SCIENCE CHINA

Physics, Mechanics & Astronomy

• Article •

November 2013 Vol. 56 No. 11: 2143–2150 doi: 10.1007/s11433-013-5321-0

Modelling the spreading rate of controlled communicable epidemics through an entropy-based thermodynamic model[†]

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Received April 23, 2013; accepted July 29, 2013; published online September 29, 2013

A model based on a thermodynamic approach is proposed for predicting the dynamics of communicable epidemics assumed to be governed by controlling efforts of multiple scales so that an entropy is associated with the system. All the epidemic details are factored into a single and time-dependent coefficient, the functional form of this coefficient is found through four constraints, including notably the existence of an inflexion point and a maximum. The model is solved to give a log-normal distribution for the spread rate, for which a Shannon entropy can be defined. The only parameter, that characterizes the width of the distribution function, is uniquely determined through maximizing the rate of entropy production. This entropy-based thermodynamic (EBT) model predicts the number of hospitalized cases with a reasonable accuracy for SARS in the year 2003. This EBT model can be of use for potential epidemics such as avian influenza and H7N9 in China.

epidemics, entropy, inflexion point

PACS number(s): 02.90.+p, 05.90.+m, 89.90.+n

Citation:

Wang W B, Wu Z N, Wang C F, et al. Modelling the spreading rate of controlled communicable epidemics through an entropy-based thermodynamic model. Sci China-Phys Mech Astron, 2013, 56: 2143–2150, doi: 10.1007/s11433-013-5321-0

1 Introduction

Beginning from late 2002 to mid 2003, severe acute respiratory syndrome (SARS) spread over the world. Up to the end of May 2003 probable cases have been reported in 35 countries or regions, and the cumulative number of cases reached 8202 by May 26, 2003 according to the report by the World Health Organization (WHO). SARS in the year 2003 and avian influenza such as H7N9 in reported first in 2013 has been the focus of world attention because of the high case-fatality rate. Researchers were particularly interested in finding the period of the time between infection and the onset of infectiousness, length of period that patients remain infec-

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†Recommended by SHE ZhenSu (Associate Editor)

tious, further infections that each patient produce and the total number of infections during the epidemic. A large number of research groups have reported on SARS elsewhere [1–4]. Important achievements have been made for the transmission dynamics using various mathematical models [5–17] and reported data from Hong Kong or Canada. Donnelly et al. [5], Riley et al. [6] and Lipsitch et al. [7] made use of the available data for SARS on latent, incubation and infectious periods and have successfully fitted mathematical models to data describing the number of cases observed over time. One logical conclusion was that if SARS was unchecked, then a majority of people would be infected. The potential effectiveness of different control measures has been studied in these references.

Though SARS did not appear again since 2003, there may be other epidemic, such as H7N9 avian influenza occurring

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actually in China possibly, spreading in a similar way. Hence the study of various models for the prediction of SARS and other epidemic once it has occurred is critical for intensive study of transmission modes and mathematical modelling.

As assessed by Dye and Gay [8], the current mathematical models are complex, the data are poor, and some big questions such as accuracy of case reports and heterogeneity in transmission remain. Dye and Gay anticipated that the next generation of SARS models would become more complex.

It is now evident that SARS and maybe avian influenza in a city can be controlled through multiscale measures such as medical interventions, public-service announcements, isolation of people having contact with infected and restriction of individual and social activities. When the interventions to control a communicable epidemic are intensive and of multiple scales, it would be very difficult to find all those details of the epidemic needed by a more complex model. It is thus desired that, under intensive and multiscale interventions, the global behavior of SARS or avian influenza spread, governed by a complex and multiscale system, could be approximated without having awareness of the epidemic details.

The dynamics of an epidemics is an important topic in biology, medicine, mathematics and physics and is usually modelled through differential equations [17–21], among which is the SIR (susceptible-infected-removed) model. Research in this topic has been multi-pronged and on-going [9–17,25,26].

Most of the models for epidemics spread rely on differential equations for the susceptible, infected and removed numbers. Different spread mechanisms are embedded into the various terms in the differential equations.

