No one Set of Parameter Values Can Simulate the Epidemics Due to SARS Occurring at Different Localities

Weerachi Sarakorn and I-Ming Tang

Abstract—A mathematical model for the transmission of SARS is developed. In addition to dividing the population into susceptible (high and low risk), exposed, infected, quarantined, diagnosed and recovered classes, we have included a class called untraced. The model simulates the Gompertz curves which are the best representation of the cumulative numbers of probable SARS cases in Hong Kong and Singapore. The values of the parameters in the model which produces the best fit of the observed data for each city are obtained by using a differential evolution algorithm. It is seen that the values for the parameters needed to simulate the observed daily behaviors of the two epidemics are different.

Keywords—SARS, Mathematical Modeling, Differential Evolution Algorithm

I. INTRODUCTION

The SARS (Severe Acute Respiratory Syndrome) epidemic in 2003 created near panic among the general populations in Asia [1, 2]. Singapore has estimated that the economic lost of potential income by the country caused by the fear of this disease was over 20 billion dollars. Even though the start of the disease began in China around the middle of November 2002, the epidemic in the rest of Asia and Canada can be traced back to a single visitor to Hong Kong at the end of February, 2003 [4]. From Hong Kong, the disease was transmitted to Vietnam, Singapore, Taiwan and Canada. By the end of the epidemic, the cumulative number of probable SARS case stood at 8,427 cases with 813 deaths [5]. For some reason, the SARS epidemic ended by the end of the summer of 2003 although there have been a few reported cases in 2004. These were among military personnel or the general populace and of the presence of classes of people called “untraced” on the spread of SARS virus. All of these disease began to appear. They looked at the influence of early diagnostic, of quarantine and isolation, of cleanliness of among the general populace and of the presence of classes of people called “untraced” on the spread of SARS virus. All of these were among military personnel or scientists who undertook unauthorized studies of the live virus.

Over the past few years, there have been warnings from the public health officials throughout the world about the inevitable outbreak of the avian flu (HSN1) pandemic [6]. The panic now is not among the general populations but among public health officials in various countries and at the WHO. Elected government officials have proposed the spending of billions of dollars to stockpile unproven medicines to treat this disease if ever arises. Mathematical models [8, 9] have been proposed for developing strategies to lessen the dire consequences of a disease which at present has a mortality rate of over 50%. There have been warnings from WHO and the authors of refs. 8 and 9 that building a mathematical model is that the assumptions, the model are built on is not proven. To construct a model for the spread of a disease, the epidemic must have already occurred. Then one could compare the predictions of the model with what has actually occurred. In the absence of the actual occurrence of the epidemic, one should look at the lessons learnt from previous epidemics.

Towards the end of the SARS epidemic, many mathematical models [10-14] of the transmission of this disease began to appear. They looked at the influence of early diagnostic, of quarantine and isolation, of cleanliness of among the general populace and of the presence of classes of people called “untraced” on the spread of SARS virus. All of these models required the separation of the populace into different population groups (suppose N). At least three parameters needed in the dynamical equations to describe the time evolution of each group, one would need at least 3N numerical values. How many populations groups depend on the model is being used. In one model on AID’s [15], the population was divided into over fifty groups based on sex, age and occupation.

Due to the great amount of uncertainty that would arise when there are a large number of untraced people present and when there are many parameters to be determined, the fitting of the model to the past data to obtain the values of the parameters would be a horrendous task. In addition to this, Bombardt [16] recently showed that the SAR outbreak (2003) in Taiwan could be explained if there was time varying rate of disease transmission. The time varying rate was determined by examining the epidemic curves. In this paper, we used a differential evolution (DE) algorithm to obtain the values of the parameters in our model for the SAR epidemic in Hong Kong and Singapore. We will find that a different set of numerical values are needed to simulate the behavior of different epidemics. One set of values can not account for the
behaviors of all the epidemics due to one disease. The DE algorithm is a class of stochastic search and optimization methods. The DE algorithm used, the DE/best/2/bin scheme given by Price & Storn, [17] is briefly reviewed in Section IIc. Descriptions of the SARS epidemic in Hong Kong and in Singapore are presented in Section IIa. The model for the transmission of SARS is given in Section IIb. In Section III, the numerical values of the parameters that lead to the simulated results which most closely matched the observed results are given. The simulated curves for the cumulative number of SARS cases in the two city states are presented here. We see that the simulated curves closely fit the Gompertz description of the observed daily increases in the number of SARS cases in the two cities. We make some comments in Section IV.

