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THE EFFECT OF GLOBAL TRAVEL ON THE SPREAD OF SARS

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Abstract. The goal of this paper is to study the global spread of SARS. We propose a multiregional compartmental model using medical geography theory (central place theory) and regarding each outbreak zone (such as Hong Kong, Singapore, Toronto, and Beijing) as one region. We then study the effect of the travel of individuals (especially the infected and exposed ones) between regions on the global spread of the disease.

In honor of Professor Zhien Ma's 70th birthday

1. **Introduction.** Severe acute respiratory syndrome (SARS) is a new infectious disease first reported in November 2002 in the Guangdong province of China (WHO, March 12, 2003). SARS was carried out of the Guangdong on February 21, 2003, when an infected physician spent a single night on the 9th floor of a Hong Kong hotel (Hotel M) (Tsang et al., 2003). By the end of February, guests and visitors to the hotel's 9th floor had seeded outbreaks in the hospital systems of Hong Kong, Vietnam, and Singapore. Simultaneously, the disease began spreading around the world along air travel routes as guests at the hotel flew home to Toronto and other cities around the world (WHO, May 20, 2003). On March 15, the World Health Organization (WHO) issued emergency travel recommendations to alert health authorities, physicians and the traveling public to what was perceived to be a worldwide threat to health. The number of worldwide SARS cases exceeded 4,000 on April 23 and then rapidly soared to 5,000 on April 28, 6,000 on May 2, 7,000 on May 8, and 8,000 on May 22. During the peak of the global outbreak in early May, more than 200 new cases were being reported each day. As of August 2003, when SARS was under control globally, it had been spread to 30 countries and regions, diagnosed in more than 8,000 patients and caused 774 deaths (WHO, 8/15/2003). SARS, the first severe infectious disease to emerge in the twenty-first

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century, had taken advantage of opportunities for rapid international spread made possible by the unprecedented volume and speed of international travel.

International travel has been identified as one of the major factors associated with the global spread of infectious diseases (Ostroff and Kozarsky, 1998; Wilson, 2003). With modern fast air transport, global spread of infectious agents becomes much easier. The diffusion of SARS, a respiratory virus with a high attack rate, is even more rapid. WHO issued the first emergency travel advisory on March 15, 2003 to airlines and travelers, providing case definitions for probable and suspect cases of SARS and advising airline crews of the need to report all such cases to airport and public health authorities (WHO, March 15, 2003). Additional guidance was issued on March 27, 2003 that recommended measures to reduce the risk of the global spread of SARS, including the exit screening of air passengers departing from areas reporting local transmission (WHO, March 27, 2003). The International Air Transport Association (IATA) provided denominator data on commercial international flights and passengers, including transit passengers, for March 2003, to and from Beijing, Hong Kong SAR, Singapore, Taipei, and Toronto. There are a number of important findings from the preliminary data (WHO/CDS/CSR/GAR, 2003; Olsen et al., 2003): (1) A total of 29 secondary cases had been linked to probable cases of SARS who traveled while symptomatic. (2) No transmission had been confirmed on flights after the March 27 travel advisory, in spite of at least 21 flights with probable SARS cases on board since that date. (3) A crude estimate from the verified flights of March was that 6.5 passengers per million traveled as symptomatic probable SARS cases in March 2003, having departed from locations specified above with local transmission of SARS.

By piecing together preliminary data on the course of infection and by making use of accumulating case notifications, several epidemiological studies (Chowell et al., 2003; Lipsitch et al., 2003; Riley et al., 2003) give the quantitative assessment of the epidemic potential of SARS and the effectiveness of control measures. They all made use of dynamic mathematical models in which individuals progress through mutually exclusive classes containing susceptible, exposed (latent), infectious, and recovered (immune) individuals (SEIR). All calculate that the "basic case reproduction number"—the fundamental epidemiological quantity that determines the potential for disease spread—is of the order of 2 to 4 for the Hong Kong epidemic. They draw the conclusion that the SARS coronavirus, if uncontrolled, would infect the majority of people wherever it was introduced, but that it is not so contagious as to be uncontrollable with good, basic public-health measures: improved control measures in hospitals, quarantine of contacts of cases, and voluntary reduction in contacts in the population (Dye and Gay, 2003). These studies are significant in studying the local outbreaks and control of SARS in such places as Hong Kong, Singapore, Toronto. Mathematical models have also used to simulate the SARS outbreaks in China as well (Wang and Ruan, 2004; Zhou and Yan, 2003; Zhou et al. 2004; Zhang et al., 2005). The nosocomial spread of SARS has been studied using models introduced by Lloyd-Smith et al. (2003) (discrete, stochastic) and Webb et al. (2004) (continuous, deterministic). Transmission of SARS in small-world networks has been simulated by Masuda et al. (2004).

The goal of this paper is to study the SARS spread from a global point of view by proposing multi-region compartmental models using medical geography theory (central place theory). We regard each outbreak zone (such as Guangdong, Hong Kong, Vietnam, Singapore, Toronto, Beijing, and the United States) as one region,

study the effect of the travel of individuals (especially the infected and exposed ones) between regions on the global spread of the disease, and investigate the dynamics of the model.