Herein we are interested in the number of hospitalized cases (cumulative number of cases minus the number of deaths and the number recovered) and attempt to consider a new approach to predict this number. In our approach all the mechanisms controlling the spread are factored into a single parameter. Assuming the system controlling the spread of SARS or similar epidemic is a thermodynamic one, we define an entropy and determine the only parameter by using the principle of extreme rate of entropy production. This allows us to relate the dynamics of the spread to the information at the inflexion point of the curve describing the time variation of the number of hospitalized cases. The inflexion point is the date at which the multiple controlling measures take effect.

The model presented in this paper is based on a simple differential equation with the spread rate forced to satisfy four constraints. The model is closed by the use of maximum or minimal rate of entropy production as the system for spread is assumed to be thermodynamical. A critical point (date) at which the spread rate turns to decrease because of the overall role of interventions. The maximum number of infected individuals and the time at which this maximum occurs can be related to the number and time corresponding to the critical date. This entropy-based thermodynamic model is validated against the SARS data of the year 2003 for which we are able

to follow the history of the spread.

2 The entropy-based thermodynamic model

2.1 Basic model

Let f(t) be the number of hospitalized cases, defined as the cumulative number subtracted from the cumulative number of deaths and recovery ones since death and recovery are also parts of actions in the thermodynamical system. The epidemic increase is generally complex and can not be represented by an explicit expression. Thus, in the previous research, one can either use the master equation or mean-field to describe f(t). However, viewing the epidemic as a thermodynamic system and following the approach for the rate of vibration excitation and chemical reaction [26], we may assume that the rate of increase (decrease) be proportional to the number at the previous day, that is,

$$\frac{\mathrm{d}f(t)}{\mathrm{d}t} = \alpha(t)f(t) \tag{1}$$

Here $\alpha(t)$ is a time-dependent coefficient. The specific form for the coefficient $\alpha(t)$ depends on the balance between the spread mechanism of the epidemic and the the control mechanisms during the public intervention. For a deterministic method, one need the knowledge of all the details for the spreading and controlling of the epidemic, and a coupled system of differential equations should be used. Here, we instead use a statistic approach, by first assuming that all the spread mechanism and controlling effect be incorporated into the time-dependent function $\alpha(t)$. Though the details of epidemic are not need here, there are four obvious constraints that this function should meet:

- (1) The parameter $\alpha(t)$ must have the dimension of t^{-1} , that is $\alpha(t) \sim t^{-1}$.
- (2) At the initial stage there is an exponential increase for regular spread to start (since at the initial stage the number is near zero), that is, $\alpha(0) \to \infty$.
- (3) With the strong and active interventions the rate must decrease at a given day t=L which will be called the *inflexion point* (date). Mathematically this amounts to say that $\frac{d^2 f(t)}{dt^2}$ vanishes at t=L. Inserting eq. (1) into $\frac{d^2 f(L)}{dt^2}=0$ yields,

$$\frac{\mathrm{d}\alpha}{\mathrm{d}t} + \alpha^2 = 0, t = L$$

(4) There must be a maximum for f(t), say at the date t = D, for which we have $\alpha(D) = 0$.

We assume that the virus causing an epidemic is constantly active (high temperature or intrinsic lifetime constraint would make the epidemic disappear suddenly, but this is not considered here) so that $\alpha(t)$ is further assumed to be an analytical function.

The only analytical function that meets the four constraints and that is sufficiently simple is found to be given by

$$\alpha(t) = \frac{-c\ln(t/D)}{t}. (2)$$

where $c=\frac{1-\ln(L/D)}{\ln^2(L/D)}$. Inserting (2) into (1) leads to the following solution which is effectively the log-normal function:

$$f(t) = \frac{k}{\sqrt{2\pi}\sigma t} \exp\left(-\frac{(\ln t - \mu)^2}{2\sigma^2}\right). \tag{3}$$

Here k is a proportion constant that does not need to be known, $\mu = \ln D + \sigma^2$, and σ is to be determined in the following through the use of the principle of extreme rate of entropy production.

