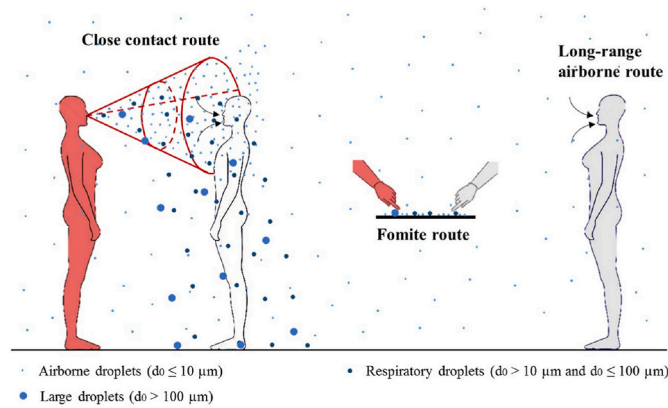


Fig. 1. The three major transmission routes: close contact, fomite and long-range airborne routes.

saliva is wrapped in the virus. Large droplets will fall to the ground quickly because of their weight, while tiny droplets will form fog clouds, soon evaporating into dry droplets nuclei in the air (Stadnytskyi et al., 2021). Droplet nuclei with pathogens can remain in the air for a long time, and if they are touched or inhaled by a healthy person, they may become infected. However, it still needs to be determined how long the droplet nuclei with the virus can survive in the air, which is related to factors such as the external environment (temperature, humidity, wind speed, etc.) and the host. The short ones die within a few hours, and the long ones can survive for days or even longer (Carraturo et al., 2020). Fig. 1 shows that when the virus is released from the respiratory tract of the infected person, it transmits through different transmission routes (Xiao et al., 2018). Therefore, it can be said that amount of infectious particles (viruses), hosts, and environmental factors affect the transmission probability (Leung, 2021). According to data from the Chinese Ministry of Health, there are three primary forms of COVID-19 transmission: contact transmission, aerosol transmission, and droplet transmission.

Contact transmission is divided into direct contact transmission and indirect contact transmission. The former refers to the infection caused by direct skin contact with the patient, while the latter refers to the infection caused by the susceptible person through contact with the environment contaminated by the patient. People treating patients with COVID-19 are particularly vulnerable to the transmission mode, which is one reason healthcare workers are so heavily infected. In the process of direct contact transmission, infectious cases are the primary source of transmission. Frequent alcohol-based hand sanitizer and soap to wash hands, avoiding contact with eyes, nose and mouth with contaminated hands, and prolonged ventilation time can minimize the contact transmission of COVID-19.

For aerosol transmission, the newly released “New Coronary Virus Pneumonia Diagnosis Program (Ninth Edition)” pointed out that “in a relatively closed environment, it is transmitted by aerosols and may cause infection after contact with infectious particles”. If the virus is adsorbed on the aerosol, it can form pathogenic microorganism aerosol.

Table 1
Information on droplets and aerosols from human exhalation.

Activity	Number of droplets produced (size>2 μm)	Aerosol (1–2 μm)	Site of origin
Normal breathing (5 min)	None - few	Some	Nose
Single strong breathing	Few - several hundred	Some	Nose
Softly counting	Few - few dozen	Some	Front of the mouth
Loudly speaking-talking	Few dozen - few hundred	Mostly	Front of the mouth
A cough (mouth open)	None - few hundred	Some	Faucial region
A cough (mouth initially closed)	Few hundred - few thousand	Mostly	Front of the mouth
Single sneezing	Few hundred thousand - few million	Mostly	Front of the mouth
	Few - few thousand	Some	Nose and faucial region

Airborne infection by pathogenic microorganisms is faster and more widespread due to the high mobility and diffusivity of the air. The diameter of aerosol particles is minimal. After being inhaled by susceptible people may be deposited in the deep respiratory tract and even in the alveolar area (Drossinos and Stilianakis, 2020). The study has shown that aerosols containing the novel coronavirus can survive 3 h on stainless steel surfaces and at least 48–72 h on plastic surfaces (van Doremalen et al., 2020). In addition, in a closed environment, there may be high concentrations of virus-containing aerosols in the air. These factors undoubtedly increase the speed of the epidemic.

Droplet transmission. Droplet transmission is the infection caused by the direct inhalation of droplets when the patient sneezes, coughs, and speaks. For ease of understanding, the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) assume that droplets are described as larger entities (>5 μm) that fall rapidly to the ground by gravity, usually within 3–6 feet of the source person. Aerosols are tiny particles (≤5 μm) that evaporate rapidly in the air and can be suspended in the air for several hours (Shiu et al., 2019). Droplets with a radius of 5–50 μm are easily inhaled into the human body (Nicas and Jones, 2009), while those more significant than 50 μm mainly adhere to susceptible individual mucous membranes (eyes, nose, lips). Correct use of personal protective equipment that can effectively block droplets and maintenance of personal and environmental hygiene can effectively reduce the infection rate of the epidemic (Lake, 2020).

The person in red is the infected one. The figure was quoted from Xiao et al. (2018).

Droplets and aerosols can be generated from “vigorous exhalation events” such as coughing and sneezing (Dhand and Li, 2020), as well as from breathing and speaking (Leung et al., 2020) Humans produce different numbers of droplet particles during different exhalation activities. Duguid (1945) was the first to explore the characteristics of droplets and aerosols produced by human expiratory activity and chest infections. The findings confirm that breathing and exhaling from the nose can generate hundreds of droplets, some of which are aerosols. In contrast, talking, coughing, and sneezing produced more aerosols than droplets (Table 1).

2.1.2. Key factors

Individuals may be repeatedly infected with the same virus, such as influenza and respiratory syncytial virus, throughout their lives. In early January 2021, “nature” magazine collected more than 100 experts’ opinions on the new Crown epidemic, and 90% of the experts believed that the new Crown virus would coexist with humans in a localized way for a long time. For the repeated and local outbreaks of the new crown epidemic, Shaman and Galanti (2020) believe that the main factors affecting the spread of the epidemic may be the following four:

1. Individual autoimmunity. After the first infection, the human immune system has a set of defense mechanisms. When the pathogen enters the host cell again, the defense mechanism can kill the pathogen efficiently and quickly. However, when the human immune system exhibits insufficient adaptive immune response, weakened immunity and immune escape, the bactericidal properties can be destroyed or circumvented, leading to re-infection. Moreover, as

- viruses evolve into new strains over time, existing immune mechanisms in the body may not be able to stop the mutated pathogens.
2. Season. Outside the tropical areas, the incidence of many common respiratory infections increases at specific times of the year. For example, in temperate regions, influenza incidence is highest in winter (Paules and Subbarao, 2017). The case data of COVID-19 also confirmed that the infection rate in winter is significantly more severe than in summer (Guo et al., 2021). On the one hand, the virus is more tolerant to low temperatures. On the other hand, people prefer to stay indoors in the cold winter, and a closed indoor environment is more conducive to spreading the virus.
 3. Virus interaction. Viruses may enhance the spread of each other but may also accomplish suppression of another strain by neutralizing a more infectious strain cross-reacting. The study has shown that most people infected with COVID-19, regardless of the severity, induce the production of some specific antibodies (Long et al., 2020). The antiviral interferon response of the host is usually considered the primary mechanism to interfere with the performance, which may inhibit the secondary infection. On the population scale, this inhibitory effect can effectively slow down the epidemic rate of the virus and change the transmission time.
 4. Drug and non-drug interventions. Drug defense measures are mainly vaccination. Given the mode of transmission of COVID-19, non-drug

intervention measures such as isolation, wearing masks and disinfection are also essential components of the public health response to the COVID-19 epidemic. These measures can reduce the transmission of COVID-19 to a certain extent. The commonly used non-drug interventions are as follows:

