

Modeling of viral infection behavior to evaluate countermeasures against infection causing social disaster

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Abstract Infection control and protection from the emerging diseases should be rationally formulated and operated based on epidemiologically determined infection characteristics. In order to respond to this requirement, this study proposes a mathematical model of the progression of the spread of viral infection in the society. In addition, the model was applied to cases of transmission of the new coronavirus COVID-19. From the results, the following is clarified: the progress of the viral infection can be simply modeled by the daily-rate basic reproduction number r and the infection detection rate k ; r is determined by the epidemiologically determined values of basic reproduction number R_0 and the infection lifetime T of virus; the daily-rate effective reproduction number r_{eff} can be defined by $r_{\text{eff}} = r(1 - k)$, and $r_{\text{eff}} < 1$ indicates that the infection is suppressed; the infection suppression can be realized to make k greater than the critical value k_{cr} corresponding to the epidemiological parameters; this model fits well with the practical infection behavior of COVID-19 and enables the quantitative evaluation of infection suppress measures; In the case of China, thorough detecting and isolation would have improved the infection condition to the suppression phase after only 10 days.

Keywords viral infection; mathematical model; reproduction number; parameter identification; COVID-19.

1. Introduction

As human life and activities continue to expand, human beings are constantly at risk of developing emerging infectious diseases. Even within the last 50 years, serious novel

fatal infectious diseases including Ebola (1976) [1], AIDS (1981) [2], SARS (2003) [3], H1N1 influenza (2009) [4] and MERS (2012) [5] have occurred causing fear to human beings. Today, since production regions have spread to every area of the world, and, the movement of people and goods has become more active, the risk of pandemic of infectious diseases worldwide has never been higher.

Therefore, mankind must have a quick and effective response to such emerging infectious diseases. At the time of onset, there are no vaccines or therapeutics for those emerging diseases. Therefore, what can be dealt with immediately is limited only the public health measures: that is detection and isolation of infected persons based on tests and medical treatments to prevent secondary infection. For the onset of emerging infectious diseases, it will also be necessary to quickly identify the epidemiological characteristics of the infectious disease and to formulate in advance rational preventive measures based on such epidemiological information.

The appropriate mathematical model of infection progress behavior can be the basis for a rational construction of the infection control measures. The most common model of the transmission process of such infectious diseases is the SIR model proposed by W. O. Kermack and A. G. McKendrick in 1927 [6]. This model can well represent the spread behavior of influenza and other infections, where the infection suppresses due to an increase in the antibody population with the infection progress. Especially, influenza is so familiar that it appears every year with small variations, and the effectiveness of this SIR model and its derivation model have been highly appreciated.

However, the SIR model may not be able to adequately describe the infection progress of emerging diseases, such as SARS infection [7–11], when robust human intervention for rapid suppression of the infection spread occurs. In

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SARS infection control measures, the infection route has been traced from the very beginning of the onset, and the infected person has been quickly detected and isolated to suppress secondary infections, and then, the virus has been successfully eliminated.

In this paper, a simple mathematical model is proposed for the progression of viral infection under a situation to execute the detection and isolation to suppress the infection spread. The model will be validated by applying it to the new coronavirus COVID-19 infection. Furthermore, the condition of infection and its control measures are evaluated for the case of China and Japan.

2. Materials and Methods

2.1 Modeling progress of viral infection

Figure 1 schematically shows the detection and isolation of infected persons and the progress of secondary infection. The progress of viral infection under the control measures of the infection involves two processes that occur in parallel: “detection and isolation of infected persons” and “secondary infection by remaining infected persons”. Here, for the modeling of the infection progress, the process of detection and isolation of infected persons and the process of secondary infection by infected persons remained in towns are formulated sequentially. First, as shown in figure (a), a part of the latently infected persons is detected with the onset of

the disease. Subsequently, as shown in figure (b), the detected infected persons are isolated from healthy persons to prevent secondary infection. Nevertheless, since another segment of infected persons remain as shown in figure (c), the secondary-infected persons are newly generated by those latently infected persons. Therefore, as shown in figures (d) to (f), these processes continue again on the second and subsequent days.

This model treats the progression of secondary infections more simply by not specifying the incubation period. The treatment of such incubation periods is the same as the standard SIR model [6], which is the most common epidemic model. According to a study based on the SIR model [12], the incubation period slows the progression of the epidemic, but has little effect on the magnitude of the epidemic such as the maximum cumulative number of infected individuals.

Table 1 shows the parameters for modeling. The numbers of infected persons are assumed to be two types: the number of unknown latently infected persons (I_{ac} , I_{res}) and the number of obviously infected persons that can be detected by testing or medical treatment (R_{sc} , R_{ac}).

