Mixing Patterns Between Age Groups Using Social Networks

S. Y. Del Valle[1*] J. M. Hyman [2], H.W. Hethcote[3], and S. G. Eubank[1†]

[1] CCS-5 Simulation Science (MS M997), Los Alamos National Laboratory,
Los Alamos, NM 87545, USA

[2] Mathematical Modeling Analysis Group (MS B284), Los Alamos National Laboratory,
Los Alamos, NM 87545, USA

[3]Department of Applied Mathematical & Computational Sciences, University of Iowa, 14 McLean Hall,
Iowa City, IA 52242, USA

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Abstract

We present a method for estimating transmission matrices that describe the mixing and the probability of infection between age groups. Transmission matrices can be used to estimate age-dependent forces of infection in age-structured, compartmental models for the study of infectious diseases. We have analyzed the social network generated by bipartite graphs for the synthetic city of Portland and identified mixing patterns. Our results show that children interact most frequently with other children close to their own age, while adults interact with a wider range of age groups and the durations of typical adult contacts are shorter than typical contacts between children.

*Corresponding author:Tel.:+1-505-665-7285; fax:+1-505-665-7464. E-mail: sdelvall@lanl.gov.
†Present address: Virginia Bioinformatics Institute, Virginia Tech, Blacksburg, VA 24061, USA

1 Introduction

A major difficulty in understanding the spread of diseases is our lack of data on the mixing patterns in the population. It is important to appropriately account for the occurrence of contacts to accurately understand disease spread and develop control measures. Correctly accounting for the mixing patterns in a population may be crucial to accurately predict the path of a disease and thus where the outbreak could be intercepted most effectively.

Mathematical models often estimate the likelihood of a disease outbreak based on the basic *reproductive number*. The basic *reproductive number* is the average number of secondary cases produced by a "typical" infectious individual during its infectious period (van den Driessche and Watmough, 2002). The rate at which infectious individuals spread the disease depends on the number of adequate contacts (i.e. contacts that would result in infection) between infecteds and susceptibles. Thus, if we determine the mixing patterns in the population, we can obtain better estimates of the basic *reproductive number*. This result can help modelers predict the severity of an outbreak and the best means of containing it.

Because of the recognition that heterogeneous contact patterns govern sexually transmitted diseases (STDs), several techniques have been developed to incorporate heterogeneous mixing in mathematical models for STDs. However, not much effort has been channeled into incorporating heterogeneous mixing for other infectious diseases. Numerous models have studied the effects of different mixing functions or mixing matrices in the form of compartmental models for STDs (Anderson *et al.*, 1990; Blythe and Castillo-Chavez, 1989; Hethcote and Yorke, 1984; Hyman and Stanley, 1989; Hyman and Li, 1997; Hyman *et al.*, 1999; Knolle, 2004). Some

of the techniques developed that incorporate non-random mixing into epidemic models include restricted mixing (Jacquez *et al.*, 1988), proportionate mixing (Hethcote and Van Ark, 1987; Nold, 1980), preferred mixing (Hethcote and Yorke, 1984), selective mixing (Koopman *et al.*, 1989), and non-proportionate mixing (Anderson and May, 1991). These techniques involve defining a form for the $n \times n$ matrix, the elements of which represent adequate contacts between individuals in age group i and age group j. However, estimating the entries in these matrices require knowledge of the forces of infection and the steady states of the endemic disease. The forces of infection are usually estimated using serological data, but these data are often not available for many diseases.

Survey studies of mixing patterns can be useful tools in understanding disease spread. Edmunds et al. (1997) studied a survey of a sample of 65 individuals and estimated contact patterns that could lead to the spread of airborne infections. They concluded that older adults mix with themselves and all other age groups at the same rate, and that younger adults do not. They also found that people have a different mixing pattern during the weekend than on weekdays. However, some of the limitations of this study are the sample size, the lack of quantification of duration of contact, and the fact that all the participants were adults, even though a great number of diseases are transmitted by children. A review article by Wallinga et al. (1999) discussed the use of networks in developing contact patterns and the spread of airborne infectious diseases. They noted that more studies are needed to better understand contact patterns to predict disease spread.