II. MATHEMATICAL MODELS AND METHODS

A. SARS Epidemic in Hong Kong and Singapore

The initial cases of an atypical pneumonia appeared in Fushan City, Guangdong Province in China in the middle of November 2002. An accurate epidemiological study of the index patient who started the global spread of this disease can be found on the CDC website (http://www.cdc.gov/mmwr/preview/mmwrhtml/mmm5212a1.htm# figure 1 on the site). He was a medical doctor visiting Hong Kong who had checked into a hotel in Hong Kong. At the hotel, he infected ten people. The index patient and three of the newly infected persons were taken to four hospitals in Hong Kong where they in turn infected more people. Three other infectious went to Singapore. There, they began the epidemic in that country. Two others went to Canada and began the epidemic in the city of Ontario. The remaining two traveled to the USA and to Europe. They did not however start any new epidemics. In the second ring of the epidemiology chain in Hong Kong, 103 of new cases were health care workers. The epidemic in Taiwan was started by a businessman who had visited Hong Kong, but no direct or indirect connections with the people in the primary or secondary ring were found. The epidemic in Taiwan is different from the others in that it began in a country where the number of people recovering each day.

Looking at the shape of the curves formed by the raw data on the cumulative number of probable SARS cases, we recognize them to be the Gompertz curves. These curves are the most commonly used curves to fit the data on the growth of a large variety of populations. The Gompertz curve is often divided into three segments. The first segment reflects the dynamics of the initial growth of the populations. In this segment, the curve indicates an exponential growth and so the curve is concave in this time region. Laird [18] defines the end of this segment to be the point at which the population is equal to 0.37 of its final number. This point is often called the inflection point in the curve. In this study, we take it to be the 27th day from the start of the epidemic. The second segment starts at the inflection point and reflects the dynamics of the growth when the limitations on the exponential growth begin to be a factor. The limitations can be due to the finiteness of the food supply or of the number of susceptible people who can be infected. The end of the second segment is the inflection point. The inflection point is defined as the intersection of the initial slope of the first segment of the curve and slope of the Gompertz curve in the saturation region, the region in which no increase in the number of infected people is observed. The third segment extends from the inflection point into the saturation region. In this study, the inflection point is set to be the 54th day of the epidemic.

B. Mathematical Model

Since the SARS epidemics have only been of short durations and so the number of births and deaths from natural causes would be small, the Kermack-McKendrick model [19] is used. We have added an additional class, the untraced classes, to the model. In our model, the population is divided into ten categories; S1 denotes the number of susceptible people in the general population; S2, the number of susceptible people who are at high risk (health care workers and close relatives); Scs, the number of susceptible people who who are quarantined; Scg, the number of susceptible high risk people who are quarantined; Es, the number of people known to have been exposed to SARS and who are therefore quarantined; E, the number of people who have been exposed but are untraced; Q and J, the number of known infectious people who are quarantined or who are quarantined and isolated, respectively; I is the number of infectious persons who are untraced and R is the number of people who have recovered. A verbal description of what is happening is described as follows.

