The Basic Reproduction Number in a Multi-city Compartmental Epidemic Model

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Abstract. A directed graph with cities as vertices and arcs determined by outgoing (or return) travel represents the mobility component in a population of individuals who travel between n cities. A model with 4 epidemiological compartments in each city that describes the propagation of a disease in this population is formulated as a system of $4n^2$ ordinary differential equations. Terms in the system account for disease transmission, latency, recovery, temporary immunity, birth, death, and travel between cities. The basic reproduction number $\mathcal{R}_0$ is determined as the spectral radius of a nonnegative matrix product, and easily computable bounds on $\mathcal{R}_0$ are obtained.

1 Introduction

Modeling the spatial spread of infectious diseases is a complex task. One possible approach is to consider the travel of individuals between discrete geographical regions (cities), considering that the transmission does not take place during travel. The situation is then that of a directed graph, with the vertices representing the cities and the arcs representing the links between these cities. Disease transmission is assumed to occur between individuals present in a given city.

Sattenspiel and Dietz [7] introduced such a model with travel between cities, and a similar type of model was considered in [8]. More recently Fulford et al [4] and Wang and Zhao [10] have formulated and discussed other models for the spread of a disease among discrete geographical regions.

We consider the time evolution of a disease with 4 epidemiological compartments in each city for residents of n cities who may travel between them. The model formulated here is an extension of that of [1], which is adapted from [7]. We give a rigorous derivation of the *basic reproduction number* $\mathcal{R}_0$, which represents the average number of new infections produced in a totally susceptible population by the introduction of an infective individual (see [3, 5, 9]).

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Easily computable bounds on $\mathcal{R}_0$ are derived. Local analysis and numerical simulations indicate that $\mathcal{R}_0$, is a sharp threshold with the disease dying out or becoming endemic according as $\mathcal{R}_0 < 1$ or $\mathcal{R}_0 > 1$.

2 The SEIRS epidemic model

The total number of cities considered is n. The number of residents of (*i.e.*, individuals who normally live in) city i who are present in city j at time t is denoted by N_{ij}, and $N_i^r = \sum_{j=1}^n N_{ij}$ denotes the resident population of city i at time t. Also, $N_i^p = \sum_{j=1}^n N_{ji}$ denotes the population of city i at time t, *i.e.*, the number of individuals who are physically present in city i.

As in [1, 7], residents of city i leave this city at a per capita rate $g_i \geq 0$ per unit time with a fraction $m_{ji} \geq 0$ of these outgoing individuals going to city j. If $g_i > 0$, then $\sum_{j=1}^n m_{ji} = 1$, with $m_{ii} = 0$, and $g_i m_{ji}$ is the travel rate from city i to city j. Residents of city i who are in city j return to i with a per capita rate of $r_{ij} \geq 0$, with $r_{ii} = 0$. With these assumptions, an individual resident in a given city who is present in another city, must first return to their city of residence before travelling to a third city. The outgoing matrix $[g_i m_{ji}]$ and the return matrix $[r_{ij}]$, which represent the outgoing travel from i to j and the return to i from j, respectively, are assumed to have the same zero/nonzero pattern. Thus the directed graph with vertices representing cities and arcs representing travel between these cities can be determined by either matrix. The terms m_{ji} and r_{ij} implicitly take into account the distance between cities i and j.

In each of the n cities, an epidemic model is superimposed; see Hethcote [5] for a recent review of mathematical models of infectious diseases. In [7], an SIR epidemic model with 3 compartments (susceptible, infective, recovered) is formulated in each city (called region), with two types of mobility (infants and adults) in each region. In [8], each region has an SIR model and, as in [7], there is no birth or natural death of individuals. Here we construct an SEIRS model with 4 compartments (susceptible, exposed, infective, recovered) and include birth in the city of residence and natural death in any city. Our general SEIRS model is applicable for diseases with a latent period that confers immunity upon recovery (*e.g.*, pertussis), and can be reduced to simpler models by formally setting parameter(s) (or inverse(s)) to zero. For example, tuberculosis has a long latent period and treated infectives move back into the susceptible class; thus an SEIS model is appropriate. Some childhood diseases (*e.g.*, scarlet fever) have short latent periods and confer permanent immunity upon recovery, thus an SIR model is appropriate; others (*e.g.*, measles) have a longer latent period, thus an SEIR model is preferred. For a disease with no latent period and that confers no immunity (*e.g.*, gonnorhea) an SIS model, as formulated and analyzed in [1], is adequate.