Control social distance. Viral transmission is more likely to occur within the distance covered by human breathing activities. Table 1 shows significant differences in the number of droplets and aerosols produced by different human exhalation activities. The influence range of droplets produced by different exhalation activities is also different. Fig. 2 shows the droplet trajectory of the infected person when sneezing, coughing, and simply exhaling. (a) When sneezing, droplets travel for 6 m at a speed of 50 m/s within 0.12s; (b) When coughing, the droplets travel at a speed of 10 m/s for 2 m within 0.2s; (c) When exhaling, the droplets travel 1 m at 1 m/s in 1s (Mahjoub Mohammed Merghani et al., 2021). The Department of Disease Control and Prevention recommends covering the mouth and nose with elbows or disposable toilet paper when coughing or sneezing and promptly disposing of the toilet paper. Because coughing and sneezing produce more particles and have an enormous scope of influence, covering with elbows or paper towels can reduce the spread of the virus. It further explains that maintaining social distance, preferably more than 2 m, can reduce the risk of virus

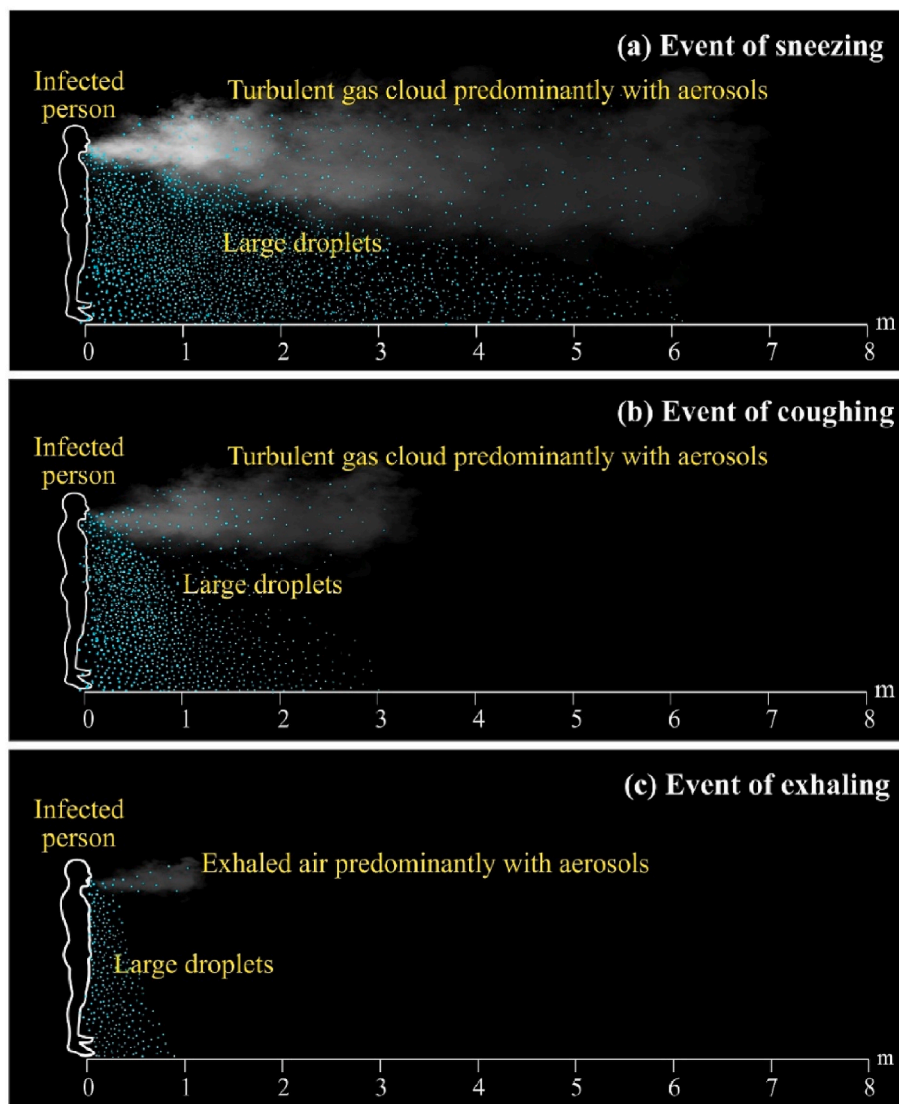


Fig. 2. Droplet trajectories generated by different exhalation activities (Jayaweera et al., 2020).

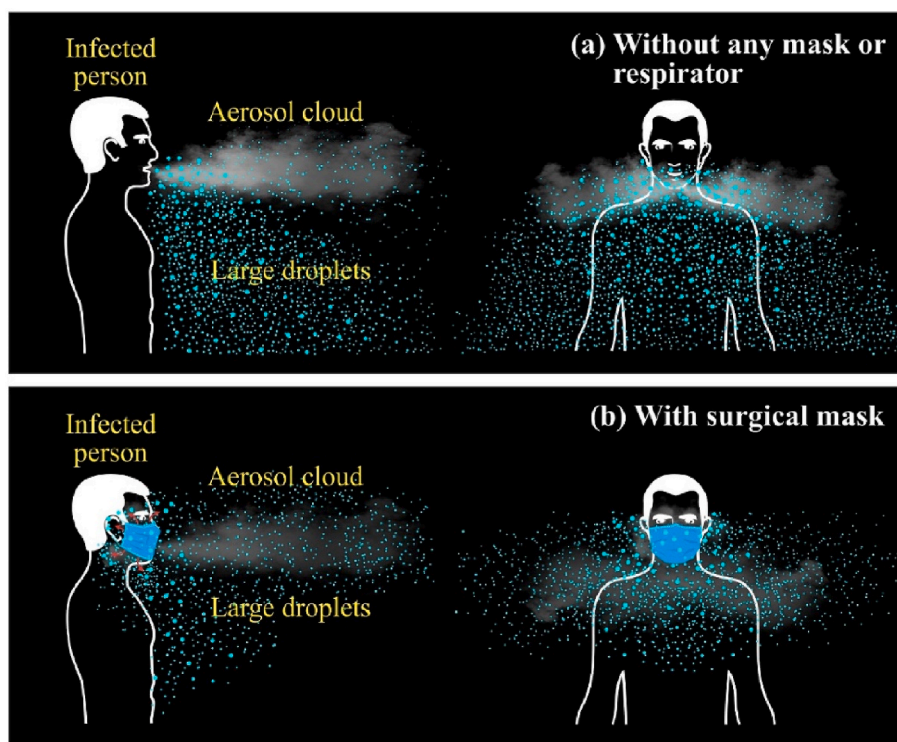


Fig. 3. Particle leakage with and without masks (Jayaweera et al., 2020).

transmission (Jayaweera et al., 2020) (see Fig. 3).

Wear masks. In the early epidemic of infectious diseases, without any vaccination and specific anti-infection treatment, medical surgical masks play an important role in preventing the spread of droplets and aerosols.

Limit indoor gatherings. Crowd gatherings also affect the spread of the virus to a certain extent. In dense public places (shopping malls, squares, classrooms, etc.), the crowd is highly concentrated, and the mobility of individuals is considerable, which is easy to cause the spread of infectious diseases. Usually, when the area (spatial range) is fixed, the more people there are, the smaller the distance between people and the greater the risk of virus transmission. This figure depicts the trajectory of droplets and aerosols infecting patients with and without medical masks (Mahjoub Mohammed Merghani et al., 2021). With surgical masks worn, only about 20–30% of droplets and aerosols are expected to leak, mainly from loose sides. A medical mask can effectively limit the spread range of virus-carrying particles produced by infected people during exhalation, play the role of a “firewall” for susceptible people reduces the risk of virus infection.

Ventilation disinfection. The survival time of the virus on the surface of the object will directly affect its ability to spread. Studies have shown that viruses with epidemic potential, such as the SARS, Ebola, and influenza viruses, can survive on the surface of objects for a while and have the risk of transmission. Therefore, regular ventilation and disinfection can effectively shorten the survival time of viruses in the air and on objects, thus inhibiting the spread of viruses.