The approach will be validated against the SARS data of the year 2003. The essentially new feature of the present model is the simplicity as there are no free parameters to be fitted. The only parameter σ , characterizing the width of the distribution function, in eq. (3) can be determined by a thermodynamic approach as described below.

2.2 Principle of extreme rate of entropy production

The principle of extreme rate of entropy production can be found elsewhere [27]. This has been successfully used to obtain the distribution of droplet production during its impingement on solid walls [20]. Though the principle of maximum/minimum entropy production principle at least in some cases has been proved to be incorrect, it is still useful as a method to determine parameters in a model. Certainly, the width of the curve $f(t) \propto t$ can be characterized by σ . The wider the curve is, the larger is the (Shannon) entropy. The intrinsic spread mechanism of virus and the large mixing activity of the population tend to make the curve wider (so σ larger). However, the medical and social interventions to control the epidemic constitute a dissipation mechanism which would prohibit the curve to become infinitely wide (σ infinitely large). The width would cease to increase when the maximum dissipation rate is reached. The dissipation rate is proportional to the rate of the entropy production. Maximum dissipation rate corresponds to extreme rate of entropy production, which again corresponds to

$$\frac{\mathrm{d}^2 S(\sigma, \eta)}{\mathrm{d}\sigma^2} = 0. \tag{4}$$

Here $S(\sigma, \eta)$ is the Shannon entropy defined as:

$$S(\sigma, \eta) = -\int_0^\infty F(t) \ln F(t) dt^{\eta},$$

where $F(t) = t^{1-\eta} f(t)$ with $\eta = 3$ in the usual entropy definition. Integration leads to

$$S(\sigma, \eta) = \eta \left(\ln \left(\sqrt{2\pi} \sigma \right) + \eta \left(\ln D + \sigma^2 \right) + \frac{1}{2} \right),$$

so that eq. (4) holds if and only if

$$\sigma = \frac{1}{\sqrt{2\eta}} \approx 0.408, \quad \text{for} \quad \eta = 3. \tag{5}$$

At this value for σ , the intrinsic spread mechanism is balanced by the dissipation mechanism (controlling effect).

2.3 Maximum number of hospitalized cases

Inserting eq. (3) into the definition of inflexion point $\frac{d^2 f(t)}{dt^2}\Big|_{t=L} = 0$ and considering $\mu = \ln D + \sigma^2$, we obtain the following relationship between the two typical dates D (for maximum number of hospitalized cases) and L (inflexion point):

$$D = L \exp\left(\frac{1}{2}\sigma^2 + \frac{1}{2}\sqrt{4\sigma^2 + \sigma^4}\right).$$

Using eq. (3) again, f(D) is found to be related to f(L) by

$$f(D) = f(L) \exp\left(-\sigma^2 - \frac{1}{2}\sqrt{4\sigma^2 + \sigma^4} + \frac{1}{2}\left(\frac{3}{2}\sigma + \frac{1}{2}\sqrt{4 + \sigma^2}\right)^2\right).$$

With σ given by eq. (5), we have two important relations:

$$\frac{D}{L}\Big|_{\eta=3} = 1.649, \frac{f(D)}{f(L)}\Big|_{\eta=3} = 2.120.$$
 (6)

these important ratios can be applied to predict the maximal number of possible hospitalized cases and the day this maxima appears, once the inflexion point is identified through the data at the earlier stage of epidemic spreading. See below for more detailed explanation.

2.4 Initial date for regular spreading

Once we know the inflexion date, it is crucial to determine when is the initial date for regular spreading of the epidemic. In other words, we must know the number L (cumulated days to reach the inflexion point counting from the initial date). This can be done by using the rate of increase $\frac{\mathrm{d}f(t)}{\mathrm{d}t}$ at t=L. A simple calculation using eq. (3) yields

$$\frac{\mathrm{d}f(t)}{\mathrm{d}t}\Big|_{t=L} = -\frac{1}{\sigma^2 L} f(L) \ln \frac{L}{D}$$

which yields

$$L = \left(\frac{1}{2} + \frac{1}{2}\sqrt{\frac{4}{\sigma^2} + 1}\right) \frac{f(L)}{\frac{\mathrm{d}f(t)}{\mathrm{d}t}\Big|_{t=L}} = \frac{3f(L)}{\frac{\mathrm{d}f(t)}{\mathrm{d}t}\Big|_{t=L}}$$
(7)