Let S_{ij}, E_{ij}, I_{ij} and R_{ij} denote respectively the number of susceptible, exposed, infective and recovered individuals resident in city i who are present

in city j at time t; thus $N_{ij} = S_{ij} + E_{ij} + I_{ij} + R_{ij}$ for all $i, j = 1, \ldots, n$. Disease transmission is modelled using standard incidence, namely

$$\sum_{j=1}^{n} \sum_{k=1}^{n} \kappa_j \beta_{ikj} \frac{S_{ij} I_{kj}}{N_j^p} \tag{1}$$

where the disease transmission coefficient $\beta_{ikj} > 0$ is the proportion of adequate contacts in city j between a susceptible from city i and an infective from city k that actually results in transmission of the disease and $\kappa_j > 0$ is the average number of such contacts in city j per unit time. Let $1/d$, $1/\varepsilon$, $1/\gamma$ and $1/\nu$ denote the average lifetime, exposed period, infective period and period of temporary immunity, respectively. Note that d, ε, γ and ν are assumed to be positive and the same for all cities. Birth and death are assumed to occur with the same rate constant, thus the total population remains a fixed constant.

For residents of city i present in city i (with $i = 1, \ldots, n$), the following 4 differential equations describe the dynamics of the susceptible, exposed, infective and recovered individuals,

$$\frac{dS_{ii}}{dt} = \sum_{k=1}^{n} r_{ik} S_{ik} - g_i S_{ii} - \sum_{k=1}^{n} \kappa_i \beta_{iki} \frac{S_{ii} I_{ki}}{N_i^p} + d(N_i^r - S_{ii}) + \nu R_{ii} \tag{2a}$$

$$\frac{dE_{ii}}{dt} = \sum_{k=1}^{n} r_{ik} E_{ik} - g_i E_{ii} + \sum_{k=1}^{n} \kappa_i \beta_{iki} \frac{S_{ii} I_{ki}}{N_i^p} - (\varepsilon + d) E_{ii} \tag{2b}$$

$$\frac{dI_{ii}}{dt} = \sum_{k=1}^{n} r_{ik} I_{ik} - g_i I_{ii} + \varepsilon E_{ii} - (\gamma + d) I_{ii} \tag{2c}$$

$$\frac{dR_{ii}}{dt} = \sum_{k=1}^{n} r_{ik} R_{ik} - g_i R_{ii} + \gamma I_{ii} - (\nu + d) R_{ii} \tag{2d}$$

and, for $j \neq i$, the following equations describe the dynamics of residents of city i present in city j,

$$\frac{dS_{ij}}{dt} = g_i m_{ji} S_{ii} - r_{ij} S_{ij} - \sum_{k=1}^{n} \kappa_j \beta_{ikj} \frac{S_{ij} I_{kj}}{N_j^p} - d S_{ij} + \nu R_{ij} \tag{2e}$$

$$\frac{dE_{ij}}{dt} = g_i m_{ji} E_{ii} - r_{ij} E_{ij} + \sum_{k=1}^{n} \kappa_j \beta_{ikj} \frac{S_{ij} I_{kj}}{N_j^p} - (\varepsilon + d) E_{ij} \tag{2f}$$

$$\frac{dI_{ij}}{dt} = g_i m_{ji} I_{ii} - r_{ij} I_{ij} + \varepsilon E_{ij} - (\gamma + d) I_{ij} \tag{2g}$$

$$\frac{dR_{ij}}{dt} = g_i m_{ji} R_{ii} - r_{ij} R_{ij} + \gamma I_{ij} - (\nu + d) R_{ij} \tag{2h}$$

As there are n cities, there are $4n^2$ equations. These equations, together with nonnegative initial conditions and fixed N_i^r, constitute the SEIRS epidemic

model. The following result is easily shown and assures that the system is well posed.