2. Medical Geography and Central Place Theory.

2.1. Medical Geography.

Medical geography is a discipline that uses spatial analytic techniques to identify relationships between geographic variables and illness and can be used to study how geographic processes such as movement of people and spatio-temporal changes (i.e., changes in geographic space over time) affect disease diffusion. Medical geography theory has been used to study spatial aspects of influenza, measles, cholera, and hepatitis B (Meade et al, 2000; Gatrell, 2002).

Diseases can occur in a specific geographic location by originating there or by being transported there (Meade et al, 2000; Gatrell, 2002; Mayer, 2000). Diseases originate in a particular place because certain precipitating ecologic factors favor that location as the locus of initiation. SARS originated in restaurant workers in Guangdong, presumably because of poor sanitary conditions and contact between humans and the zoonotic vector. If a disease does not originate in a specific location, it is transported from place to place by spatially contagious diffusion, hierarchical diffusion, or a combination of both.

Spatially contagious diffusion (SCD) involves diseases spreading from person to person through close contact. The extent of diffusion is related to the initial intensity of infection and the ability of people to become infected (Gould, 1993). For especially infectious SARS, SCD is responsible for transmission within a particular geographic location. For example, in Hong Kong, the number of infected individuals increased daily because of direct contact between infected individuals and others within the community. Hierarchical diffusion (HD) is another method of disease diffusion. With SARS, SCD was responsible for diffusion within Hong Kong, while HD was responsible for its spread to other major cities around the world. Indeed, SARS appeared to have jumped from one major city to another without affecting smaller cities in between (e.g., from Hong Kong to Singapore).

2.2. Central Place Theory.

Central place theory categorizes cities and towns on an urban hierarchy based on factors such as population size, services available in that city, and interconnectedness with other cities (King, 1984). In turn, cities are ranked as first, second, third, and so on. First-order cities are highly developed service centers such as Hong Kong and Toronto. Both are large, urban, global economic centers with highly developed infrastructure and transportation networks. They also have major research universities and a whole array of goods and services available. A second-order city has fewer services but would still be considered a major city. As one moves down the urban hierarchy, fewer goods and services are available and the population becomes smaller. When one arrives at the lowest-order center, only essential goods and services, such as a post office, gas station, and neighborhood grocery store, are available. The interconnectedness between geographic locations determines the flow of people and diseases between them. A higher degree of interconnectedness results in increased disease diffusion. Generally, a disease originating in a lower-order city will ascend (and descend) its particular urban hierarchy. SARS, for example, ascended the urban hierarchy from rural Guangdong Province to Shenzhen to Hong Kong. From there, SARS diffused to

other first-order cities around the world. Once SARS was established in another urban hierarchy, it began to descend to lower-order cities.

2.3. **Combination Diffusion of SARS.** The diffusion of SARS is a combination of both SCD and HD. For example, SARS was transmitted to family members and healthcare workers in Hong Kong by SCD and was transported to Toronto, Singapore, and Hanoi by HD. In turn, Toronto, Singapore, and Hanoi demonstrated SCD within their respective cities and also were the source for transmission to other cities and towns down their urban hierarchy (Affonso et al., 2004; Boulos, 2004; Litaker et al., 2003). Based on documented accounts of the initial index patient in Hong Kong and his or her contact with others in Hong Kong, it is evident that HD was responsible for the spread of disease from Hong Kong to other cities in Asia and around the world (CDC, March 21, 2003; WHO, May 20, 2003). On February 21, 2003, the index patient (patient A) stayed at Hotel M in Hong Kong. One infected guest (patient B) traveled to Hanoi (a lower-order city), became ill on February 23, 2003, and infected 59 healthcare workers in Hanoi. Patient B spread SARS within Hanoi by SCD. Three other guests at the hotel (patients C, D, E) carried the disease to Singapore and in turn infected dozens of healthcare workers and family members. One of the infected Singaporean healthcare workers, a physician, traveled to Germany and is linked to several cases there. Diffusion from one first-order center to other first-order centers also occurred. Patient F, also a guest at the Hotel M in Hong Kong, was linked to the diffusion of SARS to family members, healthcare workers, and other patients in a Toronto hospital before the disease spread to the community by SCD.

2.4. **Multi-Regional Models.** Spatial heterogeneities can be included by adding an immigration term where infective individuals enter the system at a constant rate. This clearly allows the persistence of the disease, because if it dies out in one region, then the arrival of an infective from elsewhere can trigger another epidemic (Murray, 1989). Another way of introducing spatial effects into the model is to divide the population into multiple subpopulations and allow infective individuals in one patch to infect susceptible individuals in another, an idea very similar to the central place theory (King, 1984). The equilibrium behavior of such models for various diseases has been studied widely (Lajmanovich and Yorke, 1976: Hethcote, 1978; Nold, 1980; Hethcote and Thieme, 1985; Dushoff and Levin,1995; Sattenspiel and Dietz, 1995; Lloyd and May,1996; Sattenspiel and Herring, 1998, 2003; Arino and van den Driessche, 2003).