2.2. COVID-19 propagation model construction based on multi-agent in an indoor space

2.2.1. Intelligent simulation of COVID-19 propagation framework

The indoor space COVID-19 propagation model is structurally composed of three parts: the simulation preparation stage, the simulation operation stage, and the simulation result stage. The preparation stage of simulation provides input data for the model, which can be used to configure the agent, simulation space environment, and interactive

information among various elements. The simulation phase is the core part of the model, which shows the evolution process of virus transmission and state transformation between infected and susceptible agents through environmental interaction. The influence of different population densities and mask-wearing rates on the spread of COVID-19 was simulated by setting the relevant parameters of agents. The overall framework of the model is shown in Fig. 4.

2.2.2. Basic agent attributes

The agent model comprises agents with specific action goals, which can perceive the environment and make decisions under specific conditions. By defining the attributes and behaviors of agents, some phenomena in the real world can be simulated. The modeling objects are divided into micro-individuals, single groups, and compound groups in constructing the infectious disease model. Micro-individual takes a single individual as the research object, fully considering individual differences. A single group regards a class of individuals with the same characteristics and explores the differences between individuals with different characteristics. A compound group is composed of individuals in a relatively independent geographical area, and the migration of internal individuals connects subgroups.

In the process of the COVID-19 virus spreading, Susceptible agents (S, Susceptible) and Infected agents (I, Infected) are important behavior subjects for virus prevention and control. A susceptible agent is a healthy agent that has not been infected yet, but lacks immunity and has a certain probability of being infected after contact with a latent or infected person. The agent class in the virtual geospatial environment has specific attributes. Table 2 shows the primary attributes of agents.

2.2.3. Agent-based model development

According to the movement of individuals in a limited space area, an agent-based COVID-19 transmission model is constructed, and the virus is transmitted by randomly moving individuals in space. Firstly, a plane space of a specific size is created, and a certain number of agents are randomly distributed in the plane space. The position of each agent in the initial state is unique, and all agents in the plane are in an

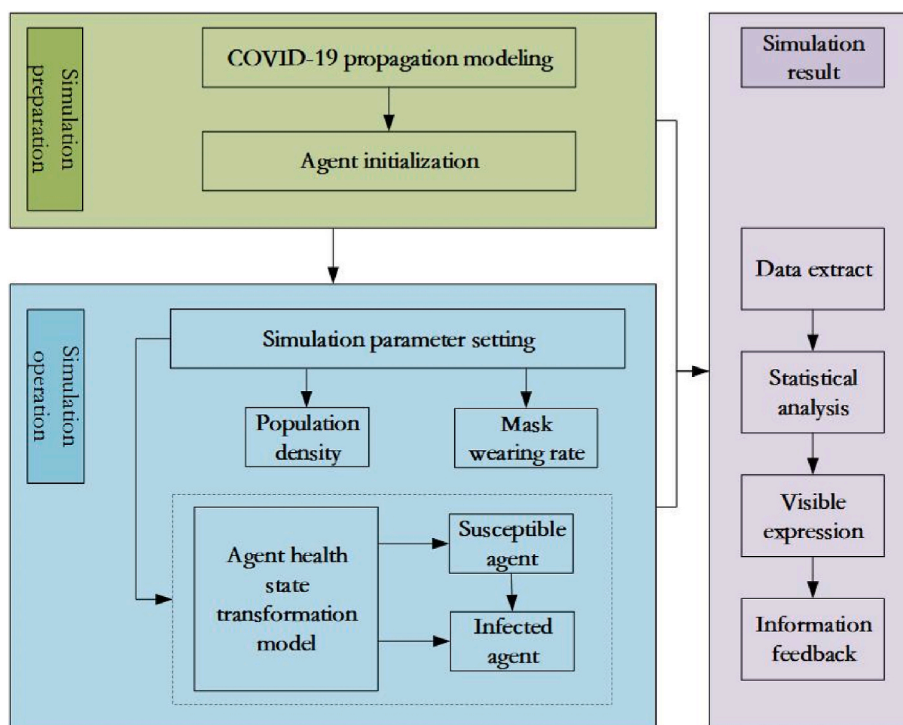


Fig. 4. COVID-19 agent simulation model framework diagram.

Table 2

Basic attributes of agents.

Attribute name	Meaning	Attribute name	Meaning
Who	Unique identification code	exposed_period	Exposed days
Xcor	X coordinate of agent in virtual space	infected_period	Infected days
Ycor	Y coordinate of agent in virtual space	infected?	Whether the infected agent
shape	Agent shape	susceptible?	Whether the susceptible agent
Size	Agent size		

independent state. All agents can move randomly in any direction in discrete time and space. Most of the changes in the status of infected people are determined based on probability. However, there are two influences of “time” and “space” in spreading infectious diseases. If the susceptible person has been in contact with the infected person at some point, the probability of the susceptible person being infected is higher. Secondly, the closer the spatial distance between susceptible and infected people is, the higher the probability of infection. Conversely,

the farther the spatial distance between susceptible and infected people is, the lower the probability of infection will be. The steps to determine whether a susceptible person is infected are as follows:

Calculate the sum of the doses of the individual virus of infected persons received by a susceptible individual. If the infected dose received by the susceptible individual i in contact with the infected individual j at time t is $d_i(t)$, the calculation formula is as follows:

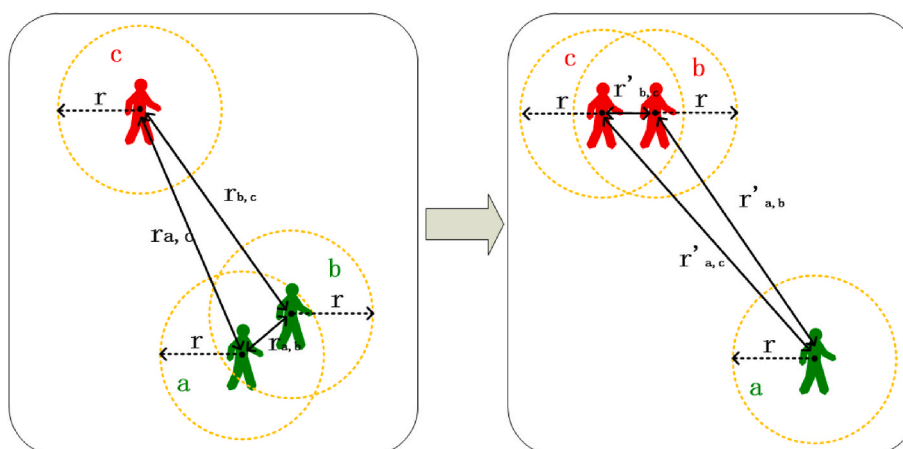


Fig. 5. Transmission of COVID-19 between individuals.

$$d_i(t) = \frac{d}{r_{ij}} \quad r_{ij} < r \quad (1)$$

where d is the dose value of infection, r_{ij} is the distance between susceptible and infected individuals, and r is the maximum infection range. At time t , the total infection doses $D_i(t)$ received by the susceptible individuals equals the sum of the infection doses given by all infected agents who have contact with them.

$$D_i(t) = \sum_{n=1}^n d_i(t) \quad (2)$$

n is the number of infected individuals who have contact with susceptible individuals at t time.

Compare the total infection dose received by the susceptible person with the infection critical value. Suppose the total infection dose received by the susceptible person is greater than the critical infection value. In that case, there is a certain probability that the infected body of the susceptible person will be infected. Otherwise, it will not be infected:

$$D_i(t) \begin{cases} \geq d_i \cap k \leq p \\ < d_i \end{cases} \quad (3)$$

where d_i is the critical value of infection, k is a random number, and p is the probability of infection.

The spreading process of the agent is shown in Fig. 5, where r is the maximum infection range of the infected person. When the distance between two individuals is less than r , and one individual is infected, the other is at risk of infection. For example, at a specific time t , individuals a and b are healthy, and individual c is infected. Although the distance $r_{a,b}$ between individual a and individual b is smaller than r , both individuals a and b are healthy. There will be no infection between the two

individuals. The distance $r_{a,c}$, $r_{b,c}$ between individual c and individual a and individual b is more extensive than r , so there is no danger that individual a and individual b will be infected by individual c . The new position is shown on the right after the individual moves randomly. The distance $r_{b,c}$ between individual b and individual c is less than r , and individual b will receive a certain amount of virus dose from individual c . Individual b will be at risk of infection when the dose value reaches the critical value.