3 Application and validation of the model

3.1 Use of the EBT model

The model is used as follows:

Step 1 (data recording). Using the reported data we determine the number F = f(L) at the inflexion date (the date that $\frac{\mathrm{d}f(t)}{\mathrm{d}t}$ tends to decrease). Also determine $\frac{\mathrm{d}f(t)}{\mathrm{d}t}\Big|_{t=L}$ by using the reported date. Determine the proportion constant k in (3) by setting f(L) = F. Then use eq. (7) to determine L.

Step 2 (Prediction). Once L and f(L) are known, use eq. (6) to predict D and f(D) and plot the curve $f(t) \sim t$ using eq. (3) to predict the number f(t) for L < t.

Hence it is essential to determine the inflexion point. Specifically, this is done as follows. We record the reported number f(t) for each day and draw the curve g(t) = f(t) - f(t-1). Once we observe that g(t) reaches a peak (denoted as G) at t = L, then L is considered as the inflexion point. However, special cautions must be made.

- (a) in the early period of the epidemic, it is possible to have report delay of cases so that a false peak would occur.
- (b) for a city or region where the cumulative number of cases remains always small, it is difficult to observe a clear peak. In this case this approach is not valid.
- (c) There is also a possibility to have multiple inflexion points due to new outbreaks, as is in the case of Hong Kong, Singapore and Canada for SARS in the year 2003.

Numerically, L is calculated as:

$$L = 3\overline{F}/G,\tag{8}$$

where $\overline{F}=(2F-G)/2$ is the number of f averaged over two consecutive dates (at and before the inflexion date). Still using the log-normal function, we can relate the maximum H=f(D) and the date D to F and G by $H\approx 2.12\overline{F}$ and $D\approx L+2\overline{F}/G$ where none of the constants depend on the details of the epidemic.

3.2 Test of the model for the epidemic of SARS in 2003: cities in China

First let us consider Beijing. Using the reported date as shown in Figure 1, we identify April 27 to be the critical date since $\frac{df(t)}{dt}$ experiences an evident decrease after that date (we also observe a decrease before April 25, but that decrease is due to the report delay). Using the reported date we have

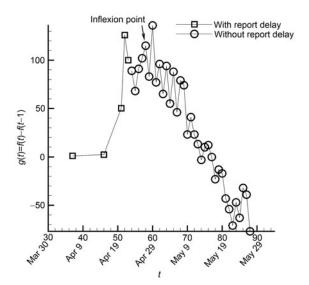


Figure 1 Inflexion point for Beijing. Note that the first peak is not an inflexion point but is simply due to report delay in the early period.

f(L) = 980 and $\frac{df(t)}{dt}\Big|_{t=L} = 116$. Hence L = 24 according to eq. (8). This indicates that the initial date for irregular spread is April 3. Using eq. (6) we predict D and f(D) to be D = 42 (May 13) and f(D) = 1955, while according to the report, D = 44 (May 15) and f(D) = 1991. The predicted curve f = f(t) follows well the curve, as can be seen in Figure 2.

For Hong Kong, we observe three distinct inflexion points as can be seen in Figure 3. The prediction using the information at the three inflexion points (IP1, IP2, IP3) show that the predicted curve using the first inflexion point is the closest to the reported data (Figure 4).

For Hebei, the number of cases is not large, however, the prediction is in good agreement (Figures 5 and 6).

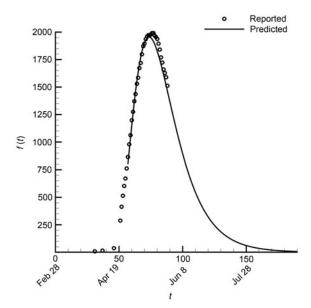


Figure 2 Time history of the number of hospitalized cases for Beijing.