We shall use the multiple subpopulation approach and the medical geography theory (spatially contagious diffusion, hierarchical diffusion, central place theory) to propose multi-regional compartmental models to study global transmission of SARS. The SCD of SARS in each region will be described by the SEIR type of models, and the HD of SARS will be modeled by connecting these submodels.

3. **The Model.** We consider n geographical regions. Each region is mainly occupied by one community. We suppose that a population from the same community and living in the same region is homogenous. That is, they have the same biological and epidemiological parameters. The residents of each community are classified into 5 classes: susceptible, exposed, quarantined, infectious, and recovered. By the process of SARS control, we assume that the individuals who are in the quarantined class cannot travel; those members in susceptible, exposed and recovered

classes may travel among the regions; and a very small fraction of infectious individuals may travel as well. Residents in the susceptible class or the exposed class are assumed to leave a region i at a certain constant rate, σ_i. The probability that a person travels from region i to any other region j is given by ν_{ij}. A person from region i who travels to region j returns home at a rate ρ_{ij}.

Let $S_{ij}(t), E_{ij}(t), I_{ij}(t), Q_{ij}(t)$, and $R_{ij}(t)$ denote the number of susceptible, exposed, infective, quarantined, and recovered individuals from community i who are present in region j at time t, respectively. Set

$$N_{ij} = S_{ij} + E_{ij} + I_{ij} + R_{ij}, \quad i, j = 1, 2, \ldots, n$$

and

$$N_i^r = \sum_{j=1}^{n} N_{ij}, \quad N_i^p = \sum_{j=1}^{n} N_{ji}.$$

Then, N_i^r is the number of residents from region i, and N_i^p is the number of individuals (residents and travelers) who are physically present in region i at time t.

If we adopt a standard incidence rate, then the infection rate of individuals from region i in site k is given by

$$\sum_{j=1}^{n} \beta_{ikj} \frac{S_{ik} I_{jk}}{N_j^p},$$

where $\beta_{ikj} = \kappa_k \eta_{ikj}$. Here, κ_k is the fraction of infected persons who can transmit SARS at region k. It measures the quarantined intensity of SARS patients at the region k. If $\kappa_k = 0$, no patient can spread the SARS disease at the region k. On the other hand, if $\kappa_k = 1$, patients are free to transmit SARS at the region k. Furthermore, η_{ikj} is the adequate contacts in region k between a susceptible individual from region i and an infectious individual from region j.

We suppose that the birth rate of community i in site j is a constant b_{ij}, and newborn infants are susceptible. Let $1/d_{ij}, 1/e_{ij}, 1/\alpha_{ij}, 1/\xi_{ij}$, and $1/\eta_{ij}$ denote the average lifetime, exposed period, quarantined period, infectious period, and hospitalized time of persons from community i who are present at site j, respectively. Further, let g_{ij} denote the transition rate of exposed individuals of community i to infectious class at site j, and θ_{ij} the transition rate of quarantined individuals of community i to infectious class at site j. Denote the disease-induced death rate of individuals from community i at site j by ϵ_{ij}. We suppose that all exposed individuals who can be traced will either enter into the quarantined class, or enter into the infective class if they are diagnosed as suspected cases. After the quarantined period, most individuals will return to the susceptible class except those who are diagnosed as infectious members. The infected individuals will be either recovered or removed (including by death). Let c_i denote the screening coefficient for SARS infectives at the border of site i. If $c_i = 1$, then infected members can pass through site i freely; if $c_i = 0$, then infected individuals cannot pass through the border of site i. Under the above assumptions, we can write the equations for

each subpopulation from region i who remain in this region as

$$\begin{aligned}
\frac{dS_{ii}}{dt} &= b_{ii} + \sum_{k=1,k\neq i}^{n} \rho_{ik} S_{ik} - (\sigma_i + d_{ii}) S_{ii} - \sum_{k=1}^{n} \beta_{iik} \frac{S_{ii} I_{ki}}{N_k^p} + \alpha_{ii} Q_{ii} + \eta_{ii} R_{ii}, \\
\frac{dE_{ii}}{dt} &= \sum_{k=1,k\neq i}^{n} \rho_{ik} E_{ik} + \sum_{k=1}^{n} \beta_{iik} \frac{S_{ii} I_{ki}}{N_k^p} - (\sigma_i + d_{ii} + e_{ii} + g_{ii}) E_{ii}, \\
\frac{dQ_{ii}}{dt} &= e_{ii} E_{ii} - (d_{ii} + \alpha_{ii} + \theta_{ii}) Q_{ii}, \\
\frac{dI_{ii}}{dt} &= \sum_{k=1,k\neq i}^{n} c_k \rho_{ik} I_{ik} + g_{ii} E_{ii} + \theta_{ii} Q_{ii} - (c_i \sigma_i + d_{ii} + \epsilon_{ii} + \xi_{ii}) I_{ii}, \\
\frac{dR_{ii}}{dt} &= \sum_{k=1,k\neq i}^{n} \rho_{ik} R_{ik} + \xi_{ii} I_{ii} - (\sigma_i + d_{ii} + \eta_{ii}) R_{ii}.
\end{aligned} \tag{3.1}$$