Based on the epidemical studies that determine the infection characteristics, the infection lifetime T and the basic reproduction number R_0 can be applicable to the modeling. The infection lifetime T corresponds to the average duration until eliminating the chance of the infection by isolation. And, the basic reproduction number R_0 corresponds to the average number of infected persons caused by the genera-

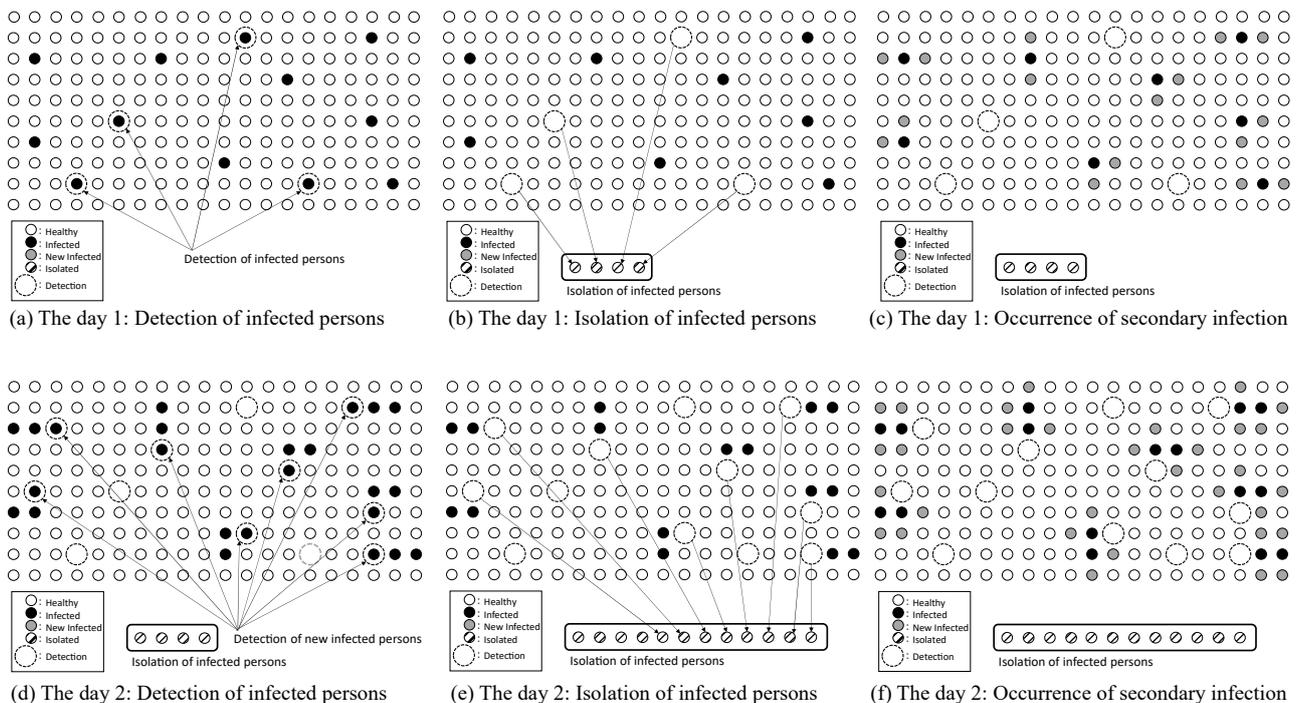


Fig. 1 Schematic diagram of the virus infection process under control measures. (a) The day 1: Detection of infected persons. (b) The day 1: Isolation of infected persons. (c) The day 1: Occurrence of secondary infection. (d) The day 2: Detection of infected persons. (e) The day 2: Isolation of infected persons. (f) The day 2: Occurrence of secondary infection.

tion of secondary infection by a certain infected individual during lifetime T [13].

Furthermore, these values reflect into the model by transforming to the daily-rate basic reproduction number r of the virus derived in Eq. (20) describing later. The value of r represents the average number of individuals infected after one day by a certain infected individual, that is, it is defined as the reproduction number per day per infected person.

On the other hand, the infected person detection rate k corresponds to the proportion of detected infectious persons to the whole population of infected persons. However, since the total of infected persons includes latently infected persons that cannot be known exactly, this value can be determined not as a definite value but as the estimated value by the application of the model to the detected number of infected persons.

Such an infection process can be formulated as follows. In this model, the initial value is the number $I_{res(0)}$ of latently infected persons already remaining in towns and the total number $R_{ac(0)}$ of detected infectious persons if control measures have already started.

The infection process on day 1 can be formulated as shown in Eq. (1) to (3). Equation (1) corresponds to figure (a) described above, and the detected infectious persons $R_{sc(1)}$ are screened as multiplying the detection rate k to $I_{res(0)}$. Equation (2) corresponds to figure (b) and indicates that even if $R_{sc(1)}$ is isolated from $I_{res(0)}$, the active infected persons $I_{ac(1)}$ having infectious activity remain in towns. Equation (3) corresponds to figure (c), and, the number of latently infected persons $I_{res(1)}$ including newly infected persons by secondary infection can be determined by multiplying $I_{ac(1)}$ by the daily-rate basic reproduction number r .