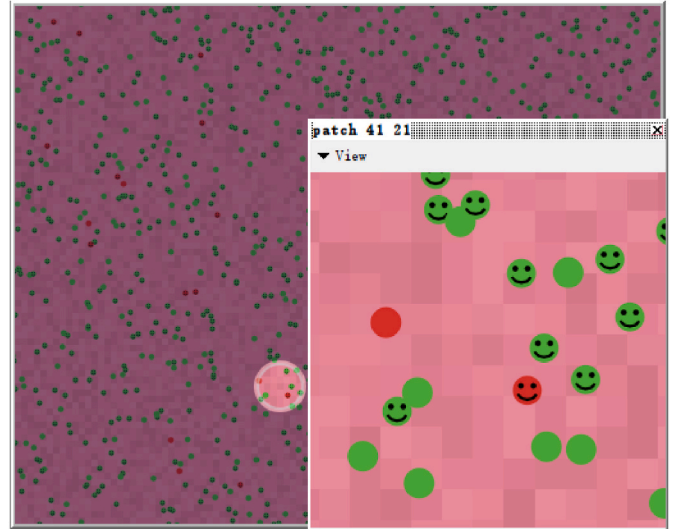


Fig. 7. Representation of individuals in different state.

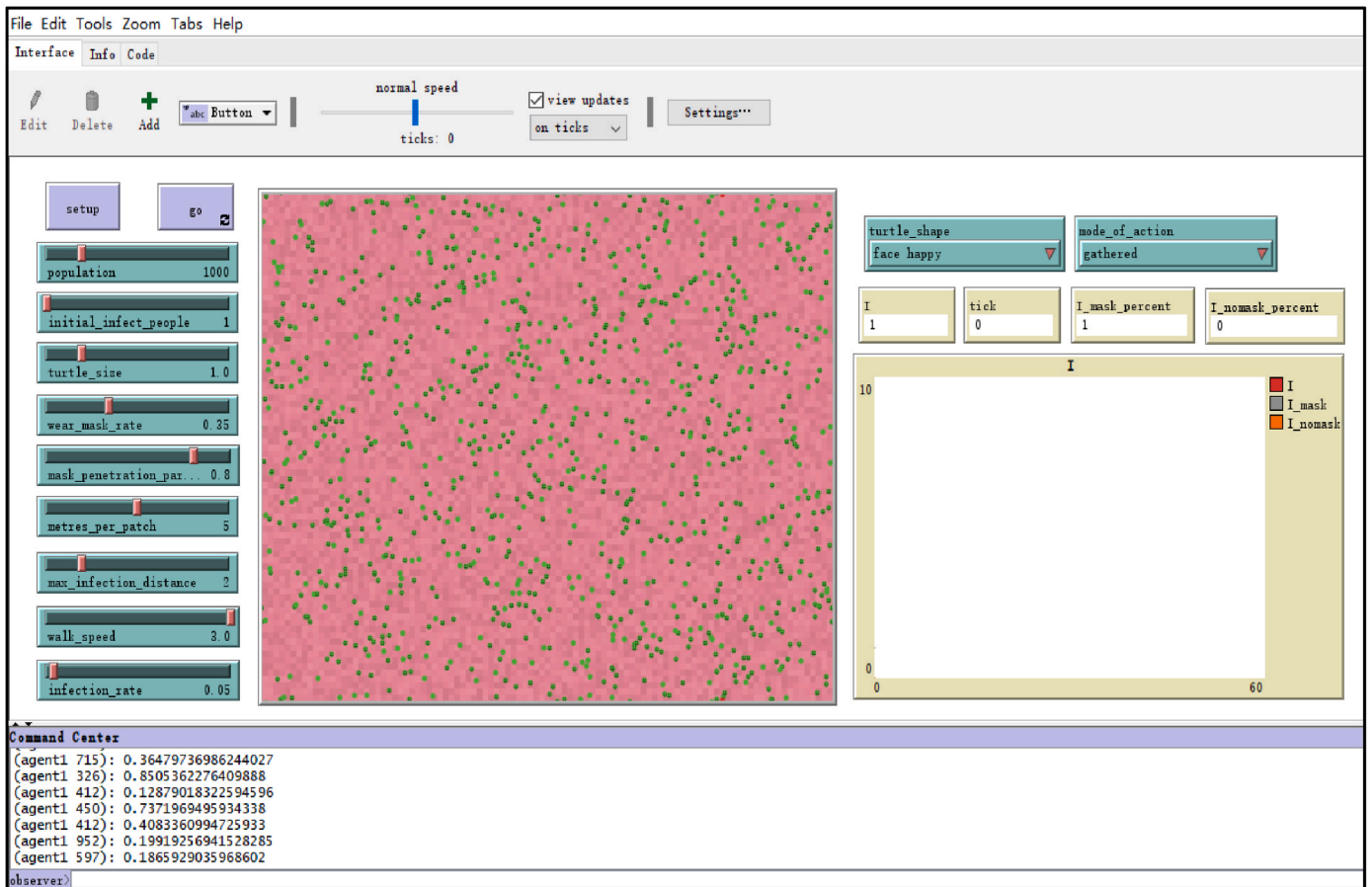


Fig. 6. NetLogo interface of COVID-19 spread model based on agent.

The model is developed and implemented using the NetLogo programming environment, and the interface is shown in Fig. 6. NetLogo is a programmable simulation platform developed based on the Java language, used to simulate multi-agent modeling environments for natural and social phenomena. It is particularly suitable for modeling complex systems, which their conditions vary with time. NetLogo uses the Logo language for programming and adds intelligent agents and concurrency mechanisms on top of the Logo language. Modelers can issue instructions to hundreds or thousands of independent “agents” running simultaneously to explore the connection between micro-individual behavior and emerging macro-group phenomena.

In the experiment, the factor of wearing masks was considered emphatically. The shape of individuals who do not wear masks is set as smiling faces. Circles represent individuals who wear masks, and the green smiling face represents susceptible individuals who do not wear masks. The green circle indicates susceptible individuals wearing masks. The red smiling face means an infected person without a mask. The red circle indicates the infected person wearing a mask (see Fig. 7).

3. Results

3.1. Simulation experiments and analyses

The time of virus transmission is short. Sometimes, the process can be completed even in a few seconds, so we use the COVID-19 model based on an agent to simulate the 1-h virus transmission in a limited space. Only susceptible and infected agents are set in the initial state of the model. When a susceptible person accumulates more than a specific

viral load through contact or airborne transmission, it has a certain probability of being infected. Once infected, the individual is contagious in a specific incubation period. Since the model is simulated in minutes and recovered in one day, the model does not consider the agent who is cured or dies after infection.

3.1.1. Model basic assumptions

Crowd individuals in a limited space area are regarded as dynamic agents, and a static environment with a particular spatial range is constructed through agents. The following assumptions support the model:

Hypothesis 1. : The transmission environment is limited to a fixed and closed area, with no population inflow and outflow. The simulation time step is 1 h.

Hypothesis 2. : During the running of the model, all individuals move freely in the crowd. The simulation place is suitable for gathering places where most individuals are moving, such as residential quarters, supermarkets, shopping malls and squares, without considering the short-term stay of some individuals.

Hypothesis 3. : The viral dose contained in each infected person is the same, not affected by age, physical fitness, and other factors.