For $i \neq j$, the dynamical equations are

$$\begin{aligned}
\frac{dS_{ij}}{dt} &= b_{ij} + \sigma_i \nu_{ij} S_{ii} - (\rho_{ij} + d_{ij}) S_{ij} - \sum_{k=1}^{n} \beta_{ijk} \frac{S_{ij} I_{kj}}{N_k^p} + \alpha_{ij} Q_{ij} + \eta_{ij} R_{ij}, \\
\frac{dE_{ij}}{dt} &= \sigma_i \nu_{ij} E_{ii} + \sum_{k=1}^{n} \beta_{ijk} \frac{S_{ij} I_{kj}}{N_k^p} - (\rho_{ij} + d_{ij} + e_{ij} + g_{ij}) E_{ij}, \\
\frac{dQ_{ij}}{dt} &= e_{ij} E_{ij} - (d_{ij} + \alpha_{ij} + \theta_{ij}) Q_{ij}, \\
\frac{dI_{ij}}{dt} &= c_i \sigma_i \nu_{ij} I_{ii} + g_{ij} E_{ij} + \theta_{ij} Q_{ij} - (c_j \rho_{ij} + d_{ij} + \epsilon_{ij} + \xi_{ij}) I_{ij}, \\
\frac{dR_{ij}}{dt} &= \sigma_i \nu_{ij} R_{ii} + \xi_{ij} I_{ij} - (\rho_{ij} + d_{ij} + \eta_{ij}) R_{ij}.
\end{aligned} \tag{3.2}$$

4. **Analysis.** We now consider the system (3.1)-(3.2). First, we find its disease-free equilibrium. For convenience in notation, we arrange the order of the variables in the system (3.1)-(3.2) by the following manner. First, we sort them by the index of communities, then by the number of sites, and finally by epidemiological classes: susceptible, exposed, quarantined, infected, and recovered. For $1 \leq i \leq n$, we consider

$$\begin{aligned}
&b_{ii} + \sum_{k=1,k\neq i}^{n} \rho_{ik} S_{ik} - (\sigma_i + d_{ii}) S_{ii} = 0, \\
&b_{ij} + \sigma_i \nu_{ij} S_{ii} - (\rho_{ij} + d_{ij}) S_{ij} = 0, \qquad j = 1, \ldots, n, i \neq j.
\end{aligned} \tag{4.3}$$

Since the coefficients of S_{ij} consist of an M matrix, it is easy to see that (4.3) admits a unique positive solution $S_i^* = (S_{i1}^*, \ldots, S_{in}^*)$. Set $E_i^* = Q_i^* = I_i^* = R_i^* = 0$. Then

$$P_0 = (S_1^*, E_1^*, Q_1^*, I_1^*, R_1^*, \ldots, S_n^*, E_n^*, Q_n^*, I_n^*, R_n^*)$$

is a disease-free equilibrium.

Set

$$w_{ii}^E = \sigma_i + d_{ii} + e_{ii} + g_{ii}; \quad w_{ij}^E = \rho_{ij} + d_{ij} + e_{ij} + g_{ij}, \quad i \neq j;$$

$$w_{ii}^I = c_i\sigma_i + d_{ii} + \epsilon_{ii} + \xi_{ii}; \quad w_{ij}^I = c_j\rho_{ij} + d_{ij} + \epsilon_{ij} + \xi_{ij}, \quad i \neq j;$$

$$w_{ij}^Q = d_{ij} + \alpha_{ij} + \theta_{ij}.$$

Define

$$M_i^E = \begin{pmatrix} -w_{i1}^E & 0 & \cdots & \sigma_i\nu_{i1} & 0 & \cdots & 0 \\ 0 & -w_{i2}^E & \cdots & \sigma_i\nu_{i2} & 0 & \cdots & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ \rho_{i1} & \rho_{i2} & \cdots & -w_{ii}^E & \rho_{i,i+1} & \cdots & \rho_{in} \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \cdots & \sigma_i\nu_{in} & 0 & \cdots & -w_{in}^E \end{pmatrix},$$

$$M_i^I = \begin{pmatrix} -w_{i1}^I & 0 & \cdots & c_i\sigma_i\nu_{i1} & 0 & \cdots & 0 \\ 0 & -w_{i2}^I & \cdots & c_i\sigma_i\nu_{i2} & 0 & \cdots & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ c_1\rho_{i1} & c_2\rho_{i2} & \cdots & -w_{ii}^I & c_{i+1}\rho_{i,i+1} & \cdots & c_n\rho_{in} \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \cdots & c_i\sigma_i\nu_{in} & 0 & \cdots & -w_{in}^I \end{pmatrix},$$

$$M_i^Q = \begin{pmatrix} -w_{i1}^Q & 0 & \cdots & 0 \\ 0 & -w_{i2}^Q & \cdots & 0 \\ \cdots & \cdots & \cdots\cdots & \\ 0 & 0 & \cdots & -w_{in}^Q \end{pmatrix}.$$

The matrix M_i^E characterizes the loss of exposed persons of community i in the n regions and the travel by exposed persons of community i among the n regions. M_i^Q, M_i^I, corresponding to quarantined class and infectious class, have similar meanings.