Proposition 1. *The nonnegative orthant $\mathbb{R}_+^{4n^2}$ is positively invariant under the flow of (2), and for all $t > 0$, $S_{ii} > 0$ and $S_{ij} > 0$ provided that $g_i m_{ji} > 0$. Furthermore, solutions of (2) are bounded.*

2.1 The underlying travel model

Summing (2a) to (2d) gives the evolution of the number of residents of city i present in city i,

$$\frac{dN_{ii}}{dt} = d(N_i^r - N_{ii}) + \sum_{k=1}^{n} r_{ik} N_{ik} - g_i N_{ii} \tag{3a}$$

Similarly, summing (2e) to (2h) gives the evolution of the number of residents of city i who are present in city $j \neq i$,

$$\frac{dN_{ij}}{dt} = g_i m_{ji} N_{ii} - r_{ij} N_{ij} - d N_{ij} \tag{3b}$$

From (3), it can be shown that the resident population N_i^r of city i is constant, whereas the current population N_i^p need not be. The total population $\sum_{i=1}^n N_i^r = \sum_{i=1}^n N_i^p$ in the system is constant.

Equations (3) subject to the initial values $N_{ij} \geq 0$ at $t = 0$ with fixed $N_i^r > 0$ constitute the travel model, which is identical to that in the SIS model [1], where the following is proved.

Theorem 1. *The travel model (3) has the (globally) asymptotically stable equilibrium*

$$\hat{N}_{ii} = \left(\frac{1}{1 + g_i C_i} \right) N_i^r \tag{4}$$

and, for $j \neq i$

$$\hat{N}_{ij} = g_i \frac{m_{ji}}{d + r_{ij}} \left(\frac{1}{1 + g_i C_i} \right) N_i^r \tag{5}$$

where $C_i = \sum_{k=1}^n \frac{m_{ki}}{d + r_{ik}}$ for $i = 1, \ldots, n$.

2.2 The basic reproduction number

The system is at an equilibrium if the time derivatives in (2) are zero. City i is at the disease free equilibrium (DFE) if $I_{ji} = 0$ for all $j = 1, \ldots, n$, giving $E_{ji} = R_{ji} = 0$ and $S_{ji} = \hat{N}_{ji}$ from (4) and (5). The n-city model given by (2) is at the DFE if every city is at the DFE. The DFE of (2) always exists, and in the case in which the disease is absent in all cities, (2) reduces to the underlying travel model (3).

To discuss local stability of the DFE in the n-city model given by (2), we use the method of [3, 9], and $\mathcal{R}_0$, the basic reproduction number for the whole system, is the spectral radius of the next generation matrix.

Ordering the infected variables (exposed and infectives) as

$$E_{11}, \ldots, E_{1n}, E_{21}, \ldots E_{2n}, \ldots E_{nn}, I_{11}, \ldots, I_{1n}, I_{21}, \ldots I_{2n}, \ldots, I_{nn}$$

gives the lower triangular block matrix

$$V = \left[\begin{array}{c:c} A & 0 \\ \hdashline C & B \end{array}\right] = \left[\begin{array}{c:c} \bigoplus_{k=1}^{n} A_k & 0 \\ \hdashline -\mathrm{diag}(\varepsilon) & \bigoplus_{k=1}^{n} B_k \end{array}\right]$$

where each block A, B and C is $n^2 \times n^2$. For $k = 1, \ldots n$, A_k is an $n \times n$ matrix with

$$A_k = \begin{bmatrix} r_{k1}+\varepsilon+d & 0 & \cdots & 0 & -g_k m_{1k} & 0 \cdots & 0 \\ 0 & r_{k2}+\varepsilon+d & & & -g_k m_{2k} & 0 \cdots & 0 \\ & & & & & & \\ -r_{k1} & -r_{k2} & & g_k+\varepsilon+d & & & -r_{kn} \\ & & & & & & \\ 0 & \cdots & & & -g_k m_{nk} & 0 & r_{kn}+\varepsilon+d \end{bmatrix}$$