$$R_{sc(1)} = kI_{res(0)} \tag{1}$$

$$I_{ac(1)} = I_{res(0)} - R_{sc(1)} = (1 - k)I_{res(0)} \tag{2}$$

$$I_{res(1)} = rI_{ac(1)} = r(1 - k)I_{res(0)} \tag{3}$$

Based on the formulation of these infection processes, Eq. (4) formulates the accumulative number of infected persons $R_{ac(1)}$ detected after one day of infection processes. Actually, since the number of latently infected persons cannot be known exactly, infection control measures are examined based on the accumulative number of detected infectious persons corresponding to $R_{ac(1)}$ formulated in this Eq. (4). Therefore, the validity and effectiveness of this model should be evaluated based on the consistency between the published practical number of detected infected persons and R_{ac} determined according to the series of formulations of this model.

$$R_{ac(1)} = R_{ac(0)} + R_{sc(1)} = R_{ac(0)} + kI_{res(0)} \tag{4}$$

The infection process on days 2 and 3 is described similarly. The infection behavior on the second day is formulated by Eq. (5) to (8).

$$R_{sc(2)} = kI_{res(1)} = kr(1 - k)I_{res(0)} \tag{5}$$

$$I_{ac(2)} = I_{res(1)} - R_{sc(2)} = r(1 - k)^2 I_{res(0)} \tag{6}$$

$$I_{res(2)} = rI_{ac(2)} = r^2(1 - k)^2 I_{res(0)} \tag{7}$$

$$R_{ac(2)} = R_{ac(1)} + R_{sc(2)} = R_{ac(0)} + kI_{res(0)} + kr(1 - k)I_{res(0)} \tag{8}$$

Similarly, the infection behavior on day 3 can be formulated as Eq. (9) to (12).

$$R_{sc(3)} = kI_{res(2)} = kr^2(1 - k)^2 I_{res(0)} \tag{9}$$

$$I_{ac(3)} = I_{res(2)} - R_{sc(3)} = r^2(1 - k)^3 I_{res(0)} \tag{10}$$

$$I_{res(3)} = rI_{ac(3)} = r^3(1 - k)^3 I_{res(0)} \tag{11}$$

$$R_{ac(3)} = R_{ac(2)} + R_{sc(3)} \\ = R_{ac(0)} + kI_{res(0)} + kr(1 - k)I_{res(0)} + kr^2(1 - k)^2 I_{res(0)} \tag{12}$$

Table 1 Parameters used in the infection progress model

Item	Symbol	Unit	Note
Number of active infected persons for infection	I_{ac}	persons	
Number of residual infected person in a town	I_{res}	persons	Initial value: $I_{res(0)}$
Number of infected persons detected	R_{sc}	persons	
Accumulated number of infected persons detected	R_{ac}	persons	Initial value: $R_{ac(0)}$
Infection lifetime of virus	T	day	
Fundamental reproduction number of virus	R_0	persons	
Daily-rate reproduction number	r	persons/day	
Daily-rate effective reproduction number	r_{eff}	persons/day	
Infected person detection rate	k	(no unit) or %	
Critical rate of infected person detection	k_{cr}	(no unit) or %	

Based on these, the general formula of this infection process can be expressed as a series of formulas on the n th day as in formulas (13) to (16). The expressions of R_{sc} , I_{ac} and I_{res} are all represented by exponential functions with base $r(1 - k)$. On the other hand, the accumulative number of infected persons R_{ac} is represented by adding a geometric series having a common ratio of $r(1 - k)$ to an initial value $R_{ac(0)}$.

$$R_{sc(n)} = kI_{res(n-1)} = kr^{n-1}(1-k)^{n-1}I_{res(0)} \tag{13}$$

$$I_{ac(n)} = I_{res(n-1)} - R_{sc(n)} = r^{n-1}(1-k)^n I_{res(0)} \tag{14}$$

$$I_{res(n)} = rI_{ac(n)} = r^n(1-k)^n I_{res(0)} \tag{15}$$

$$\begin{aligned} R_{ac(n)} &= R_{ac(n-1)} + R_{sc(n)} \\ &= R_{ac(0)} + kI_{res(0)} + kr(1-k)I_{res(0)} + kr^2(1-k)^2 I_{res(0)} \\ &\quad + \dots + kr^{n-1}(1-k)^{n-1}I_{res(0)} \\ &= R_{ac(0)} + kI_{res(0)} \sum_{i=1}^n \{r(1-k)\}^{i-1} \\ &= R_{ac(0)} + \frac{1 - \{r(1-k)\}^n}{1 - r(1-k)} kI_{res(0)} \end{aligned} \tag{16}$$

2.2 Decision index of infection progressing condition

The progress of the infection is classified into three phases: spread phase; equilibrium phase; suppression phase. The phases can be determined by the increase or decrease of the number of latently infected persons, that is, the magnitude relationship between $I_{res(n)}$ and $I_{res(n-1)}$. The relationships as $I_{res(n)} > I_{res(n-1)}$, $I_{res(n)} = I_{res(n-1)}$ and $I_{res(n)} < I_{res(n-1)}$ respectively correspond to the spread, equilibrium, and suppression phases of infection.