Set $N_i^{p*} = \sum_{j=1}^n S_{ji}^*$. Then we define

$$M_{ij}^{IE} = \begin{pmatrix} \beta_{i1j}\frac{S_{i1}^*}{N_j^{p*}} & 0 & \vdots & 0 \\ 0 & \beta_{i2j}\frac{S_{i2}^*}{N_j^{p*}} & \vdots & 0 \\ \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \vdots & \beta_{inj}\frac{S_{in}^*}{N_j^{p*}} \end{pmatrix}, \quad M_i^{EQ} = \begin{pmatrix} e_{i1} & 0 & \cdots & 0 \\ 0 & e_{i2} & \cdots & 0 \\ \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \cdots & e_{in} \end{pmatrix},$$

$$M_i^{EI} = \begin{pmatrix} g_{i1} & 0 & \cdots & 0 \\ 0 & g_{i2} & \cdots & 0 \\ \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \cdots & g_{in} \end{pmatrix}, \quad M_i^{QI} = \begin{pmatrix} \theta_{i1} & 0 & \cdots & 0 \\ 0 & \theta_{i2} & \cdots & 0 \\ \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \cdots & \theta_{in} \end{pmatrix}.$$

Basically, M_{ij}^{IE} describes the distributions in which susceptible persons of community i are infected by an infectious member from community j at each region; M_i^{EQ} describes the transition rates of community i from exposed class to quarantined class at every region; M_i^{EI} describes the transition rates of community i from exposed class to infected class at every region; M_i^{QI} describes the transition rates of community i from quarantined class to infected class at every region.

Based on the above matrices, we define

$$A_i = \begin{pmatrix} M_i^E & 0 & 0 \\ M_i^{EQ} & M_i^Q & 0 \\ M_i^{EI} & M_i^{QI} & M_i^I \end{pmatrix}, \quad B_{ij} = \begin{pmatrix} 0 & 0 & M_{ij}^{IE} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

Clearly, A_i represents the interactions inside community i, and B_{ij} represents the interactions between community i and community j.

Now we consider the basic reproduction number for the system (3.1)-(3.2). The *basic reproduction number*, denoted by $\mathcal{R}_0$, is "the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual" (see Diekmann et al., 1990). For the case of a single infected compartment, $\mathcal{R}_0$ is simply the product of the infection rate and the mean duration of the infection. For the system (3.1)-(3.2) with multiple infected compartments, the basic reproduction number can be defined as the number of new infections produced by a typical infective individual in the population at the disease-free equilibrium (see van den Driessche and Watmough, 2002). Following the idea in van den Driessche and Watmough (2002), we classify the five classes into two compartments: infected and uninfected. In our case, the infected compartment consists of exposed class, quarantined class, and infected class; others belong to the uninfected compartment. Then we define

$$\mathcal{F}_i = \left[\sum_{k=1}^{n} \beta_{i1k} \frac{S_{i1} I_{k1}}{N_k^p}, \sum_{k=1}^{n} \beta_{i2k} \frac{S_{i2} I_{k2}}{N_k^p}, \ldots, \sum_{k=1}^{n} \beta_{ink} \frac{S_{in} I_{kn}}{N_k^p}, 0, \ldots, 0 \right]^T.$$

Here, $\mathcal{F}_i$ is a $3n \times 1$ vector and represents the input rate of new infections in community i. Furthermore, we define $\mathcal{V}_i = -\left[v_i^E, v_i^Q, v_i^I\right]$, where

$$\begin{aligned} v_i^E &= \left[\sigma_i \nu_{i1} E_{ii} - w_{i1}^E E_{i1}, \sigma_i \nu_{i2} E_{ii} - w_{i2}^E E_{i2}, \ldots, \sigma_i \nu_{in} E_{ii} - w_{i1}^E E_{in}\right]^T, \\ v_i^Q &= \left[e_{i1} E_{i1} - w_{i1}^Q Q_{i1}, e_{i2} E_{i2} - w_{i2}^Q Q_{i2}, \ldots, e_{in} E_{in} - w_{in}^Q Q_{in}\right]^T, \\ v_i^I &= \left[h_{i1}, h_{i2}, \ldots, h_{in}\right]^T, \end{aligned}$$

in which

$$\begin{aligned} h_{ii} &= \sum_{k=1, k\neq i}^{n} c_k \rho_{ik} I_{ik} + g_{ii} E_{ii} + \theta_{ii} Q_{ii} - w_{ii}^I I_{ii}, \\ h_{ij} &= c_i \sigma_i \nu_{ij} I_{ii} + g_{ij} E_{ij} + \theta_{ij} Q_{ij} - w_{ij}^I I_{ij} \quad \text{for } i \neq j. \end{aligned}$$

Here, $\mathcal{V}_i(x)$ is the net decreasing rate of infected compartments in community i due to the transitions, movements, and death inside the community.