Any realistic model for the spread of infectious diseases must take into account the mech-

anism of its transmission, the heterogeneities of risk between individuals, the spatial and local nature of interactions among the population, and the probability of transmission per contact (Isham and Medley, 1996; Grenfell and Harwood, 1997; Wallinga et al., 1999). However, some standard compartmental models assume homogeneously mixing populations and thus ignore many of these important properties that are crucial for the modeling of human disease-transmission. Therefore, while traditional compartmental models have proved to be useful in developing theoretical epidemiological insights, the complex nature of the mixing patterns in the population and transmission routes could have severe implications.

Diseases are often spread through social contact; thus, contact information is key to controlling an epidemic. Network modeling can be traced back to the work of Erdös and Renyi in the 1960s, which introduced the idea of random networks. A more recent application of network modeling developed to study the spread of disease is social networks (Meyers *et al.*, 2004; Newman, 2002; Zaric, 2002; Read and Keeling, 2003). In social network modeling, the structure of a community is represented by a graph consisting of nodes, representing people, and edges, representing contact between two people. Social networks allow for more realistic representation of populations and their social contact structure, which are crucial in understanding and modeling infectious disease spread.

Here we use a social network generated by the synthetic population of Portland, Oregon, consisting of more than 1.6 million individuals to determine mixing patterns between age groups. We analyze the simulated movement of these individuals to estimate the likelihood of contact and infection. A transmission matrix is estimated based on the mixing patterns observed in

the population. This matrix can be used in mathematical models to determine age-dependent forces of infection.

2 Realistic Social Networks

EpiSimS (Epidemic Simulation System) is a discrete-event, stochastic simulation model used for the spread of disease in large urban populations (Barret *et al.*, 2005; Chowell *et al.*, 2003; Eubank, 2002, Eubank *et al.*, 2004, Eubank *et al.*, To appear). The original EpiSimS model was based on the city of Portland, Oregon, in which the simulated movement of more than 1.6 million individuals was constructed. Every person in the simulation was created according to actual demographic distributions drawn from the 2000 census data, so that the synthetic population matched the correct demographics (e.g. age distribution, household statistics, and residential population density). The city of Portland was mapped into 181,230 locations such as households, schools, and shopping centers. Information on the number of actual physical locations in Portland were obtained from the Enhanced Census TIGER data set. All physical locations were aggregated by census block and 2 locations were generated per street.

Schedules of daily activities were obtained from activity surveys based on thousands of households. Each person in the simulation was assigned a sequence of daily activities based on their demographics and their role within their household. The activities consist of: working, staying at home, shopping, visiting, socializing, going to school, going to college, and other. Then, routes were assigned to each person in order to satisfy the set of activities that they carried out throughout the day.

Finally, the movement of people along their chosen routes in the synthetic city of Portland is simulated. The simulation starts by creating a network represented as a bipartite graph, G_{PL}, where P describes people and L locations (Figure 1). Each person-location is represented as a vertex in the network and the edges represent the movements of individuals between locations. Each edge in G_{PL} has different weights, which represent the duration in each location. Because for some locations such as large buildings, thousands of individuals may go to the same location, EpiSimS creates an ad-hoc model for mixing within a location. For example, schools are divided into classrooms and shopping malls are divided into stores. In this "sub-location" model, people are assigned to rooms based on activity type. Assignments overlap, so a "worker/teacher" may have a contact with a student. In each room a person is represented as a vertex and each contact between two people is represented as an edge (Figure 1). The simulation keeps track of every single individual on a second-by-second basis and is therefore able to determine the contacts, including identities of those in contact, the location, the duration of the contact, and the nature of the activity where the contact took place.