As shown in Eq. (15), since $I_{res(n)}$ is an exponential function with base $r(1 - k)$, the relationship between $I_{res(n)}$ and $I_{res(n-1)}$ can be expressed by Eq. (17). As shown in Eq. (18), this coefficient can be defined with the new symbol r_{eff} , consequently, Eq. (17) can be rewritten as Eq. (19).

$$I_{res(n)} = r(1-k)I_{res(n-1)} \tag{17}$$

$$r_{eff} = r(1-k) \tag{18}$$

$$I_{res(n)} = r_{eff} \cdot I_{res(n-1)} \tag{19}$$

This value of r_{eff} is the coefficient corresponding to the degree of increase/decrease of latently infected persons between the day and previous day, that is, this means the daily-rate effective reproduction number of the virus. Therefore, the spread, equilibrium and suppression phases of infection correspond to $r_{eff} > 1$, $r_{eff} = 1$ and $r_{eff} < 1$, respectively. From Eq. (18), this value is affected by both

the daily-rate effective reproduction number r and the infected person detection rate k .

On the other hand, the daily-rate basic reproduction number r is derived from the basic reproduction number R_0 and the infection lifetime T of the virus. Since R_0 means the number of infected persons after T days of infection caused by one infected person, when $I_{res(0)} = 1$ and $k = 0$ in Eq. (15), the number of infected person after T days can be expressed as $I_{res(T)} = R_0$, that is, Eq. (20) can be established. Therefore, r can be determined from Eq. (21).

$$R_0 = r^T \tag{20}$$

$$r = R_0^{1/T} \tag{21}$$

The infected person detection rate k can be expressed as in Eq. (22) based on Eq. (18). Therefore, the value of k can be determined by applying the model to the trend of the accumulative number of infected persons R_{ac} that is updated daily and identifying the parameters of Eq. (16) and r_{eff} with the non-linear least square method.

$$k = 1 - \frac{r_{eff}}{r} \tag{22}$$

Furthermore, the critical value k_{cr} of k corresponds to the equilibrium phase of the infection, that is, the case where $r_{eff} = 1$ in Eq. (22), and then, it can be determined from Eq. (23). As shown in Eq. (24), if k is bigger than k_{cr} , r_{eff} becomes lower than 1, that is, the infection has been suppressed.

$$k_{cr} = 1 - \frac{1}{r} = 1 - R_0^{-(1/T)} \tag{23}$$

$$k > k_{cr} \Rightarrow \therefore 1 - \frac{r_{eff}}{r} > 1 - \frac{1}{r} \Rightarrow \therefore r_{eff} < 1 \tag{24}$$

3. Results and Discussion

3.1 COVID-19 and its infection characteristics

COVID-19 is a new type of coronavirus that began to affect humans in Wuhan, China around November 2019. As of March 12, 2020, COVID-19 epidemic has spread to 110 countries around the world and has become a large-scale case with an estimated 120,000 infected persons and more than 4,600 deaths [14]. Due to the worldwide spread and high mortality, control measures are urgently required to suppress COVID-19 infection.

Epidemiological studies have been actively ongoing for COVID-19 infection [15–19]. Consequently, the infection characteristics have been determined based on infection cases in Wuhan city before 23rd January [20]. At the very beginning of the infection spread, the basic reproduction number R_0 and the lifetime T had been estimated extremely high value as $R_0 = 7.93$ (before 29th December 2019) and $T = 6.7$ (before 9th January 2020), respectively. And, the

average values of R_0 and T before 23rd January are estimated as $R_0 = 2.90$ and $T = 2.9$, respectively. From these values and Eq. (21), the daily-rate basic reproduction number r of COVID-19 can be determined to 1.3621 at the very beginning of the infection and 1.4436 as the average value.

Since these values are almost constant around 1.4, r has been set to the constant value of 1.4436 in this paper. Since r is determined by both R_0 and T as shown in Eq.(21), the reduction of R_0 reduces r , while the shortening of T increases r . Contact control and detection promotion to suppress infection synchronously reduced R_0 and T , and as mentioned in the paragraph above, the similar situation happened with COVID-19. As a result of the decrease of R_0 and T acting in the opposite effect on r and canceling each other, r has kept a relatively close value of around 1.4. On the other hand, r of SARS can be calculated as $r = 1.150$, COVID-19 seems much more infectious than SARS.

The critical value k_{cr} is also clearly determined in accordance with Eq. (23). The value of k_{cr} is 0.307 (30.7%) for

COVID-19. Therefore, COVID-19 infection can be suppressed by making k larger than $k_{cr} = 30.7\%$.

3.2 Application to infection cases in China

Changes in infection control measures change the exponential growth rate of R_{ac} and generate inflection points on the R_{ac} curve. The existence of such inflection points can be easily recognized by looking at the R_{ac} curve. Then, those inflection points can be identified by searching to maximize the degree of agreement between the R_{ac} curve and Eq. (16). With such treatment, the epidemic can be divided into several periods during which the infection control measures are working uniformly.