Set

$$E^i = \left[E_{i1}, E_{i2}, \ldots, E_{in}\right]^T, \; Q^i = \left[Q_{i1}, Q_{i2}, \ldots, Q_{in}\right]^T, \; I^i = \left[I_{i1}, I_{i2}, \ldots, I_{in}\right]^T,$$

and define

$$x = \left[E^1, Q^1, I^1, E^2, Q^2, I^2, \ldots, E^n, Q^n, I^n\right].$$

If $\mathcal{F} = (\mathcal{F}_1, \ldots, \mathcal{F}_n)^T$ and $\mathcal{V} = (\mathcal{V}_1, \ldots, \mathcal{V}_n)^T$, we define $F = D_x \mathcal{F}(P_0)$ and $V = D_x \mathcal{V}(P_0)$. Then it is easy to see that

$$V = -\begin{pmatrix} A_1 & 0 & \cdots & 0 \\ 0 & A_2 & \cdots & 0 \\ \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \cdots & A_n \end{pmatrix}$$

and

$$F = \begin{pmatrix} B_{11} & B_{12} & \cdots & B_{1n} \\ B_{21} & B_{22} & \cdots & B_{2n} \\ \cdots & \cdots & \cdots & \cdots \\ B_{n1} & B_{n2} & \cdots & B_{nn} \end{pmatrix}.$$

According to Diekmann et al. (1990) and van den Driessche and Watmough (2002), the matrix FV^{-1} is called the *next generation matrix*, and its spectral radius is defined as the reproduction number for system (3.1)-(3.2), that is,

$$\mathcal{R}_0 := \rho(FV^{-1}). \tag{4.4}$$

If we define

$$C = \begin{pmatrix} B_{11} + A_1 & B_{12} & \cdots & B_{1n} \\ B_{21} & B_{22} + A_2 & \cdots & B_{2n} \\ \cdots & \cdots & \cdots & \cdots \\ B_{n1} & B_{n2} & \cdots & B_{nn} + A_n \end{pmatrix},$$

then we have $C = F - V$. By Theorem 2 in van den Driessche and Watmough (2002) with $J_1 = C$, we have the following.

Lemma 4.1. *There hold two equivalences:*

$$\mathcal{R}_0 > 1 \Leftrightarrow s(C) > 0, \qquad \mathcal{R}_0 < 1 \Leftrightarrow s(C) < 0. \tag{4.5}$$

By Lemma 4.1, it easily follows that $\mathcal{R}_0 < 1$ implies P_0 is asymptotically stable and that $\mathcal{R}_0 > 1$ implies P_0 is unstable.

5. **An Example.** Let us consider 2 regions, Hong Kong ($i = 1$) and Toronto ($i = 2$). Then, we have

$$M_1^E = \begin{pmatrix} -w_{11}^E & \rho_{12} \\ \sigma_1 & -w_{12}^E \end{pmatrix}, \quad M_2^E = \begin{pmatrix} -w_{21}^E & \sigma_2 \\ \rho_{21} & -w_{22}^E \end{pmatrix},$$

$$M_1^Q = \begin{pmatrix} -w_{11}^Q & 0 \\ 0 & -w_{12}^Q \end{pmatrix}, \quad M_2^Q = \begin{pmatrix} -w_{21}^Q & 0 \\ 0 & -w_{22}^Q \end{pmatrix},$$

$$M_1^I = \begin{pmatrix} -w_{11}^I & c_2\rho_{12} \\ c_1\sigma_1 & -w_{12}^I \end{pmatrix}, \quad M_2^I = \begin{pmatrix} -w_{21}^I & c_2\sigma_2 \\ c_1\rho_{21} & -w_{22}^I \end{pmatrix},$$

$$M_{11}^{IE} = \begin{pmatrix} \beta_{111}\frac{S_{11}^*}{N_1^{p*}} & 0 \\ 0 & \beta_{121}\frac{S_{12}^*}{N_1^{p*}} \end{pmatrix}, \quad M_{22}^{IE} = \begin{pmatrix} \beta_{212}\frac{S_{21}^*}{N_2^{p*}} & 0 \\ 0 & \beta_{222}\frac{S_{22}^*}{N_2^{p*}} \end{pmatrix},$$

$$M_{12}^{IE} = \begin{pmatrix} \beta_{112}\frac{S_{11}^*}{N_2^{p*}} & 0 \\ 0 & \beta_{122}\frac{S_{12}^*}{N_2^{p*}} \end{pmatrix}, \quad M_{21}^{IE} = \begin{pmatrix} \beta_{211}\frac{S_{21}^*}{N_1^{p*}} & 0 \\ 0 & \beta_{221}\frac{S_{22}^*}{N_1^{p*}} \end{pmatrix},$$