Hypothesis 4. : Only direct mechanisms and objective processes are simulated. Many factors influence the spread of COVID-19. This paper only simulates its objective process based on the direct influence mechanism. This direct influence mechanism includes a close-range transmission mechanism, and protection mechanism (mainly wearing medical masks), without considering other influence mechanisms (such

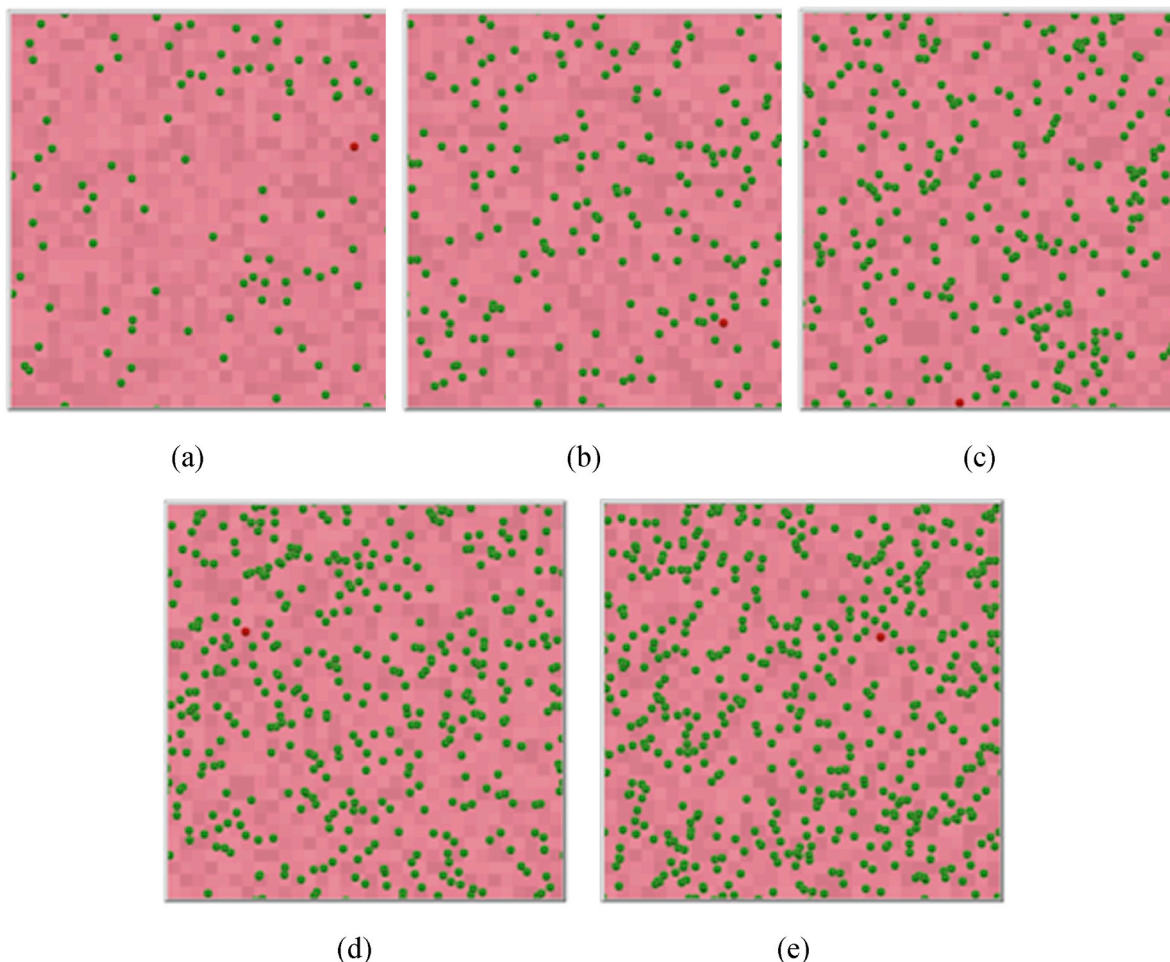


Fig. 8. Distribution of different population densities in a limited space.

Table 3
Simulation parameter settings.

Parameter	Meaning	Numerical value
Patch	The size of the simulation space	About 1000 patches
initial infect people	Number of initial infections	1
turtle size	Size of the agent	0.8
mask penetration particles	Proportion of particles filtered by wearing a mask	25%
walk speed	Walking speed	random-float 1.1
max infection distance (r)	Maximum infection distance	2
infection rate (p)	Infection rate	0.05
d_i	critical value of infection	1
D	dose value of infection	0.2
K	random number	[0,1]
mode of action	Mode of motion	random
population	Total number of people	100, 200, 300, 400, 500
wear mask rate	Proportion of people wearing masks	0, 25%, 50%, 75%, 100%

as air circulation, meteorological factors, etc.).

3.1.2. Parameter settings

The research experiment on infectious diseases cannot be carried out in a natural population. The relevant data can only be obtained from the existing reports and records, but these data are not comprehensive enough. The current research mainly uses computer simulation for analysis. In the following we explain various input values in NetLogo.

Total area: The NetLogo interface display sets the patch with (0,0) as the origin, and the fixed point is a rectangular patch of (31,31). The total area is $1024 = 32 \times 32$, and the active area is about 1000 patches.

Total number: To explore the impact of population aggregation on infectious particles transmission, five population density levels were set in the simulation to describe the spread of the epidemic under different population densities. In the active area of about 1000 patches, the first density is 10%, and the number of individuals is 100; the second density is 20%, and the number of individuals is 200; the three-level density is 30%, and the number of individuals is 300. The four-level density was 40%, and the number of individuals was 400. The five-level density is 50%, and the number of individuals is 500. Initially, individuals given five population densities are randomly distributed within the region (see Fig. 8).

Number of initial infections: The initial number of infected persons per simulation is 1, and the location of the infected person is randomly distributed.

The proportion of particles filtered out by wearing masks: It is assumed that all the masks worn by individuals in the experiment are medical-surgical. Mahjoub Mohammed Merghani et al. (2021) showed that about 20%–30% of the drops and aerosols leaked when wearing medical surgical masks.

Walking speed: The walking speed of ordinary people is about 1.1 m/s, but individuals may stay or walk. The random floating-point number of 1.1 is taken as the walking speed in the experiment.

Maximum infection distance: The maximum range of virus particles received by susceptible people from infected people.

Infection rate: The early infection rate in China was determined to be 0.05, according to the data of the National Health Commission.

The proportion of wearing masks: In order to analyze the effectiveness of wearing masks, the proportions of wearing masks were set to 0, 25%, 50%, 75%, and 100%, respectively. Model simulation parameter settings are shown in Table 3.

3.2. Analysis of simulation results

3.2.1. Spatial and temporal distribution characteristics of COVID-19

The total number of people in a simulated space of about 1000 patches is 500. It is assumed that there is an initial infected person, and the disease is slowly spreading along with the constant movement and contact of the people. Fig. 9 shows the change in rate of susceptible person S and the infected person I with time. In the beginning, there was

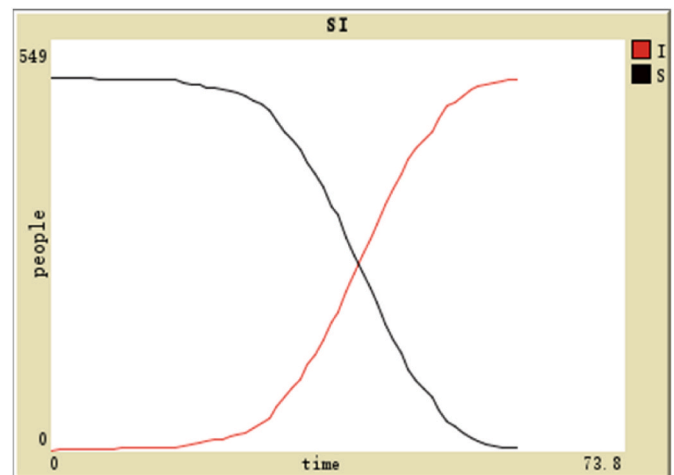


Fig. 9. Changes in susceptible and infected people over time.

only one infected person. As the infected people keep moving and contacting the susceptible, the virus starts to spread. The number of infected people is increasing over time. Finally, everyone is infected. Therefore, the number of susceptible will eventually become infected without any prevention and control measures.

Fig. 10 shows the evolution process of the virus over time, as well as the movement rules of individuals, and further studies the spatial distribution characteristics of the virus in the transmission process. It shows the distribution of the number of susceptible and infected people in the plane space when $t = 0, 20, 40, 60$ different moments. From Fig. 10, we can see that the infected population initially showed a clustered distribution, and then spread around and eventually led to more and more people being infected. The simulation results show that the crowd moves in a fixed space, without the inflow and outflow of the crowd, and almost everyone will eventually be infected with the virus. When an infectious disease breaks out, limiting the range of individual activities, reducing crowd gathering, and controlling the outbreak area can effectively control the spread of the disease.