For a fixed k, and $j \neq k$, the (k,j) entry of A_k is $-r_{kj}$, the (j,k) entry is $-g_k m_{jk}$, the j^{th} diagonal entry is $r_{kj}+\varepsilon+d$, the (k,k) entry is $g_k+\varepsilon+d$, and other entries are zero. Matrices B_k have the same entries as A_k but with ε replaced by γ.

Since A_k and B_k have the Z-sign pattern and have all positive column sums, A_k and B_k are nonsingular M-matrices [2, p. 136]. The inverse of V is the nonnegative matrix

$$V^{-1} = \left[\begin{array}{c:c} \bigoplus_{k=1}^{n} (A_k)^{-1} & 0 \\ \hdashline \left(\bigoplus_{k=1}^{n} (B_k)^{-1}\right) \mathrm{diag}(\varepsilon) \left(\bigoplus_{k=1}^{n} (A_k)^{-1}\right) & \bigoplus_{k=1}^{n} (B_k)^{-1} \end{array}\right]$$

Matrix F is a block matrix

$$F = \left[\begin{array}{c:c} 0 & G \\ \hdashline 0 & 0 \end{array}\right]$$

where G is an $n^2 \times n^2$ matrix having n^2 blocks, with each block G_{ij} an $n \times n$ diagonal matrix of the form $G_{ij} = \mathrm{diag}(g_{ijq})$, where $g_{ijq} = \kappa_q \beta_{ijq} \hat{N}_{iq} / \hat{N}_q^p$, for $q = 1, \ldots, n$.

Since V^{-1} is lower triangular by blocks, FV^{-1} can be given by blocks. By [9, Theorem 2], the basic reproduction number for system (2) is, factoring ε out of the expression,

$$\mathcal{R}_0 = \varepsilon \cdot \rho \left\{ G \left(\bigoplus_{k=1}^{n} (A_k B_k)^{-1} \right) \right\} \tag{6}$$

where $\rho\{\cdot\}$ is the spectral radius, and the following result holds.

Theorem 2. *Let $\mathcal{R}_0$ be defined as in (6). If $\mathcal{R}_0 < 1$, then the DFE of (2) is locally asymptotically stable. If $\mathcal{R}_0 > 1$, then the DFE of (2) is unstable.*

From (6), to compute $\mathcal{R}_0$, it is sufficient to invert an $n \times n$ matrix. The following bounds hold for $\mathcal{R}_0$.

Theorem 3. *For system (2),*

$$\min_{i,j,k=1,\ldots,n} \frac{\kappa_k \beta_{ijk} \varepsilon}{(\gamma + d)(\varepsilon + d)} \leq \mathcal{R}_0 \leq \max_{i,j,k=1,\ldots,n} \frac{\kappa_k \beta_{ijk} \varepsilon}{(\gamma + d)(\varepsilon + d)}$$

Proof. The i, j block of $G\left(\oplus (A_k B_k)^{-1}\right)$ is $G_{ij}(A_j B_j)^{-1}$ for all i, j. As G_{ij} is diagonal, left multiplication with $(A_j B_j)^{-1}$ amounts to multiplying row q of $(A_j B_j)^{-1}$ by $\kappa_q \beta_{ijq} \hat{N}_{iq} / \hat{N}_q^p$ for $q = 1, \ldots, n$. Let $v_{kl}^{-1}(j)$ denote the (k, l) entry of $(A_j B_j)^{-1}$, for $k, l = 1, \ldots, n$. Consider the first column of $G_{i1}(A_1 B_1)^{-1}$, and denote the sum of entries in the first column of $G_{i1}(A_1 B_1)^{-1}$ by $[\mathbb{1}^T G_{i1}(A_1 B_1)^{-1}]_1$, with $\mathbb{1}^T = (1, \ldots, 1)$. Then