$$M_1^{EQ} = \begin{pmatrix} e_{11} & 0 \\ 0 & e_{12} \end{pmatrix}, \quad M_2^{EQ} = \begin{pmatrix} e_{21} & 0 \\ 0 & e_{22} \end{pmatrix},$$

$$M_1^{EI} = \begin{pmatrix} g_{11} & 0 \\ 0 & g_{12} \end{pmatrix}, \quad M_2^{EI} = \begin{pmatrix} g_{21} & 0 \\ 0 & g_{22} \end{pmatrix},$$

$$M_1^{QI} = \begin{pmatrix} \theta_{11} & 0 \\ 0 & \theta_{12} \end{pmatrix}, \quad M_2^{QI} = \begin{pmatrix} \theta_{21} & 0 \\ 0 & \theta_{22} \end{pmatrix}.$$

As in Gumel et al. (2004), we fix $d_{ij} = 0.000034, \alpha_{ij} = \eta_{ij} = 0, g_{ij} = 0.1, \theta_{ij} = 0.125, \epsilon_{ij} = 0.0074, \xi_{ij} = 0.03615$ for all i, j, $b_{11} = 221, b_{22} = 136$. We assume that b_{12} and b_{21} are so small that they can be treated as zeros. Thus, $b_{12} = b_{21} = 0$. The parameters e_{ij} are initially assumed to be zero until March 30, 2003 and are switched to 0.1. Further, for simplicity, we neglect the movement of individuals from the Greater Toronto Area (GTA) to Hong Kong. This means $\sigma_2 = 0$. If we further ignore the movement of residents of Hong Kong between Hong Kong and GTA, we have $\sigma_1 = \rho_{12} = 0$. This means that we focus on the diffusion of SARS from Hong Kong to GTA and the development of SARS in residents of GTA. We also assume $\rho_{21} = 0.00013$. This means that about 20 residents returned to GTA from Hong Kong per day, because about 150,000 Canadians lived in Hong Kong (DFAIT, 1998; St. John et al., 2005). Suppose $c_1 = c_2 = 0$. This means that infectious individuals cannot pass through the borders. As a consequence,

$$w_{11}^E = 0.200034, \quad w_{12}^E = 0.200034, \quad w_{21}^E = 0.200164, \quad w_{22}^E = 0.200034,$$
$$w_{11}^Q = 0.125034, \quad w_{12}^Q = 0.125034, \quad w_{21}^Q = 0.125034, \quad w_{22}^Q = 0.125034,$$
$$w_{11}^I = 0.043584, \quad w_{12}^I = 0.043584, \quad w_{21}^I = 0.043584, \quad w_{22}^I = 0.043584.$$

Therefore,

$$A_1 = \begin{pmatrix} -0.200034 & 0 & 0 & 0 & 0 & 0 \\ 0 & -0.200034 & 0 & 0 & 0 & 0 \\ 0.1 & 0 & -0.125034 & 0 & 0 & 0 \\ 0 & 0.1 & 0 & -0.125034 & 0 & 0 \\ 0.1 & 0 & 0.125 & 0 & -0.043584 & 0 \\ 0 & 0.1 & 0 & 0.125 & 0 & -0.043584 \end{pmatrix},$$

$$A_2 = \begin{pmatrix} -0.200164 & 0 & 0 & 0 & 0 & 0 \\ 0.00013 & -0.200034 & 0 & 0 & 0 & 0 \\ 0.1 & 0 & -0.125034 & 0 & 0 & 0 \\ 0 & 0.1 & 0 & -0.125034 & 0 & 0 \\ 0.1 & 0 & 0.125 & 0 & -0.043584 & 0 \\ 0 & 0.1 & 0 & 0.125 & 0 & -0.043584 \end{pmatrix}.$$

As in Gumel et al. (2004), we fix $\beta_{111} = \beta_{112} = \beta_{211} = \beta_{212} = 0.15$, $\beta_{121} = \beta_{122} = \beta_{221} = \beta_{222} = 0.2$. Then we have

$$B_{11} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0.15 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \quad B_{12} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0.24375 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$B_{21} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0.1231 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \quad B_{22} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0.2 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