The susceptible population is divided into two categories since the health care workers and the close relatives will come into contact with the infected populations more often than would the general population. They would therefore a higher risk of contacting the diseases. In all other regards, the two categories are identical. We let the parameter ‘p’ indicate how much more the high risk group would be susceptible to the diseases. We further let q1 and q2 be the fractions of the two susceptible populations who have come into contact with an infected person and k be the number of contacts that an infectious person makes per day. If b is the probability of transmission per contact, then 1-b is the probability that the contact will not result in the transmission of the disease.
Adopting a policy of quarantining a person who may have come in contact (both causal and repeated) with a sick person, then \( q_1 k (1-b) S_1 \) and \( q_p k (1-b) S_2 \) people would be quarantined each day. The people who enter into the quarantine will leave when the authorities are sure that they did not catch the disease. This means that they would have to stay for at least the number of days in the incubation period. A susceptible person belong to either susceptible classes would become exposed if they encountered an infectious person. The infectious person can be a person whose health status is not known or one who is under quarantine or is in isolation. Since the opportunity for a member in the general population to met people belonging to the latter two groups is reduced, the probability that a quarantined (or a quarantined and isolated) person will transmit the disease to a susceptible person in the general population would be \( q_0 \) (or \( 1-q_0 \)). Normally, \( 0 < q < 1 \).

The rates at which people enter into the known exposed group (\( E_q \)) are \( q_1 \beta \) and \( q_p \beta \) from the two susceptible groups, while the rates at which people enter into the untraced exposed group \( E \) are \( (1-q_1) \beta \) and \( (1-q_p) \beta \). \( d_1 \) and \( d_2 \) are the rates at which the traced (quarantined) and untraced infectious persons become known and are moved into isolation, respectively. \( \alpha _1 \), \( \alpha _2 \) and \( \alpha _3 \) are the rates at which the infectious individuals from the three groups (infectious who are quarantined, infectious who are untraced and who are isolated) respectively. \( \delta _1 \), \( \delta _2 \) and \( \delta _3 \) are the mortality rates due to SARS of the three infectious groups.

The mathematical formulation of the model is done by noting that the time rate of change of each population group is equal to the number going in minus the number leaving. Expressing in mathematical terms what is happening verbally, we get

\[
\frac{dS_1}{dt} = -\beta S_1 \left[ \frac{qQ+I+J}{N_1} \right] + \theta S_{q1}, \quad (1a)
\]

\[
\frac{dS_2}{dt} = -p\beta S_2 \left[ \frac{qQ+I+J}{N_1} \right] + \theta S_{q2}, \quad (1b)
\]

\[
\frac{dS_{q1}}{dt} = q_1 k (1-b) S_1 \left[ \frac{qQ+I+J}{N_1} \right] - \theta S_{q1}, \quad (1c)
\]

\[
\frac{dS_{q2}}{dt} = q_2 p (1-b) S_2 \left[ \frac{qQ+I+J}{N_1} \right] - \theta S_{q2}, \quad (1d)
\]

\[
\frac{dE}{dt} = \beta (q_1 S_1 + q_2 S_2) \left[ \frac{qQ+I+J}{N_1} \right] - \gamma E, \quad (1e)
\]

\[
\frac{dE_q}{dt} = \beta ((1-q_1) S_1 + (1-q_2) S_2) \left[ \frac{qQ+I+J}{N_1} \right] - \gamma E_q, \quad (1f)
\]

\[
\frac{dQ}{dt} = \gamma E_q (\alpha _1 + d_1 + \delta _1) Q, \quad (1g)
\]

\[
\frac{dI}{dt} = \gamma E (\alpha _2 + d_2 + \delta _2) I, \quad (1h)
\]

\[
\frac{dR}{dt} = \alpha _3 Q + \alpha _1 I + \alpha _2 J, \quad (1j)
\]

with \( N_1 = S_1 + S_2 + S_{q1} + S_{q2} + E_q + E + Q + I + J + R \).

In the present work, we assume that the rates at which the infectious populations (\( Q \) and \( I \)) enter into the population group labeled \( J \) are the same, i.e., \( d_1 = d_2 \) and that the values of the recovery rates \( \alpha _1 \) and \( \alpha _2 \) are the same and \( 1/\alpha _3 = 1/d_1 + 1/\alpha _3 \).

The numerical values of the other parameters are determined by the differential evolution algorithm (DE), which is described in the next section (IIc). Using the numerical values generated by the DE at each update, equations (1a) to (1j) are numerically solved. The criteria for determining the optimal set of numerical values is given at the end of Section IIc. The cumulative number of probable SARS cases at time \( t \), are obtained from the solutions of the equations when the optimal set of parameter values are used. Not unsurprising, the plot of cumulative number of cases versus time is a Gompertz curve (See Figures. (1) and (2)).