$$\begin{aligned}
&[\mathbb{1}^T G_{i1}(A_1 B_1)^{-1}]_1 \\
=&\kappa_1 \beta_{111} \frac{\hat{N}_{11}}{\hat{N}_1^p} v_{11}^{-1}(1) + \kappa_2 \beta_{112} \frac{\hat{N}_{12}}{\hat{N}_2^p} v_{21}^{-1}(1) + \cdots + \kappa_n \beta_{11n} \frac{\hat{N}_{1n}}{\hat{N}_n^p} v_{n1}^{-1}(1) \\
&+ \kappa_1 \beta_{211} \frac{\hat{N}_{21}}{\hat{N}_1^p} v_{11}^{-1}(1) + \kappa_2 \beta_{212} \frac{\hat{N}_{22}}{\hat{N}_2^p} v_{21}^{-1}(1) + \cdots + \kappa_n \beta_{21n} \frac{\hat{N}_{2n}}{\hat{N}_n^p} v_{n1}^{-1}(1) + \cdots \\
&+ \kappa_1 \beta_{n11} \frac{\hat{N}_{n1}}{\hat{N}_1^p} v_{11}^{-1}(1) + \kappa_2 \beta_{n12} \frac{\hat{N}_{n2}}{\hat{N}_2^p} v_{21}^{-1}(1) + \cdots + \kappa_n \beta_{n1n} \frac{\hat{N}_{nn}}{\hat{N}_n^p} v_{n1}^{-1}(1) \\
=&\frac{\kappa_1}{\hat{N}_1^p} \left(\beta_{111} \hat{N}_{11} + \beta_{211} \hat{N}_{21} + \cdots + \beta_{n11} \hat{N}_{n1} \right) v_{11}^{-1}(1) + \cdots \\
&+ \frac{\kappa_n}{\hat{N}_n^p} \left(\beta_{11n} \hat{N}_{1n} + \beta_{21n} \hat{N}_{2n} + \cdots + \beta_{n1n} \hat{N}_{nn} \right) v_{n1}^{-1}(1)
\end{aligned} \tag{7}$$

Suppose that

$$\min_{i,j,k=1,\ldots,n} \frac{\kappa_k \beta_{ijk} \varepsilon}{(\gamma + d)(\varepsilon + d)} = \frac{\kappa_{k_m} \beta_{i_m j_m k_m} \varepsilon}{(\gamma + d)(\varepsilon + d)}$$

and

$$\max_{i,j,k=1,\ldots,n} \frac{\kappa_k \beta_{ijk} \varepsilon}{(\gamma+d)(\varepsilon+d)} = \frac{\kappa_{k_M} \beta_{i_M j_M k_M} \varepsilon}{(\gamma+d)(\varepsilon+d)}$$

Then

$$\kappa_{k_m} \beta_{i_m j_m k_m} \varepsilon \leq \ldots \leq \kappa_k \beta_{ijk} \varepsilon \leq \ldots \leq \kappa_{k_M} \beta_{i_M j_M k_M} \varepsilon$$

Using these inequalities in (7) and the definition of N_i^p,

$$\begin{aligned} \kappa_{k_m} \beta_{i_m j_m k_m} \varepsilon \left(v_{11}^{-1}(1) + \cdots + v_{n1}^{-1}(1) \right) &\leq [\mathbb{1}^T G_{i1} (A_1 B_1)^{-1}]_1 \\ &\leq \kappa_{k_M} \beta_{i_M j_M k_M} \varepsilon \left(v_{11}^{-1}(1) + \cdots + v_{n1}^{-1}(1) \right) \end{aligned}$$