Hence, by (4.4), we obtain $\mathcal{R}_0 = 4.587436164$. Further, if we vary ρ_{21}, the returning rate of residents of GTA from Hong Kong but keep other parameters fixed, we find that the basic reproduction number $\mathcal{R}_0 = 4.587436164$ is invariant. Now, we

increase ρ_{12} from 0; i.e., we allow residents of Hong Kong at GTA to return but keep other parameters as above. Then numerical calculations indicate that the basic reproduction number $\mathcal{R}_0 = 4.587436164$ is still invariant. Hence, the return of residents does not affect the basic reproduction number if infectious individuals are barred at borders and if neither Hong Kong nor GTA residents leave their native cities. However, since the basic reproduction number is greater than 1, this returning rate influences the level of SARS transmission. For example, suppose that we adopt the same parameter values as above, except for taking $e_{ij} = 0.1$ for all times. In Hong Kong, we fix the number of initial infective individuals with residence of Hong Kong as 1; the numbers of initial exposed individuals, quarantined individuals and recovered individuals with residence of Hong Kong as 0; the number of susceptible individuals with residence of Hong Kong as 6.5×10^6; the number of initial exposed individuals with residence of GTA at Hong Kong as 1; the number of susceptible individuals with residence of GTA as 1.9354×10^4; and the numbers of initial quarantined individuals and recovered individuals with residence of GTA as 0. In GTA, we fix all the initial values as 0 except for susceptible individuals with residence of GTA as 4×10^6 and with residence of Hong Kong as 3.1451×10^4 (Gumel et al., 2004). Then, when $\rho_{21} = 0.00013, 0.0013, 0.013$, infected individuals at GTA are 2.6, 26, 247, respectively, with $t = 100$. Next, we consider the effect of screening at borders. If we take $c_1 = c_2 = 0$, $c_1 = c_2 = 0.5$, and $c_1 = c_2 = 1$, respectively, and keep other parameters and initial values unchanged, we have Figure 1 which clearly shows the importance of the screening at borders.

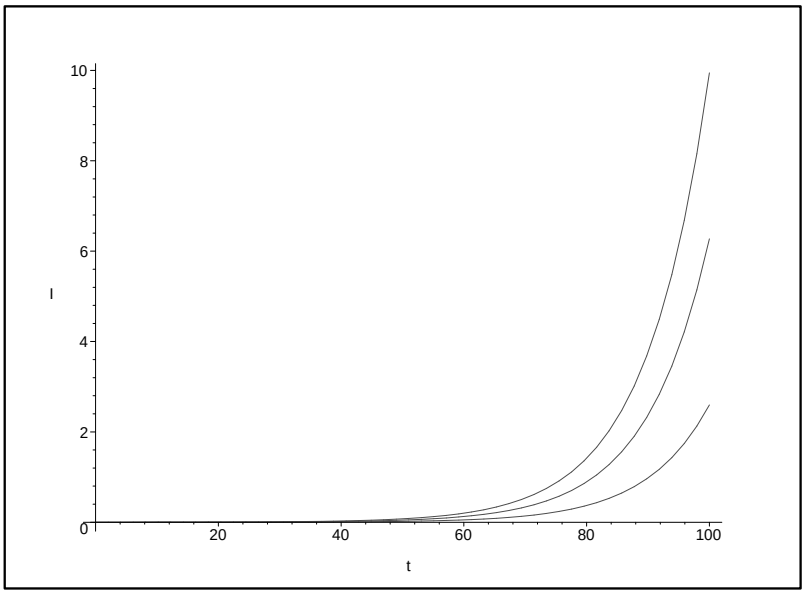

FIGURE 1. Vertical axis represents the number of infected persons with residence of GTA in GTA. Lower curve, middle curve, and top curve are the graphs of the numbers versus time t when $c_1 = c_2 = 0$, $c_1 = c_2 = 0.5$, and $c_1 = c_2 = 1$, respectively.

6. **Discussion.** In February 2003, a Canadian and a US resident were both infected when they and the index SARS patient stayed at the same hotel in Hong

Kong at almost the same time. The US resident was already symptomatic and hospitalized in Hong Kong. She returned to the United States as a suspect case and was treated with caution; so, she did not cause a SARS outbreak in the United States. The Canadian resident returned to Canada as asymptomatic and caused a SARS outbreak in Toronto (WHO, May 20, 2003). Therefore, travel by the exposed and infective individuals is one of the main channels to spread the disease, and travel by the undiagnosed asymptomatic individuals is potentially more harmful than that of the infectives.

To understand the global spread of SARS, we propose a multi-regional model to study the effect of international travel on the geographical transmission of the disease. We first calculate the basic reproduction number (R_0) using the techniques in Diekmann et al. (1990) and van den Driessche and Watmough (2002). This quantity is defined as the expected number of secondary cases produced in a completely susceptible population by a typical infective individual and determines the potential for an infectious agent to start an outbreak: the disease spreads if $R_0 > 1$ and dies out if $R_0 < 1$. The epidemic dynamics and the basic reproduction number depend on many parameters, including the travel parameters, that is, σ_i, ν_{ij}, and ρ_{ij}. The results can be used to determine when travel will induce inter-regional spread of the disease ($R_0 > 1$) and how to bring the disease under control ($R_0 < 1$).

As an example, we consider a simplified model for two regions, say Hong Kong and Toronto, and study how the disease spread from one region to another. We found that the return of residents does not affect the basic reproduction number if infectious individuals are barred at borders and if both Hong Kong and GTA residents do not leave their native cities. The outcome and conclusions on global control strategies for SARS may be useful in controlling outbreaks of other similar infectious diseases.

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