3.2.2. Influence of population density

Population density is the core index and variable that causes the rapid spread of infectious diseases. Through the simulation, we can accurately investigate the epidemic's influence effect and infection situation in different population densities and provide accurate guidance for epidemic prevention in different population densities. Because the spread of epidemic diseases is random in space and quantity, the single simulation result may not be representative. In the experiment, all results were randomly simulated 100 times with the same parameters, and the average value of 100 simulation results was finally taken. Through

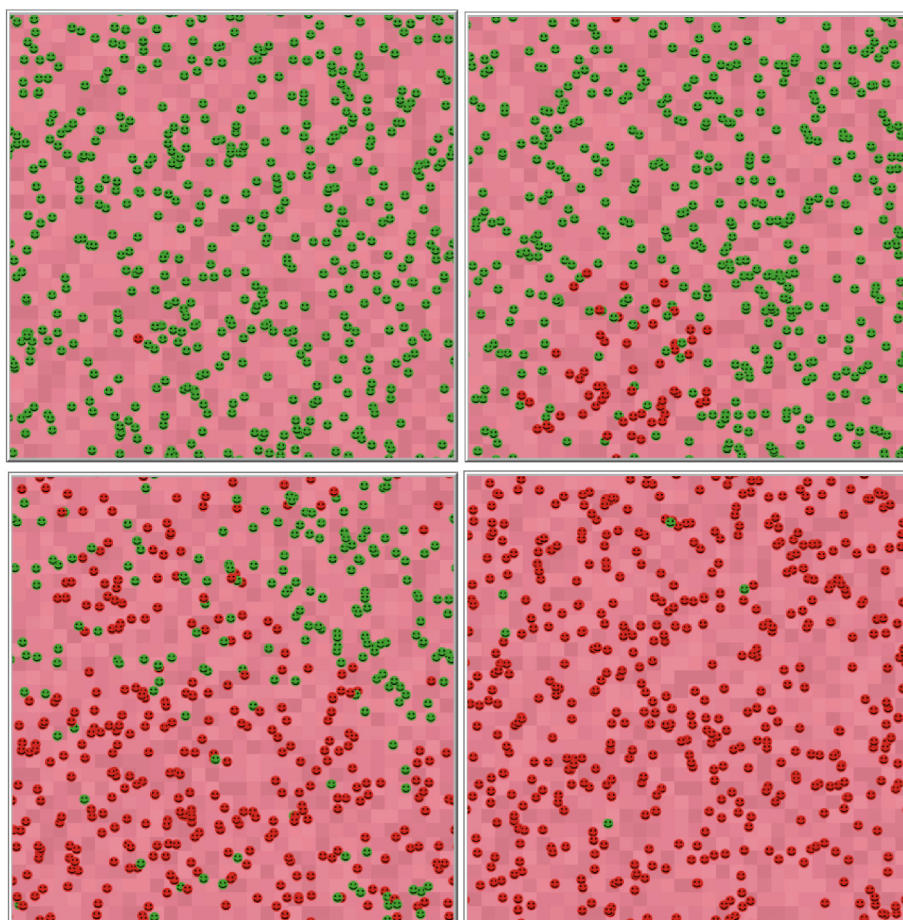


Fig. 10. Spatial distribution of susceptible and infected people over time.

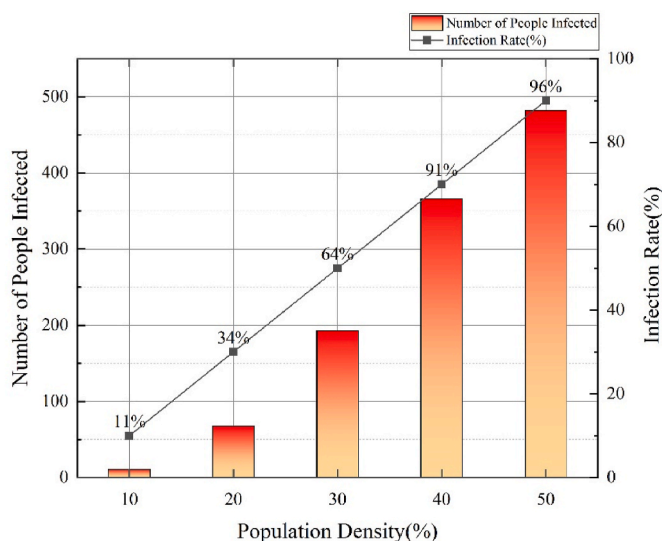


Fig. 11. The number of infected people in 1 h with different population densities.

100 simulations, the average number of infected people in five population density levels after 1 h without any protective measures. The results are shown in Fig. 11.

The experimental results show that the epidemic infection rate increases with population density. The number of first-density infections was about 11, and the infection rate was 11%. The number of second-

density infections was about 68, and the infection rate was 34%. The number of people infected with the three-level density was about 193, and the infection rate was 64%. The number of people infected with the four-level density was 366, the infection rate was 91%, and the number of people infected with the five-level density was about 482, and the infection rate was 96%. Therefore, with the increasing number of people in a limited area, the space occupied by individuals per capita will become smaller and smaller. The per capita occupied space of the first-level density ranges from 10 patches to only two patches of the five-level density. The smaller range of individual activities also means the distance between individuals is closer. The epidemic will spread rapidly when infected people are in dense spaces.

Because of the risk of epidemic transmission caused by population movements, lockdown isolation has become the mainstream prevention policy. However, at present, the epidemic situation gradually tends to be normalized. In non-high-risk areas, prevention and control regulations are often in a " lax " state, especially in suburban areas far from urban centers. The suburban society's risk awareness, prevention and control ability, and response measures are relatively lacking; coupled with population mobility, organizational weakening, and insufficient resources, the ability to prevent and control the epidemic is low. Once an emergency occurs, it is easy to lead to the rapid spread of the epidemic. In 2021, a super-spreading event occurred in Tonghua City, Jilin Province, resulting in about 140 people being infected. L was identified as the super-spreader of this event, which directly infected more than 80 people and indirectly infected about 60 people. L gave three training sessions in two days at site A in Tonghua City. The classroom where L trained was about 20 square meters, with windows and doors closed and about 2.5 h between training sessions. L and most participants did not wear masks during the three training sessions. A total of 97 participants,

74 of whom tested positive for nucleic acid. The incidence of the three lectures was 90% (36/40), 90% (28/31), and 38% (10/26), respectively. The event proves that the virus will spread rapidly in a closed space without population flow, and the infection rate will increase with population density.

3.2.3. Proportion of wearing masks

The population of 300 was selected to analyze further the protective effect of wearing masks on individuals. During the experimental simulation, it was assumed that people wore disposable medical masks correctly. The average value of 100 experimental results was taken to represent the relationship between the proportion of people wearing different masks and the number of final infections in a fixed occasion within 1 h. The results are shown in Fig. 12. It can be found from the figure that if 300 people do not wear masks, nearly two-thirds of them will be infected. As the proportion of people wearing masks increases, the number of infected people gradually decreases. If only 25% of people wear masks, there will be nearly 139 people infected, 27.98% less than the total number of infections who do not wear masks. If 50% of people wear masks, the final number of infections is about 66, which is 52.52% less than only 25%. If 75% of people wear masks, the final number of infections is about 28, 57.58% less than that of only 50%. When all are masks, the number of infections is about two after an hour, 92.85 percent fewer than the 75 percent who wore them. Among the infected people with different proportions of wearing masks, the infection rate of wearing masks and the infection rate of not wearing masks decreased with the increase in the proportion of wearing masks. The infection rate of wearing masks was lower than that of not wearing masks when the proportion of wearing masks was 25%, 50%, and 75%, respectively. Therefore, wearing masks can effectively reduce the risk of virus transmission.