Figure 2 to 5 show the results of fitting the proposed model to the accumulative number of detected infectious persons R_{ac} of COVID-19 in China [21]. The infection stages in China is divided by the changing behavior of R_{ac} into four periods (1st period: 1/16 to 1/23; 2nd period: 1/23 to 2/3; 3rd period: 2/3 to 2/16; 4th period: 2/17 to 3/18).

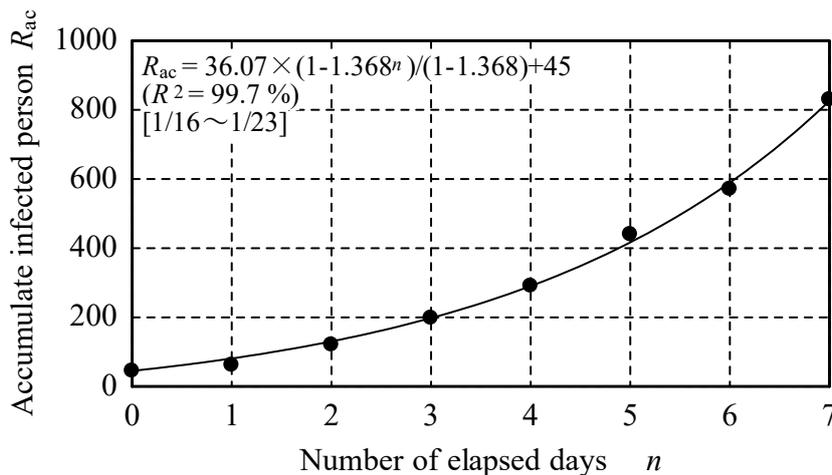


Fig. 2 Fitting result of model to accumulative number of detected infectious persons R_{ac} of 1st period (1/16~1/23) in China.

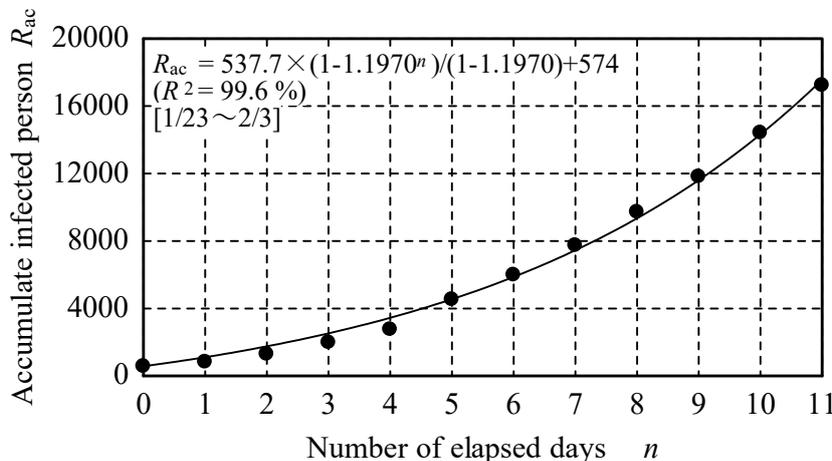


Fig. 3 Fitting result of model to accumulative number of detected infectious persons R_{ac} of 2nd period (1/23~2/3) in China.

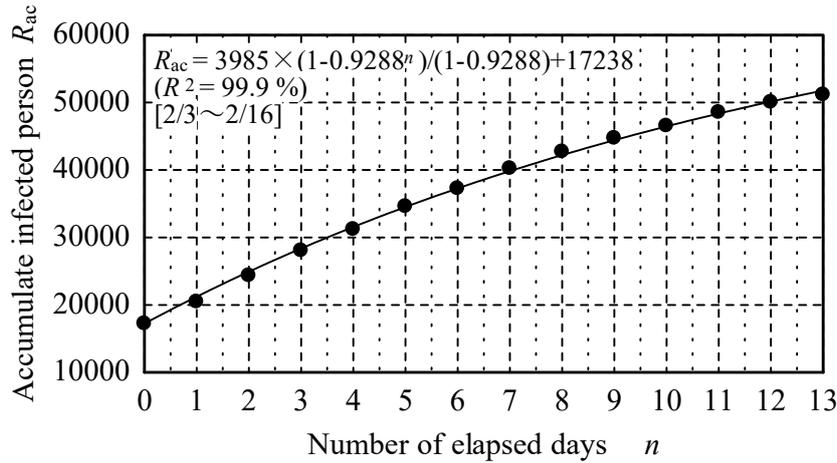


Fig. 4 Fitting result of model to accumulative number of detected infectious persons R_{ac} of 3rd period (2/3~2/16) in China.