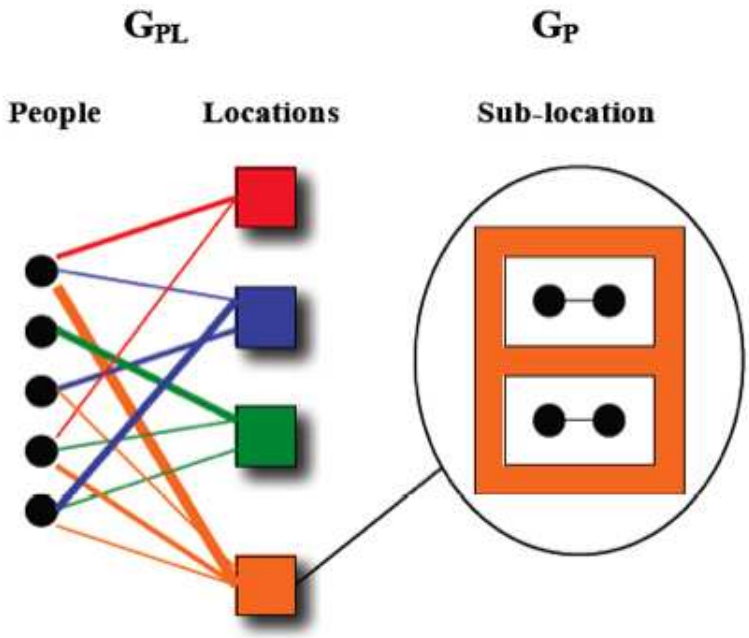

Figure 1: Schematic representation of EpiSimS social contact network. A bipartite graph G_{PL} with two types of vertices representing five people and four locations. The edges connecting the people and the locations represent movement of individuals between locations throughout the day. The thickness of the edges represents the time spent at different locations. A location is divided into rooms and each contact between two people in a room is represented by an edge. The result is G_P, a person-person social network.

EpiSimS integrates all of this information into a computer model in order to simulate disease transmission in the social network and it also provides estimates of physical contact patterns for large human populations. Because we are interested in human contact patterns and their impact on the spread of infectious diseases, we focus on G_P, a graph containing only people (Figure 1). The simulation generates time dependent person-person social contact networks

based on the sequence of activities each person carries out throughout the day.

We begin by analyzing some of the properties of the social contact network, G_P, generated by the synthetic population of Portland. The G_P graph consists of 1,615,860 nodes and 13,143,900 edges. Figure 2 shows the degree distribution of G_P aggregated over one day. We observe that the distribution decays as two power laws, $P(k) \propto k^{-\gamma}$ with $\gamma = 3.4$ for the range 65 to 135 and $\gamma = 5.16$ for the range 112 to 365. The G_P graph is not fully connected, but has a giant component with 1,591,010 people and an average degree of 16.27. We also estimated the average number of contacts per day per person in each age group (Figure 3). In general, older adults have fewer contacts than children and middle-aged adults. The average number of contacts generated by the synthetic population of Portland, Oregon is consistent with previous studies (Edmunds *et al.*, 1997). The average number of people contacted per day per person, the probability of transmission per contact, and the duration of infection could give us an estimate of how many secondary cases could potentially acquire infection from one index case.

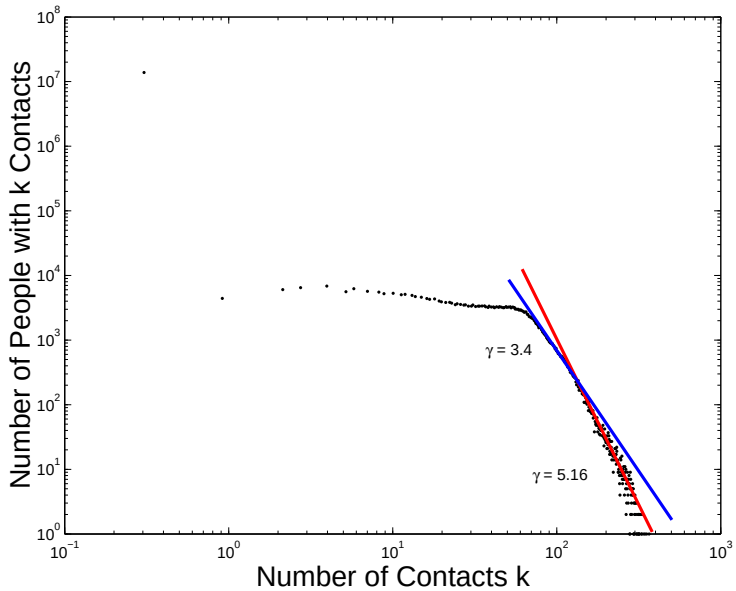

Figure 2: The number of people who have k contacts per-day in the population on log-log scale. The distribution decays as two power laws, $P(k) \propto k^{-\gamma}$ with $\gamma = 3.4$ for the range 65 to 135 and $\gamma = 5.16$ for the range 112 to 365.