4. Conclusion

In this paper, a multi-agent-based simulation model of COVID-19 virus prevention and control is constructed to spread and prevent COVID-19. This model simulates the spatiotemporal propagation process of the COVID-19 epidemic in a limited area. Simulation results show that the virus will continue to spread without any containment measures until it infects everyone in a fixed area. Simulations were performed with different population densities and different mask-wearing rates. The simulation results show that when the population does not flow in and out, the population density will seriously affect the spread of the epidemic. When the population density is 10%, the infection rate is 11%. For every 10% increase in population density, the infection rate increases by three times. The increase in crowd density means that the social distance between people is decreasing, and campuses, shopping malls, hospital outpatient clinics, large vehicles, and other places are often densely populated. They are places where the new crown virus is easy to spread. Wearing a mask is necessary during the spread of COVID-19. While this protection does not result in a significant drop in infection rates, this limited drop can keep the spread of the virus under control. In our study, when the population density was 30%, the number of infections wearing masks was consistently lower than that of not wearing masks. When everyone wore masks, the infection rate was 1.67%, while when no one wore masks When wearing a mask, the infection rate was 72.33%. Without a mask, the virus will ultimately be out of control. People's life and work are mainly carried out indoors, primarily when various blockade measures are implemented during the epidemic. Nevertheless, even when the epidemic is severe, community personnel must have a certain degree of mobility to ensure the unimpeded flow of rescue personnel, materials, equipment, and others., and to ensure the supply of basic living materials for citizens. This contradiction in epidemic prevention and control can easily lead to the importation of new coronavirus cases and the outbreak of clustered epidemics. Reducing unnecessary indoor gathering activities, advocating the

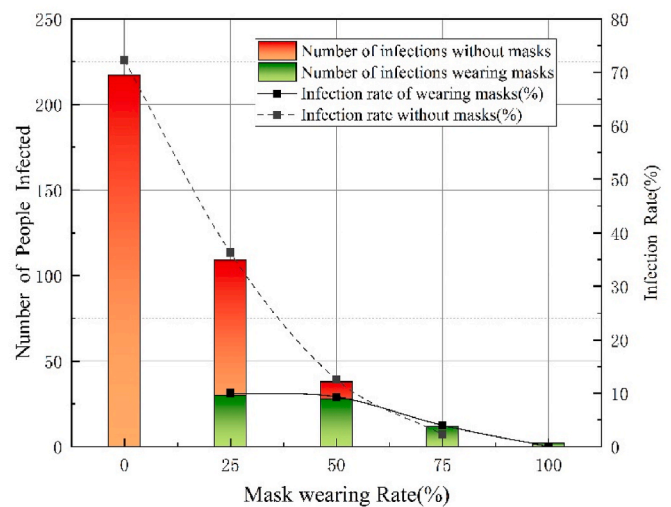


Fig. 12. The number of infected people with different proportions of people wearing masks within 1 h.

correct wearing of medical masks, and timely vaccination against the new coronavirus can effectively prevent the increase in new cases. In future research, in terms of epidemic prevention and control, how to coordinate various prevention and control measures to achieve more effective prevention and control effects can be further studied. The model can be further extended with demographic, geographic, and environmental factors. Predict the development trend of the urban epidemic situation and provide more effective decision-making support for urban health security.

Credit author statement

Hamed Karimian: Conceptualization, Verification. **Qin Fan:** Methodology, Writing-Original draft. **Qun Li:** Data processing. **Hamed Karimian & Youliang Chen:** Supervision, Writing-Reviewing and Editing. **Juan Shi:** Visualization, Data collection.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

References

- Assaf, D., Gutman, Y., Neuman, Y., Segal, G., Amit, S., Gefen-Halevi, S., Shilo, N., Epstein, A., Mor-Cohen, R., Biber, A., Rahav, G., Levy, I., Tirosh, A., 2020. Utilization of machine-learning models to accurately predict the risk for critical COVID-19. *Intern. Emerg. Med.* 15, 1435–1443.
- Carraturo, F., Del Giudice, C., Morelli, M., Cerullo, V., Libralato, G., Galdiero, E., Guida, M., 2020. Persistence of SARS-CoV-2 in the environment and COVID-19 transmission risk from environmental matrices and surfaces. *Environ. Pollut.* 265, 115010.
- Chen, Y., Li, D., Karimian, H., Wang, S., Fang, S., 2022. The relationship between air quality and MODIS aerosol optical depth in major cities of the Yangtze River Delta. *Chemosphere* 308, 136301.
- Chen, Y., Li, Q., Karimian, H., Chen, X., Li, X., 2021. Spatio-temporal distribution characteristics and influencing factors of COVID-19 in China. *Sci. Rep.* 11, 3717.
- Cheng, V.C., Wong, S.C., Chuang, V.W., So, S.Y., Chen, J.H., Sridhar, S., To, K.K., Chan, J. F., Hung, I.F., Ho, P.L., Yuen, K.Y., 2020. The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2. *J. Infect.* 81, 107–114.
- Dhand, R., Li, J., 2020. Coughs and sneezes: their role in transmission of respiratory viral infections, including SARS-CoV-2. *Am. J. Respir. Crit. Care Med.* 202, 651–659.