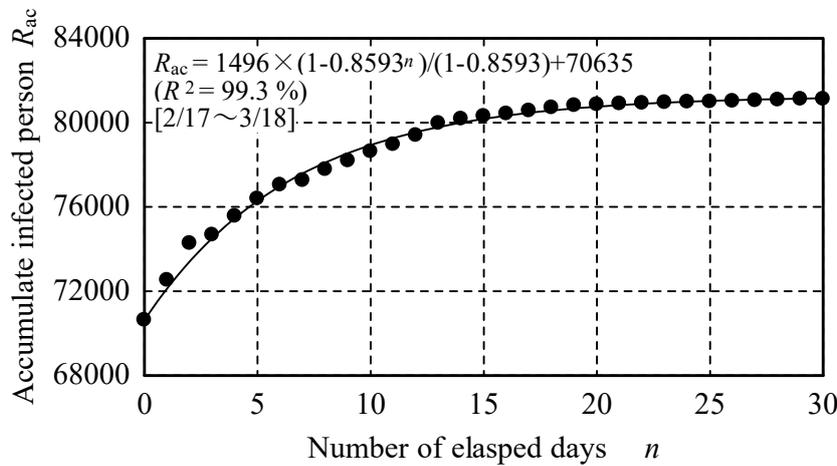


Fig. 5 Fitting result of model to accumulative number of detected infectious persons R_{ac} of 4th period (2/17~3/18) in China.

Figure 2 to 5 correspond to those four periods, respectively. In Fig. 2 and Fig. 3, the plots of R_{ac} show downwardly convex trends, that is, the infection conditions had been the spread phase before early February. On the other hand, as shown in Fig. 4 and Fig. 5, after February 3rd, the plots of R_{ac} show upwardly convex trends, indicating that the infection had already been improved to the suppression phase.

At all periods, the fitting curves are well in agreement with the changes in R_{ac} . The determination coefficient R^2 shown in parentheses in the figure corresponding to the square of the correlation coefficient R between the fitted curve and the nominal value of R_{ac} and is expressed as percentage. The closer this value is to 100%, the better the fitted curve agrees to R_{ac} values, that is, the higher the reliability of parameter identification is. In this figure, each R^2 value is equal to or greater than 99% in every period, that is, the fitted curves correspond to the plot of R_{ac} very well. This means that the increasing behavior of R_{ac} can be expressed with high correlation by an exponential function. Furthermore, it is shown that the parameter identification by fitting with model formulas can identify the characteris-

tic parameters that quantitatively represent the condition of epidemic defined by this model and the effect of infection control measures.

Table 2 shows the results of parameter identification to evaluate the progress of COVID-19 infection in China. The evaluation items are the daily-rate reproduction number r_{eff} , the infected person detection rate k and the progression status of infection determined by these.

The daily-rate reproduction number r_{eff} has decreased consistently with the passage of time and fallen below 1 after the third period. This indicates that infection control measures in China have been steadily effective. When the control measures began in earnest throughout China after January 23, the infection status had shifted to the suppression state in only 10 days.

Specifically, this effect is realized by thoroughly detecting and isolating unknown infected persons. Initially, k in China was around 5% but had been increasing steadily. Finally, it has reached over 40%, that is, sufficiently higher than $k_{cr} = 30.7\%$, since mid-February. It can be said that in China since mid-February, the detection rate k is sufficiently

Table 2 Identification of infection condition of COVID-19 in China

Item	Symbol	1st period	2nd period	3rd period	4th period
Term		1/16~1/23	1/23~2/3	2/3~2/16	2/17~3/18
Daily-rate effective reproduction number	r_{eff}	1.368	1.197	0.9288	0.8593
Infected person detecting rate	k	5.22%	17.1%	35.7%	40.5%
Infection progression phase		Spreading	Spreading	Suppressing	Suppressing

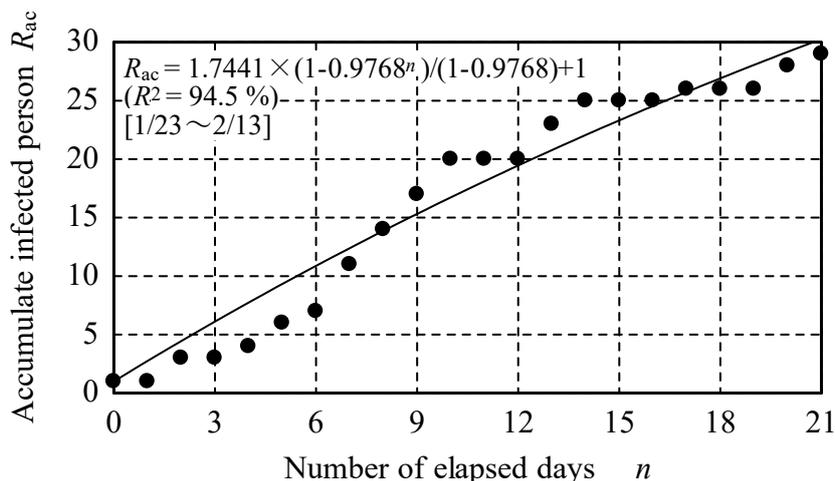


Fig. 6 Fitting result of model to accumulative number of detected infectious persons R_{ac} of 1st period (1/23~2/13) in Japan.