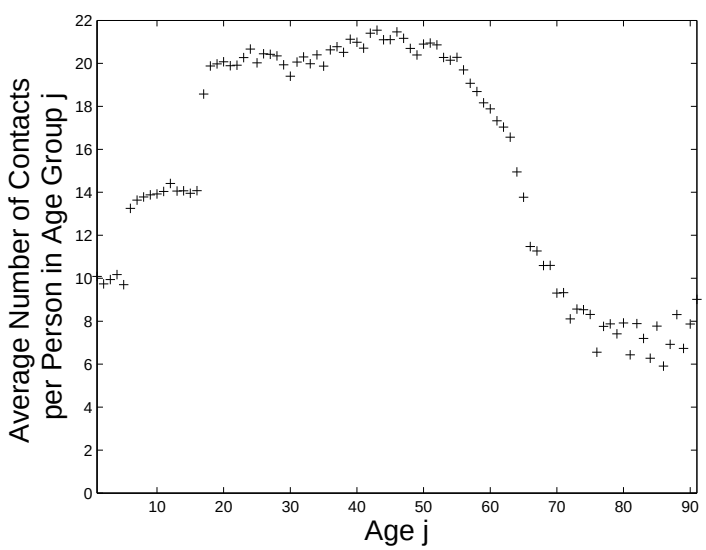

Figure 3: Average number of contacts per person per-day in age group j. The average number

of contacts per person is defined by dividing the total number of contacts made by age group j by the size of age group j.

Although the parameter values used to estimate the average number of people per room were obtained from survey data, there is still some uncertainty in their values. Thus, we performed sensitivity analysis to determine the effects of changes in the "sub-location" model on the simulation results. We found that the average degree (average number of contacts per person) is sensitive to variations in the number of people allowed into each room per day. That is, when the number of people allowed into each room increases, the average degree increases and vice versa. However, the mixing structure is not sensitive to changes in the "sub-location" model. For example, the shape of Figure 3 remains the same regardless of the parameter values used in the "sub-location" model.

2.1 Population

EpiSimS uses a synthetic population that resembles the real population of Portland, Oregon in the course of carrying out their daily activities over one randomly chosen day. The population consists of 1,615,860 individuals of ages ranging from 0 to 90 years. Figure 4 shows a histogram of the age distribution of the population. Portland is somewhat unusual because of the disproportionately large population of young adults, resulting in a double-hump distribution.

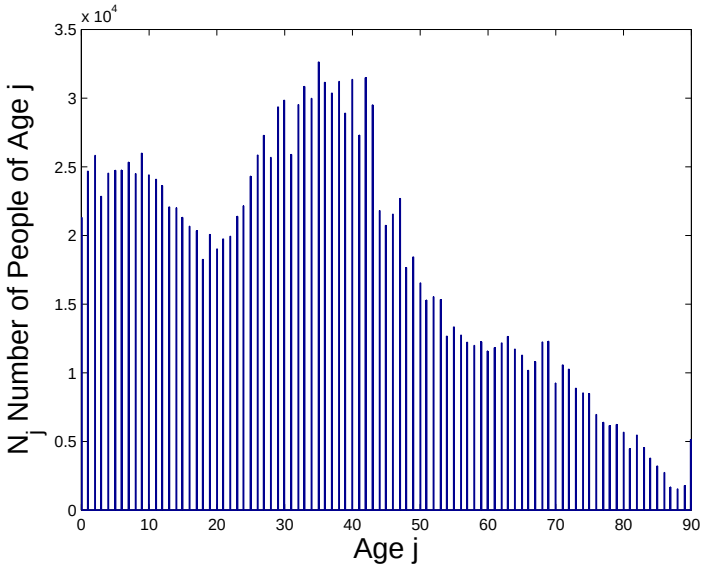

Figure 4: Age distribution of the synthetic population for the city of Portland. The population consists of 1,615,860 individuals of ages ranging from 0 to 90 years. The population is described by a double-hump distribution with mean of 34.37 and median of 33.

3 Estimating the Transmission Matrix

Here we demonstrate how the EpiSimS results can be used to estimate a transmission matrix. The force of infection λ_i is the relative rate at which susceptibles of age i acquire infection. Homogeneous mixing means that contacts of a person are randomly distributed among all others in the population. One immediate implication of the assumption of homogeneous mixing is that the force of infection is same for all ages. However, for heterogeneous mixing, the forces of infection reflect the age-related differences in the degree of mixing and contact, within and among age groups.