C. Differential Evolution Algorithm

The ideal of Differential Evolution was put forth by Price and Storm in 1996. It grew from the attempt to solve the Chebychev Polynomial fitting problem presented to Price by Storm. The DE is a sub branch of evolutionary algorithms which is a class of stochastic search and optimization methods. It is a generic algorithm for numerical optimization in which the user sets the values of three parameters; the population size \( (N_p) \), a constant which controls the amplification of the differential variation \( (F) \) and the cross over constant \( (CR) \). Price and Strom have proposed ten variants of the DE algorithm. We will be using the DE/best/2/bin variant.

We first choose the values of \( N_p \), \( F \), CR, the number of maximum updates and the convergence criteria \( (\epsilon) \) with \( F \in [0, 2] \) and \( CR \in [0, 1] \). Lopez [18] has proposed some criteria for the values of \( F \) and CR so that the differential evolution algorithm is an efficient method for determining the near optimal values of the parameters. He suggest that \( F = 0.9 \) and \( CR = 0.1 \) when \( \rho \) (a measure population diversity) > \( \epsilon \) and \( F = 0.5 \) and \( CR = 0.5 \), otherwise. Once this is done, we construct an initial set of \( n \)-dimensional vectors where \( n \) is the number of parameters whose values are to be determined. This is done by first establishing the upper and lower bounds for each parameter. We call the vectors constructed with upper bound values and with the lower bound values, \( \theta^U \) and \( \theta^L \). We now generate \( N_p \) new vectors according to the rule

\[
\theta_i = \theta^U + \beta_i (\theta^U - \theta^L), \quad i = 1,...,N_p \quad (2a)
\]

where \( \beta_i \) is random number between 1 and 1. \( \theta_i \) will be the \( n \)-dimensional vector \( [\theta_{i1}, \theta_{i2}, ..., \theta_{in}] \) where \( \theta_{ij} \) is the \( j \)-th component of the \( i \)-th (row) vector. The numerical values given by \( \theta_i \) will still be within the range of the lower and upper bounds for each parameter. We denote these initial \( N_p \) vectors as the \( G = 0 \) generation vectors.

The differential evolutionary algorithm is a method to generate a new generation of \( n \)-dimensional vectors (new
The new vectors are generated according to the following procedure:

i. From the set $\{\theta^G_i, i=1, 2, ..., N_p\}$, we randomly pick four different vectors belonging to the G-th generation and label them $j$, $k$, $l$, and $r$.

ii. The $v^{G+1}_i$ are generated according to

$$v^{G+1}_i = \theta^G_{ji} F[(\theta^G_{ji} - \theta^G_k) + (\theta^G_{ji} - \theta^G_r)]$$

(2c)

where $\theta^G_{ji}$ is the vector in the G-th generation which satisfies the criterion for being the best fit (the criterion to be given later) and $F$ is a random number between 0 and 2.

The determination of the best G-th generation best choice of numerical values, the vector $\theta^G_{ji}$ and of when the iteration should be stopped involves finding the vector $\theta^G_{ji}$ which gives the minimum values of the object function $J(\theta^G_{ji})$, defined as

$$J_k = \sum_{i=1}^{N_p} \left( \frac{X_i^{ob} (t_j) - X_i^{est} (t_j)}{X_{i, max}^{ob}} \right)^2$$

(2f)

and whether the minimum value is less than the convergence criterion. $X_i^{est} (t_j)$ is the calculated value of the i-th variable (e.g., the cumulative number of SARS cases, the number of new cases each day or the number of recovered cases) when

the numerical entries of the vector $\theta^G_{ji}$ are used in the model.

$X_i^{ob} (t_j)$ are the observed values of the variable $X_i^{est} (t_j)$ at time $t$. $X_{i, max}^{ob}$ is the maximum observed value of the variable. $m$ is the number of data points. We keep on generating new generations until the maximum number of iteration is performed or when

$$|J_{w} - J_b| < \epsilon$$

(2h)

where $J_b = min \{J(\theta^G_i), i=1,...,N_p\}$ and $J_w = max \{J(\theta^G_i), i=1,...,N_p\}$.