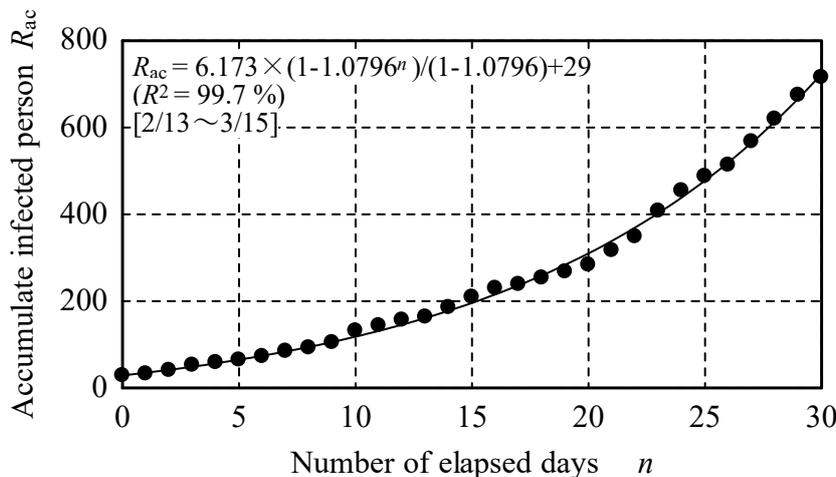


Fig. 7 Fitting result of model to accumulative number of detected infectious persons R_{ac} of 2nd period (2/13~3/15) in Japan.

high, and then, infection is effectively suppressing. In this way, this model can determine the period in which the increasing tendency of R_{ac} is common and can quantitatively evaluate the effect of infection control measures implemented during the period.

3.3 Application to infection cases in Japan

Figure 6 to 9 shows the results of fitting the proposed model to the accumulative number of detected infectious persons R_{ac} of COVID-19 in Japan [21]. The infection

stages in Japan is divided by the changing behavior of R_{ac} into six periods (1st period: 1/23 to 2/13; 2nd period: 2/13 to 3/15; 3rd period: 3/15 to 4/6; 4th period: 4/6 to 4/12; 5th period: 4/13 to 4/18; 6th period: 4/18 to 6/5). By gathering the 3rd to 5th periods into Fig. 8, these six periods are shown in the four figures. Since the R^2 is all close to 100%, the proposed model corresponds well with the epidemic behavior in Japan. In the Fig. 6 corresponding to the 1st period, the fitted curve indicates an upwardly convex trend, so that, the infection seems to have been controlled during this period. However, as shown in Fig. 7 and Fig. 8, the fit-

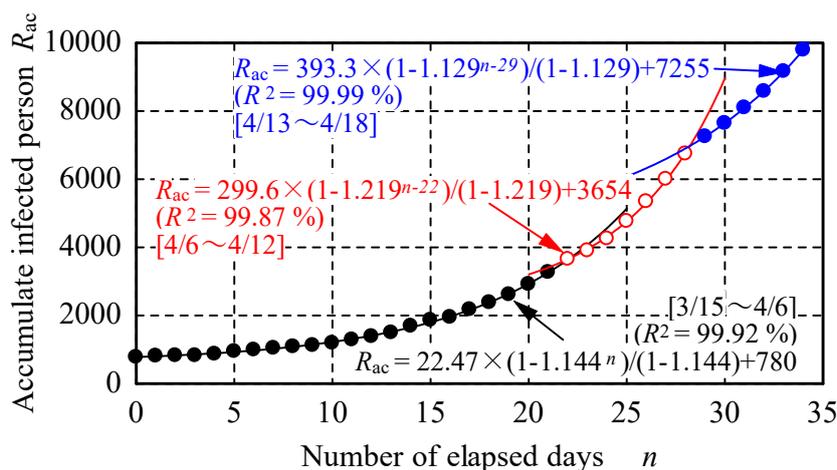


Fig. 8 Fitting result of model to accumulative number of detected infectious persons R_{ac} of 3rd to 5th periods (3/15~4/18) in Japan.

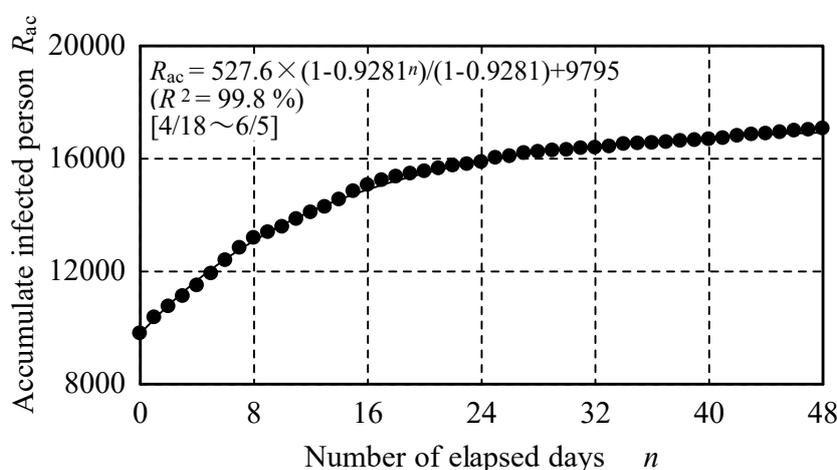


Fig. 9 Fitting result of model to accumulative number of detected infectious persons R_{ac} of 4th period (4/18~6/5) in Japan.