Empirical evidence of age-related differences in λ_i have been documented for childhood infections by Anderson and May (1982, 1991) and Grenfell and Anderson (1985). They estimated forces of infection as a function of age using serological data or records of case notifications. These studies suggest that the age-related differences in the force of infection are important factors in modeling infectious diseases. The most direct evidence against the homogeneous mixing assumption comes from studies showing that for human diseases the force of infection λ_i, tends to increase with age up to about 5-15 years, and then to decrease in later years (Anderson and May, 1991).

A standard method used in mathematical models to take account of age-dependent mixing patterns of the population is to define a transmission matrix or WAIFW (Who Acquires Infection From Whom) matrix (Anderson and May, 1991). The WAIFW matrix describes how individuals mix with other age groups. The elements of the WAIFW matrix, β_{ij}, represent the rate at which an infective of age j will infect a susceptible of age i. However, this technique requires knowledge of the forces of infection, the form of the WAIFW matrix, and the steady states of the endemic disease. The forces of infection are estimated using serological data, but these data are often not available for many diseases (Anderson and May, 1991). Furthermore, the pre-judgment of the form of the mixing matrix may be unrealistic, so that the data leads to mixing matrices with negative entries. Therefore, there is a great need to develop new methods to estimate age-dependent forces of infection.

We use the social network for the city of Portland to estimate a transmission matrix and, consequently, age-dependent forces of infection. We assume that the population is demo-

graphically divided into different age groups that can progress through various infection stages (Hyman *et al.*, 1999). For this model, we consider 91 age groups and m infection stages.

We define the force of infection λ_i as the rate of disease transmission from infected people in all age groups to susceptibles in age group i. That is, λ_i is the sum of the rate of disease transmission from all infection stages k with $1 \leq k \leq m$ in all age groups j with $1 \leq j \leq 91$ to the susceptible group S_i. This means that a susceptible person in age group i can get infected by a person in any infection stage in any age group. Thus,

$$\lambda_i = \sum_{j=1}^{91} \sum_{k=1}^{m} \lambda_{ijk}(t). \tag{1}$$

Where, λ_{ijk} is the rate of disease transmission from the infected people I_{jk} in infection stage k of age group j to the susceptibles in age group i. We calculate λ_{ijk} in (1) as the product of the number of contacts per unit time that each individual in age group i has with age group j; the probability of disease transmission per contact between an infected in stage k of age group j and a susceptible in age group i; and the fraction of those contacts that are infected. That is,

$$\lambda_{\mathbf{ijk}} = \begin{pmatrix} \text{Number of} \\ \text{Contacts per} \\ \text{Unit Time} \end{pmatrix} \begin{pmatrix} \text{Probability of} \\ \text{Disease Transmission} \\ \text{per Unit Time} \end{pmatrix} \begin{pmatrix} \text{Fraction of} \\ \text{Contacts that} \\ \text{are Infected} \end{pmatrix}.$$

In terms of the EpiSimS data, we can define the force of infection λ_{ijk} as the product of the average number of contacts, γ_{ij}; the probability of disease transmission, which is the product of the susceptibility (α_i) of a susceptible in age group i, the infectivity (ξ_{jk}) of an infective in stage k of age group j, and the probability of transmission P_{ij} based on the average duration

of contacts between age groups i and j, and the fraction of contacts that are infected. That is,

$$\lambda_{\mathbf{ijk}}(\mathbf{t}) = \ (\gamma_{ij}(t)) \quad (\alpha_i \xi_{jk} P_{ij}) \quad \left(\frac{I_{jk}(t)}{N_j(t)}\right), \tag{2}$$

where I_{jk} is the number of people in infection stage k of age group j and N_j is the size of age group j.