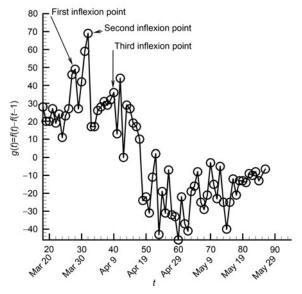


Figure 3 Inflexion point for Hong Kong. For Hong Kong we observe three distinct inflexion points.

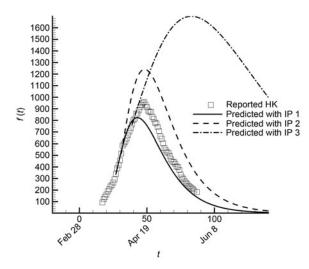


Figure 4 Time history of the number of hospitalized cases for Hong Kong.

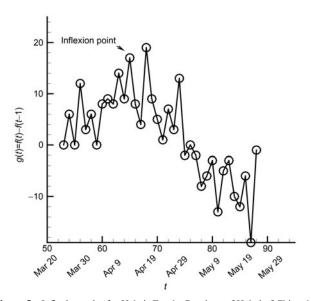


Figure 5 Inflexion point for Hebei. For the Province of Hebei of China the inflexion point is still identifiable.

3.3 Test of the model for the epidemic of SARS in 2003: other countries

Apart from China, SARS also appeared in Singapore and Canada, though the numbers of hospitalized cases were low.

For Singapore we observe three distinct inflexion points and two maximums (Figure 7). The prediction using the information at the first inflexion point fits well to the most part of the first peak (Figure 8).

For Canada we observe two inflexion points (Figure 9) and when the information of the first inflexion point is used the prediction reproduces well the lower part of the observed curve but fails to predict the peak value (Figure 10).

In summary, when the number is small, the error may be large. This is because that the thermodynamic approach is more accurate when the system is larger.

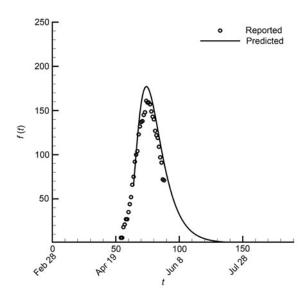


Figure 6 Time history of the number of hospitalized cases for Hebei. The predicted curve is reasonable as compared to the reported one, though the number of cases in Hebei is not large.

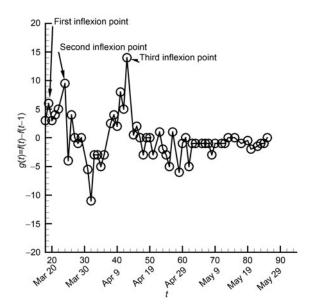


Figure 7 Inflexion points for Singapore.

3.4 Sensitivity of model to the number of hospitalized cases and the value of σ

In contrast to a deterministic approach for which one can give the specific condition under which a model is valid, for a statistic model, as for the present model, it is usually difficult to give specific conditions for validity. For the present approach, if the epidemic is sufficiently large but governed by controlling efforts of multiple scales so that an entropy is associated with the system, then the model is expected to be useful for predicting the spread increase or decrease, based on some data for the initial period of the epidemic. This can be seen from the estimated error as displayed in Table 1 for comparison of the model with SARS data. In Table 1, when

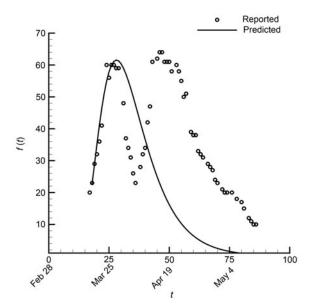


Figure 8 Comparion between predicted and reported cases for Singapore.