- Drossinos, Y., Stilianakis, N.I., 2020. What aerosol physics tells us about airborne pathogen transmission. *Aerosol Sci. Technol.* 54, 639–643.
- Duguid, J.P., 1945. The numbers and the sites of origin of the droplets expelled during expiratory activities. *Edinb. Med. J.* 52, 385–401.
- Fang, S., Li, Q., Karimian, H., Liu, H., Mo, Y., 2022. DESA: a novel hybrid decomposing-ensemble and spatiotemporal attention model for PM2.5 forecasting. *Environ. Sci. Pollut. Control Ser.* 1–17.
- Gomes, D., Serra, G.L.O., 2021. Machine learning model for computational tracking and forecasting the COVID-19 dynamic propagation. *IEEE J. Biomed. Health Inform.* 25, 615–622.
- Guo, C., Bo, Y., Lin, C., Li, H.B., Zeng, Y., Zhang, Y., Hossain, M.S., Chan, J.W.M., Yeung, D.W., Kwok, K.O., Wong, S.Y.S., Lau, A.K.H., Lao, X.Q., 2021. Meteorological factors and COVID-19 incidence in 190 countries: an observational study. *Sci. Total Environ.* 757, 143783.
- Hojjati-Najafabadi, A., Aygun, A., Tiri, R.N.E., Gulbagca, F., Lounissaa, M.I., Feng, P., Karimi, F., Sen, F., 2023. *Bacillus thuringiensis* based ruthenium/nickel Co-doped zinc as a green nanocatalyst: enhanced photocatalytic activity, mechanism, and efficient H₂ production from sodium borohydride methanolysis. *Ind. Eng. Chem. Res.* 62, 4655–4664.
- Hu, F., Qiu, L., Xia, W., Liu, C.-F., Xi, X., Zhao, S., Yu, J., Wei, S., Hu, X., Su, N., 2022. Spatiotemporal evolution of online attention to vaccines since 2011: an empirical study in China. *Front. Public Health* 9, 691746.
- Hu, F., Shi, X., Wang, H., Nan, N., Wang, K., Wei, S., Li, Z., Jiang, S., Hu, H., Zhao, S., 2021. Is health contagious?—based on empirical evidence from China family panel studies' data. *Front. Public Health* 9, 691746.
- Jayaweera, M., Perera, H., Gunawardana, B., Manatunge, J., 2020. Transmission of COVID-19 virus by droplets and aerosols: a critical review on the unresolved dichotomy. *Environ. Res.* 188, 109819.
- Jia, J.S., Lu, X., Yuan, Y., Xu, G., Jia, J., Christakis, N.A., 2020. Population flow drives spatio-temporal distribution of COVID-19 in China. *Nature* 582, 389–394.
- Joob, B., Wiwanitkit, V., 2021. Expected viscosity after COVID-19 vaccination, hyperviscosity and previous COVID-19. *Clin. Appl. Thromb. Hemost.* 27, 10760296211020833.
- Karia, R., Gupta, I., Khandait, H., Yadav, A., Yadav, A., 2020. COVID-19 and its modes of transmission. *SN Comp. Clin. Med.* 2, 1798–1801.
- Karimian, H., Karimian, H., Chen, Y., Tao, T., Yaqian, L., 2020. Spatiotemporal analysis of air quality and its relationship with meteorological factors in the Yangtze River Delta. *J. Elementol.* 25(3), 1059–1075.
- Karimian, H., Li, Q., Chen, H.F., 2013. Assessing urban sustainable development in isfahan. applied mechanics and materials. *Trans. Tech. Publ.* 244–248.
- Karimian, H., Li, Q., Li, C., Fan, J., Jin, L., Gong, C., Mo, Y., Hou, J., Ahmad, A., 2017. Daily estimation of fine particulate matter mass concentration through satellite based aerosol optical depth. *ISPRS Ann. Photogrammetry, Remote Sens. Spatial Inf. Sci.* 4, 175.
- Karimian, H., Li, Y., Chen, Y., Wang, Z., 2023. Evaluation of different machine learning approaches and aerosol optical depth in PM(2.5) prediction. *Environ. Res.* 216, 114465.
- Kissler, S.M., Tedijanto, C., Goldstein, E., Grad, Y.H., Lipsitch, M., 2020. Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. *Science* 368, 860–868.
- Lake, M.A., 2020. What we know so far: COVID-19 current clinical knowledge and research. *Clin Med (Lond)* 20, 124–127.
- Leung, N.H.L., 2021. Transmissibility and transmission of respiratory viruses. *Nat. Rev. Microbiol.* 19, 528–545.
- Leung, N.H.L., Chu, D.K.W., Shiu, E.Y.C., Chan, K.H., McDevitt, J.J., Hau, B.J.P., Yen, H. L., Li, Y., Ip, D.K.M., Peiris, J.S.M., Seto, W.H., Leung, G.M., Milton, D.K., Cowling, B. J., 2020. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nat. Med.* 26, 676–680.
- Li, Q., Miao, Y., Zeng, X., Tarimo, C.S., Wu, C., Wu, J., 2020. Prevalence and factors for anxiety during the coronavirus disease 2019 (COVID-19) epidemic among the teachers in China. *J. Affect. Disord.* 277, 153–158.
- Long, Q.X., Tang, X.J., Shi, Q.L., Li, Q., Deng, H.J., Yuan, J., Hu, J.L., Xu, W., Zhang, Y., Lv, F.J., Su, K., Zhang, F., Gong, J., Wu, B., Liu, X.M., Li, J.J., Qiu, J.F., Chen, J., Huang, A.L., 2020. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat. Med.* 26, 1200–1204.
- Mahjoub Mohammed Merghani, K., Sagot, B., Gehin, E., Da, G., Motzkus, C., 2021. A review on the applied techniques of exhaled airflow and droplets characterization. *Indoor Air* 31, 7–25.
- Mansoorianfar, M., Shahin, K., Hojjati-Najafabadi, A., Pei, R., 2022. MXene-laden bacteriophage: a new antibacterial candidate to control bacterial contamination in water. *Chemosphere* 290, 133383.
- Nepomuceno, T.C.C., Garcez, T.V., Silva, L.C.E., Coutinho, A.P., 2022. Measuring the mobility impact on the COVID-19 pandemic. *Math. Biosci. Eng.* 19, 7032–7054.
- Nicas, M., Jones, R.M., 2009. Relative contributions of four exposure pathways to influenza infection risk. *Risk Anal.* 29, 1292–1303.
- Paules, C., Subbarao, K., 2017. Influenza. *Lancet* 390, 697–708.
- Ronchi, E., Lovreglio, R., 2020. EXPOSED: an occupant exposure model for confined spaces to retrofit crowd models during a pandemic. *Saf. Sci.* 130, 104834.
- Salmi, L.R., 2022. Lessons for injury epidemiology and control learned from the COVID-19 pandemic. *Inj. Prev.* 28, 103–104.
- Shahin, K., Zhang, L., Mehraban, M.H., Collard, J.-M., Hedayatkah, A., Mansoorianfar, M., Soleimani-Delfan, A., Wang, R., 2022. Clinical and Experimental bacteriophage studies: recommendations for possible approaches for standing against SARS-CoV-2. *Microb. Pathogenesis*, 105442.
- Shaman, J., Galanti, M., 2020. Will SARS-CoV-2 become endemic? *Science* 370, 527–529.
- Shiu, E.Y.C., Leung, N.H.L., Cowling, B.J., 2019. Controversy around airborne versus droplet transmission of respiratory viruses: implication for infection prevention. *Curr. Opin. Infect. Dis.* 32, 372–379.
- Sohn, S., Huong, V.T., Nguyen, P.-D., Ly, N.H., Jang, S., Lee, H., Lee, C., Lee, J.I., Vasseghian, Y., Joo, S.-W., Zoh, K.-D., 2023. Equilibria of semi-volatile isothiazolinones between air and glass surfaces measured by gas chromatography and Raman spectroscopy. *Environ. Res.* 218, 114908.
- Stadnytskiy, V., Anfinrud, P., Bax, A., 2021. Breathing, speaking, coughing or sneezing: what drives transmission of SARS-CoV-2? *J. Intern. Med.* 290, 1010–1027.
- Tellier, R., Li, Y., Cowling, B.J., Tang, J.W., 2019. Recognition of aerosol transmission of infectious agents: a commentary. *BMC Infect. Dis.* 19, 101.
- Tiwari, S., Kumar, S., Guleria, K., 2020. Outbreak trends of coronavirus disease-2019 in India: a prediction. *Disaster Med. Public Health Prep.* 14, e33–e38.
- van Doremalen, N., Bushmaker, T., Morris, D.H., Holbrook, M.G., Gamble, A., Williamson, B.N., Tamin, A., Harcourt, J.L., Thornburg, N.J., Gerber, S.I., Lloyd-Smith, J.O., de Wit, E., Munster, V.J., 2020. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N. Engl. J. Med.* 382, 1564–1567.
- Vasseghian, Y., Sezgin, D., Nguyen, D.C., Hoang, H.Y., Sari Yilmaz, M., 2023. A hybrid nanocomposite based on CuFe layered double hydroxide coated graphene oxide for photocatalytic degradation of trimethoprim. *Chemosphere* 322, 138243.
- Wang, Y., Tian, H., Zhang, L., Zhang, M., Guo, D., Wu, W., Zhang, X., Kan, G.L., Jia, L., Huo, D., Liu, B., Wang, X., Sun, Y., Wang, Q., Yang, P., MacIntyre, C.R., 2020. Reduction of secondary transmission of SARS-CoV-2 in households by face mask use, disinfection and social distancing: a cohort study in Beijing, China. *BMJ Glob. Health* 5.
- Wu, C., Li, Q., Hou, J., Karimian, H., Chen, G., 2018. PM2.5 concentration prediction using convolutional neural networks. *Sci. Surv. Mapp.* 43, 68–75.
- Wu, J.T., Leung, K., Leung, G.M., 2020. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet* 395, 689–697.
- Xia, C., Joo, S.-W., Hojjati-Najafabadi, A., Xie, H., Wu, Y., Mashifana, T., Vasseghian, Y., 2023. Latest advances in layered covalent organic frameworks for water and wastewater treatment. *Chemosphere* 329, 138580.
- Xiao, S., Li, Y., Sung, M., Wei, J., Yang, Z., 2018. A study of the probable transmission routes of MERS-CoV during the first hospital outbreak in the Republic of Korea. *Indoor Air* 28, 51–63.
- Yesudhas, D., Srivastava, A., Gromiha, M.M., 2021. COVID-19 outbreak: history, mechanism, transmission, structural studies and therapeutics. *Infection* 49, 199–213.
- Zhong, M., Lin, B., Pathak, J.L., Gao, H., Young, A.J., Wang, X., Liu, C., Wu, K., Liu, M., Chen, J.M., Huang, J., Lee, L.H., Qi, C.L., Ge, L., Wang, L., 2020. ACE2 and furin expressions in oral epithelial cells possibly facilitate COVID-19 infection via respiratory and fecal-oral routes. *Front. Med.* 7, 580796.