Table 3 Identification of infection condition of COVID-19 in Japan

Item	Symbol	1st period	2nd period	3rd period	4th period	5th period	6th period
Term		1/23~2/13	2/13~3/15	3/15~4/6	4/6~4/12	4/13~4/18	4/18~6/5
Daily-rate effective reproduction number	r_{eff}	0.9768	1.080	1.144	1.219	1.129	0.9275
Infected person detecting rate	k	32.3%	25.2%	20.7%	15.5%	21.8%	35.7%
Infection progression phase		Suppressing	Spreading	Spreading	Spreading	Spreading	Suppressing

ted curves from middle of February for more than two months continued to show a downwardly convex trend, that is, the infection had continued to spread. Then, as shown in Fig. 9, the spread of infection ended on April 18th, and, the infection changed to a suppressing state.

Table 3 shows the results of identification of the infection status of COVID-19 in Japan. The value of r_{eff} was less than 1 in the 1st period, but, after that, the values exceed 1 from the 2nd period to the 5th period for more than two months. In particular, the fact that the value continued to increase until the 4th period indicates that the level of infection control deteriorated with the passage of time. Then, in the 6th

period from 18th April, r_{eff} was less than 1, and, the infection improved to the suppression state. The value of k also changed in inversely corresponding with r_{eff} . Despite maintaining a high value of 32.3% in the 1st period, k continued to decrease for more than 2 months after February 13th and decreased to about a half of the 1st period at the 4th period.

Figure 10 shows the estimation results of the number of latently infected persons I_{res} based on Eq. (15). The number of I_{res} seems to remain below 30 by the middle of March but to increase rapidly more than 4500 after about one month. After that, the infection status had changed to the suppression state from April 18th, and then, I_{res} on June 5th

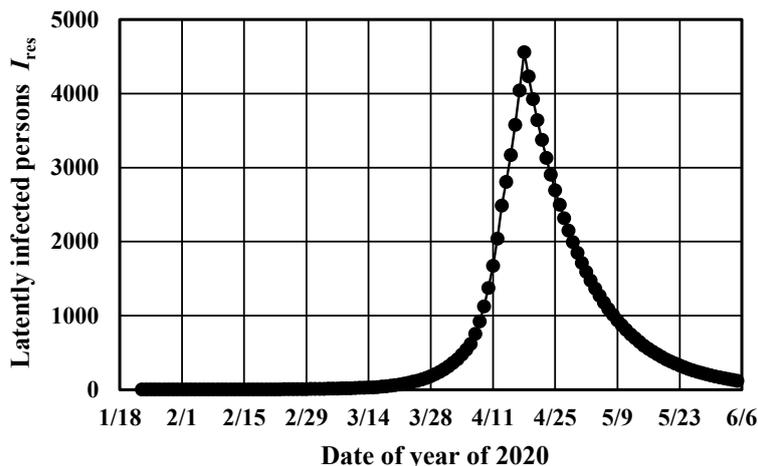


Fig. 10 Estimation of change in number of latently infected persons I_{res} in Japan.

is estimated to have decreased to 123 persons, that is, less than 1 ppm (one person in one million) of the total population.

Covid-19 has already spread all over the world. With the spread of infection, epidemiological characteristics, such as incidence and severity, are becoming different depending on the country or region [22]. In this paper, the epidemics of China and Japan have been analyzed using the infectious characteristic values identified in the very early stages of the epidemics as the common values. However, in the future, when analyzing epidemics in various regions of the world, the regional differences in infectious characteristics may be necessary to consider.

4. Conclusion

In this paper, we proposed a mathematical model that represents the progression of viral infection under the control measures against infection spread. By the application of the model to cases of new coronavirus COVID-19, the validity of the modeling has been confirmed. As a result of the examination, the followings are made clear:

- (1) The progress of the viral infection can be modeled using the daily-rate basic reproduction number r of the virus and the infection detection rate k .
- (2) The daily-rate reproduction number r is determined by the basic reproduction number R_0 and the infection lifetime T of the virus.
- (3) To grasp the infection status, the daily effective reproduction number r_{eff} can be defined as $r_{eff} = r(1 - k)$. When r_{eff} is lower than 1, the number of newly infected persons will be smaller than that of detected infected persons, that is, infection is suppressed.
- (4) The infection can be suppressed by making the infection detection rate k larger than the critical value k_{cr} .
- (5) The proposed model agrees well with the actual pro-

gression behaviors of novel coronavirus COVID-19. Based on this model, it is possible to quantitatively evaluate the control measures for infection spread.

- (6) In the cases of China, only after approximately 10 days from start of thorough detecting and isolation, the infection status had improved to the suppressing state.

Declaration of interest We declare no competing interests.

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