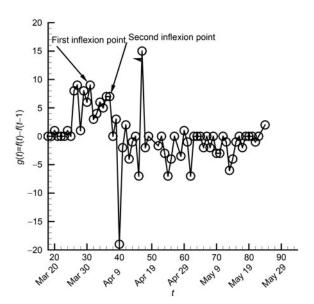


Figure 9 Inflexion points for Canada.

there are multiple inflexion points, as is in the case for Hong Kong, Singapore and Canada, we use the information at the first inflexion point. In the case of Singapore and Canada, there are two maximums but we give information only for

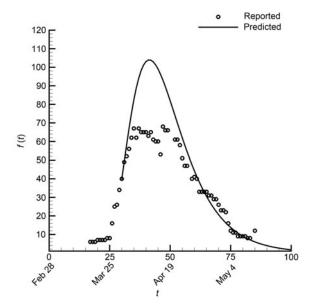


Figure 10 Comparison between predicted and reported cases for Canada.

the first one. We see that when the total number is in the order of a thousand or above, then the comparison is generally consistent, with an error within 15%.

For Hebei, Singapore and Canada, the total number is of the order of one hundred or less, with some comparison being entirely consistent. Only the case for Canada, we fails to predict the maximum value but correctly predicts the day the maximum appears.

It is interesting to note that the best fit value of σ using the reported data is close to the theoretical one ($\sigma=0.408$) (Table 2). In fitting σ , the date D (counting from the starting date) and the maximum value H are fixed to be the values given by the reported data (third and fourth columns) so that only σ is fitted. In the second column, the starting date is approximately the date when the first case was introduced into the region. The outbreak for the epidemic is assumed to take place within at most ten days so the best fit σ is obtained by using two epidemic starting days (date with the introduction of the first case and latest possible outbreak date). The range of best fit σ (fifth column) is in close approximation to the theoretical value 0.408 for Beijing and is not significantly different from the theoretical value for the other cities or regions.

Table 1 Predicted number H and date D compared with the reported ones for several cities or regions

Regions	Inflexion date			Date D		Maximum H		Error
	Date	F = f(L)	G	Pred	Rep	Pred	Rep	EHOI
Beijing	Apr27	980	116	May13	May15	1955	1991	2%
Hong Kong	Mar28	960	49	Apr12	Apr14	823	960	14%
World	Apr23	2005	222	May9	May12	4015	3700	8.5%
Mainland China	Apr27	1572	177	May14	May12	3332	3068	8.6%
Hebei	May4	92	17	May15	May13	177	161	8%
Singapore	Mar18	29	6	Mar27	Mar23	61	60	1%
Canada	Mar27	49	9	Apr10	Apr4	104	67	55%

Table 2	Best fit value of σ for several	I regions using the least sq	uare method, compared to the theoret	ical value $\sigma = 0.408$. The agreement is reasonable

Regions	Starting date	Date D	Maximum H	Best f it σ
Beijing	Mar 25/(10 days later)	May 15	1991	0.349/0.462
Hong Kong	Feb. 20/(10 days later)	Apr. 14	960	0.285/0.343
World	Feb. 20/(10 days later)	May 12	3700	0.273/0.32
Mainland China	Mar 25/(10 days later)	May 12	3068	0.307/0.404
Hebei	Apr. 17/(10 days later)	May 13	161	0.367/0.357
Singapore	March 1/(10 days later)	Apr. 15	64	0.409/0.491
Canada	Feb. 25/(10 days later)	April 8	84	0.297/0.368

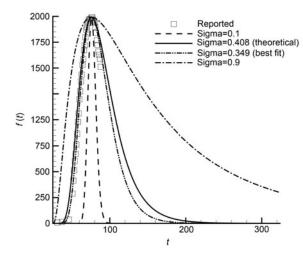


Figure 11 Role of σ on the correct reproduction of the curve f = f(t).

It can be noted that if the use of a value σ far beyond the theoretical value, the curve will not significantly affected. Herein we display in Figure 11 the role of σ on the correct reproduction of the curve f=f(t). The log-normal curves using the thermodynamical value $\sigma=0.408$ and the best fit value $\sigma=0.47$ are all close to the reported data. However, when σ is significantly different from the thermodynamical value, then the log-normal curve has a great departure from the reported data, as can be seen from the curves using $\sigma=0.1$ and $\sigma=0.9$. This shows that the shape of the curve is quite sensitive to σ and the theoretical value of σ is indeed a rational one.