Note that $\mathbb{1}^T A_j = (\varepsilon + d)\mathbb{1}^T$ and $\mathbb{1}^T B_j = (\gamma + d)\mathbb{1}^T$ for all j. This implies that $\mathbb{1}^T (A_j B_j)^{-1} = 1/[(\gamma + d)(\varepsilon + d)]\mathbb{1}^T$, *i.e.*, each column sum of $(A_j B_j)^{-1}$ is equal to $1/[(\gamma + d)(\varepsilon + d)]$. Therefore,

$$\frac{\kappa_{k_m} \beta_{i_m j_m k_m} \varepsilon}{(\gamma+d)(\varepsilon+d)} \leq [\mathbb{1}^T G_{i1} (A_1 B_1)^{-1}]_1 \leq \frac{\kappa_{k_M} \beta_{i_M j_M k_M} \varepsilon}{(\gamma+d)(\varepsilon+d)}$$

The same argument shows that this inequality remains true for every column of $G\left(\oplus (A_k B_k)^{-1}\right)$. From (6) and using a standard result on the localization of the dominant eigenvalue of a nonnegative matrix (see, *e.g.*, [6, Theorem 1.1]), the result then follows. □

If city i is isolated from the others, then the basic reproduction number in city i is $\mathcal{R}_0^i = \kappa_i \beta_{iii} \varepsilon / [(\gamma + d)(\varepsilon + d)]$. This is the product of the average number of contacts, the disease transmission coefficient, the average fraction surviving the latent period $\varepsilon/(\varepsilon+d)$, and the average time spent in the infective compartment. In the case of disease transmission coefficients equal for all populations present in a city, *i.e.*, $\beta_{ijk} = \beta_k$ for all i, j, giving $\mathcal{R}_0^i = \kappa_i \beta_i \varepsilon / [(\gamma + d)(\varepsilon + d)]$, the following easily computable bounds hold for $\mathcal{R}_0$.

Corollary 1. *Suppose that $\beta_{ijk} = \beta_k$ for all $i, j = 1, \ldots, n$. Then*

$$\min_{i=1,\ldots,n} \mathcal{R}_0^i \leq \mathcal{R}_0 \leq \max_{i=1,\ldots,n} \mathcal{R}_0^i$$

Note that in this case, if $\mathcal{R}_0^i < 1$ for all i, then $\mathcal{R}_0 < 1$, thus from Theorem 2, the DFE is locally asymptotically stable. Similarly, if $\mathcal{R}_0^i > 1$ for all i, then $\mathcal{R}_0 > 1$, thus the DFE is unstable. If $\kappa_k \beta_k = \kappa \beta$ (*i.e.*, the disease transmission parameters are identical in all cities), then $\mathcal{R}_0 = \kappa \beta \varepsilon / [(\gamma + d)(\varepsilon + d)]$, as in a classical SEIRS model with no mobility.

3 Discussion

The SEIRS epidemic model formulated in (2) describes the dynamics of an infectious disease in a population of individuals with travels between discrete

cities as incorporated in a model by Sattenspiel and Dietz [7]. The disease free equilibrium of the epidemic model (2) has population numbers given by (4) and (5). An explicit formula (6) for the basic reproduction number $\mathcal{R}_0$ is derived; the DFE of (2) is locally asymptotically stable if $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$. Numerical simulations indicate that $\mathcal{R}_0$ acts as a sharp threshold between the extinction($\mathcal{R}_0 < 1$) and the invasion ($\mathcal{R}_0 > 1$) of the disease. They also indicate that the endemic equilibrium is unique with infective numbers tending to this equilibrium whenever $\mathcal{R}_0 > 1$. Thus to control the disease, measures should be taken to reduce $\mathcal{R}_0$ below 1. However, since $\mathcal{R}_0$ depends on the disease transmission parameters, the average lifetime, the exposed and infective periods as well as the outgoing and return travel matrices, such control strategies are not in general easily quantified. However, with parameter values appropriate for a specific disease, $\mathcal{R}_0$ can be readily computed from (6) and its variation with respect to some parameters can be estimated.

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