III. PARAMETER ESTIMATION

In this work, the values which need to be estimated from the observed data are $\beta$, $p$, $q$, $q_1$, $q_2$, $\ell$, $\gamma$, $d_1$, $a_0$, and $\{X_i(0)\}$, the last being the initial values in the model. As we have mentioned, we expect the curve which will fit the data on the cumulative number of probable SARS cases will be a Gompertz curve. If the equation to be fitted were a linear one, there are standard methods to determine the values which would give a least square best fit. Since the equations are non linear ones, we have used instead the Differential Evolution Algorithm (DE/best/2/bin scheme) to find the values of the parameters which would give a least square best fit of each segment of the Gompertz curve to the observed data in the appropriate time intervals. This was done for the epidemics in Hong Kong and Singapore.

The DE/best/2/bin algorithm requires the user to set the values of $N_p$ (the population size), F (a constant factor that controls the amplification of the differential variation) and CF (crossover constant). We have set $N_p$ at 35, the maximum number of generation is 4000 and the tolerance for convergence ($\epsilon$) is set at $10^{-6}$. In our use of DE/best/2/bin, we have assumed that the values of $p$, $q$, $q_1$, $q_2$, $\ell$, $\gamma$, $d_1$, $a_0$ and $\{X_i(0)\}$ determined by a best fit of the first segment of the Gompertz curve to the data on the cumulative number of SARS cases in Hong Kong and Singapore in the time interval do not change in the second and third time intervals. We however let the values of $\beta$, $q_1$, $q_2$, and $\ell$ to be different in the three intervals. Doing this, we arrive at the values listed in Table 1 for the model for Hong Kong and Table 2 for Singapore. As we see, all the numerical values are different. This shows that the same set of numerical values can not be used to simulate the behavior of these two epidemics caused by the same disease (SARS in this case). The solid curves in Figs. 1 and 2, are the plots based on the solutions of eqns. (1a) to (1j) using the values given in Tables 1 and 2. The best fit of a Gompertz curve to the data points for Hong Kong gave a $R^2 = 0.9981$. For the data for Singapore, the best fit of the Gompertz curve gave a $R^2 = 0.9915$. Comparing the data for two city states, we see that the cumulative number of SARS cases in Singapore increased faster in the first regime that it did in Hong Kong is the same.
and $q_2$, who were quarantined, were low in the first regime but higher in the later regimes. This can be easily understood as a better understanding of what had to be done as the disease developed.

The estimated transmission rate $\beta$ in Singapore was lower than that in Hong Kong. In both cities, the fractions of susceptible general population and high risk population, $q_1$ and $q_2$, who were quarantined, were low in the first regime but higher in the later regimes. This can be easily understood as the results of a stricter application of quarantine and isolation as a better understanding of what had to be done as the disease developed.

IV. DISCUSSION.

The purpose is to show that a single set of numerical values of the parameters in a model to describe the transmission of a disease can not be used to simulate the time progression of an epidemic in a given locality. Different sets of numerical values are needed for the epidemic occurring at different localities. A model to describe the time progression of an epidemic can only be developed after the epidemic has occurred. This has tremendous implications to present development of models to describe the time progression of an epidemic caused by a virus which has not yet evolved, i.e., the H5N1 avian flu pandemic, into a contagious human to human disease.

REFERENCES

### TABLE I
VALUES OF THE PARAMETERS WHICH ENTER INTO THE MODEL FOR THE SARS EPIDEMIC IN HONG KONG

Parameter values which are common to all three segments of the Gompertz Curve

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Parameter values which are different in each segment.

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### TABLE II
VALUES OF THE PARAMETERS WHICH ENTER INTO THE MODEL FOR THE SARS EPIDEMIC IN SINGAPORE

Parameter values which are common to all three segments of the Gompertz Curve

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Parameter values which are different in each segment.

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