4 Discussion

For the spread rate of communicable epidemics with multiscale controlling effort, we have built an entropy-based thermodynamic model for which we just need some data for the early period of a communicable epidemic, that is, we just need to know the inflexion point L (the cumulative days before the inflexion point), the number f(L) of the hospitalized cases and the increase rate df(L)/dt. Then the number of hospitalized cases for t > L can be predicted through the model. Notably, the maxima (t = D, f(D)) is shown to be related to the inflexion point by the following very simple relations:

$$\frac{D}{L} = 1.649, \frac{f(D)}{f(L)} = 2.120.$$
 (9)

The EBT model is applied to predict the number for t > L and especially D and f(D) for the 2003 SARS and is hoped it can be applied to other systems for SARS or similar epidemic spread involves multiscale interventions and constitutes a thermodynamical system. Despite the possible uncertainty in the reported data for 0 < t < L and that the model does not require epidemic details such as latent, incubation and infectious periods, the comparison between model prediction and reported SARS data is sufficiently good for the cities or regions where the epidemic is severe. The prediction for the case of Beijing is somewhat consistent since the number of cases is large. This shows that when the system is sufficiently large, the thermodynamic approach is more accurate. The actual model has some difficulties to precisely predict the case of multiple inflexion points.

The model seems to work if the number of hospitalized cases is in the order of hundreds, though the epidemic of Canada for SARS in the year of 2003 contains less than one hundred hospitalized cases and the prediction is entirely consistent.

The occur of the inflexion point depends on the strong public intervention to control the epidemic. The information about the inflexion point must be given according to the recorded data, without delay in reporting.

According to eq. (9), the maximum number of hospitalized cases will appear at a day about t = 0.65L after the inflexion point t = L, and the maximum number is about two times of the number at the inflexion point.

One may define the time t = M as the day that the epidemic disappears, if at this day the number of hospitalized cases reduces to 1% of the number at the inflexion point t = L, that is, the M is determined by, according to eq. (3) such that

$$\frac{L}{M} \exp\left(\frac{(\ln L - \ln D - \sigma^2)^2}{2\sigma^2} - \frac{(\ln M - \ln D - \sigma^2)^2}{2\sigma^2}\right) = 0.01.$$

Using eq. (9) to replace D we further obtain

$$\frac{L}{M} \exp\left(\frac{(\ln L - \ln(1.649L) - \sigma^2)^2}{2\sigma^2} - \frac{(\ln M - \ln(1.649L) - \sigma^2)^2}{2\sigma^2}\right) = 0.01.$$
(10)

For SARS in Beijing, L=24, the use of (10) predicts M=150 for $\sigma=0.408$. This compares quite consistently

with the approximate disappearing date as can be seen from Figure 2.

The present model can be possibly used to predict epidemics other than SARS once the communicable epidemics receive intensive interventions. The H7N9 avian influenza is actually of great concern [28,29] and if unfortunately this should spread rapidly, we expect the present model would be useful for predicting the spread.

5 Conclusions

The advantage of the present approach is the simplicity of the model, which does not involve any free parameters nor epidemic details, though the process of the spread of epidemics is complex. The complexity of the problem is resolved here through the use of an entropy approach. She [30] recently suggested a framework for treating complex system. According to this framework, it is usually possible to define simple models for complex systems. The disadvantage of the present approach is that it is a statistical one so that it is difficult to give specific conditions under which the model remains valid. Though the use of SARS data, this supports the validity of the approach, even when the number of hospitalized cases is small for cities or countries such as Hebei Province or Canada. More comparisons needs to be done to further assess the validity. This can be considered in future studies.

This manuscript is updated from an unpublished manuscript originally written by WU Z.N. during the SARS epidemic in 2003, some previous students, notably GAN CJ, have participated in preparing some figures. The Editor Staff HOU XZ of Science China and the Associate editor Prof. SHE ZS helps to identify important points that lead to the initial improvement of the paper. Finally several referees have given detailed remarks for important improvement of this paper.

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