Let σ be the mean number of transmission events per hour of contact between fully infectious and fully susceptible people. For events that occur randomly in time, the number of occurrences in a period of time of length t obeys a Poisson probability law with parameter σt. Thus, the probability of no occurrences in time interval t is $e^{-\sigma t}$ and the probability of at least one occurrence is $1 - e^{-\sigma t}$. Using the mean duration T_{ij} of contacts between a person in age group i with people in age group j, we assume that the probability of transmission in this time interval T_{ij} is given by

$$P_{ij} = 1 - e^{-\sigma T_{ij}}. \tag{3}$$

For example, using $\sigma = 8$ in equation (3) and the average durations of contact per pair, T_{ij} from EpiSimS data, we obtain the probabilities of transmission, P_{ij} shown in Figure 5. Since children and others are more likely to spend time with others of similar ages, the average durations of contact are larger among people of similar ages. Thus, the probabilities of transmission are higher along the diagonal for all age groups. Furthermore, observe the weak coupling between middle-aged adults and young individuals, possibly due to child-parent duration of contact.

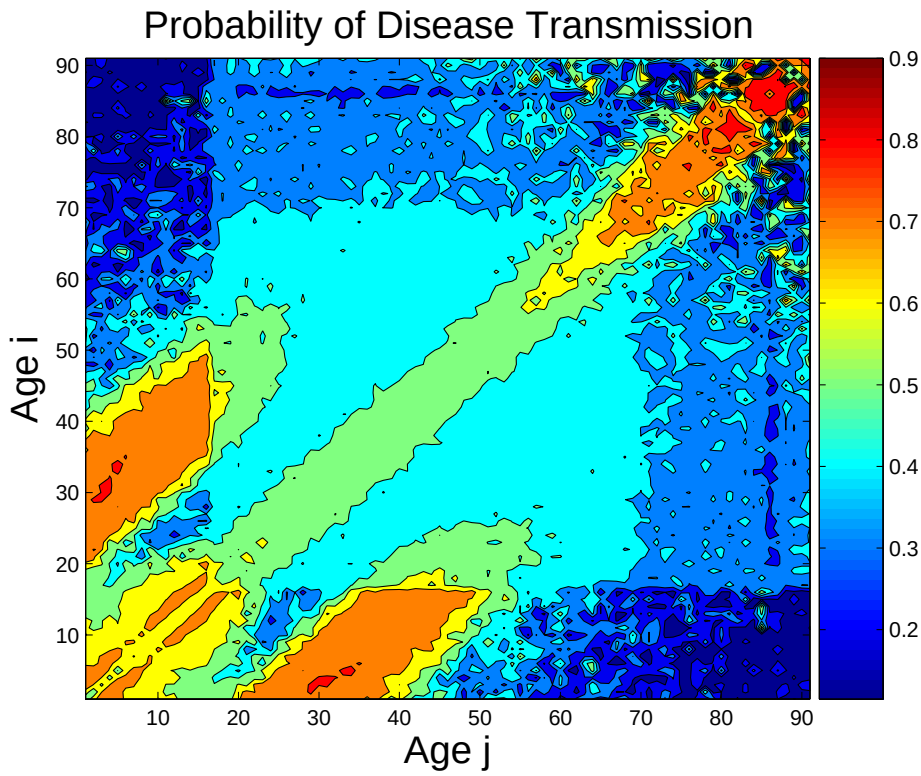

Figure 5: P_{ij}, probability of transmission based on duration of contacts between a susceptible in group i and an infected in group j. Notice that there is a high probability of transmission along the diagonal for all age groups.

Lastly, we define β_{ij} as the adequate contact rate between a susceptible in age i with people in age j, which is the product of the average number of contacts, the susceptibility, the infectivity, and the probability of disease transmission, that is, $\beta_{ij} = \gamma_{ij} * \alpha_i * \xi_{jk} * P_{ij}$. Using γ_{ij} from EpiSimS data, $\alpha_i = 1$, $\xi_{jk} = 1$, and P_{ij} from equation (3) (Figure 5), we estimate a transmission matrix β_{ij} (Figure 6), for the given social network. For simplicity, we assumed in this example that all age groups are equally susceptible ($\alpha_i = 1$), and that all infected individuals are equally infectious (ξ_{jk}), regardless of the infection stage or age group. The

transmission matrix, β_{ij} shows the rate at which an infected person in age group j will infect a susceptible person in age group i. The transmission matrix in Figure 6 exhibits two blocks of mixing, young individuals (< 20 years) and adults (> 20 years). This matrix is consistent with the prevailing opinion that the probability of disease transmission between children is high. Adults are described as likely to acquire infection from a wider range of age groups, mainly middle-aged groups. Also, observe that there is a weak coupling between middle-aged adults (parents) and children.

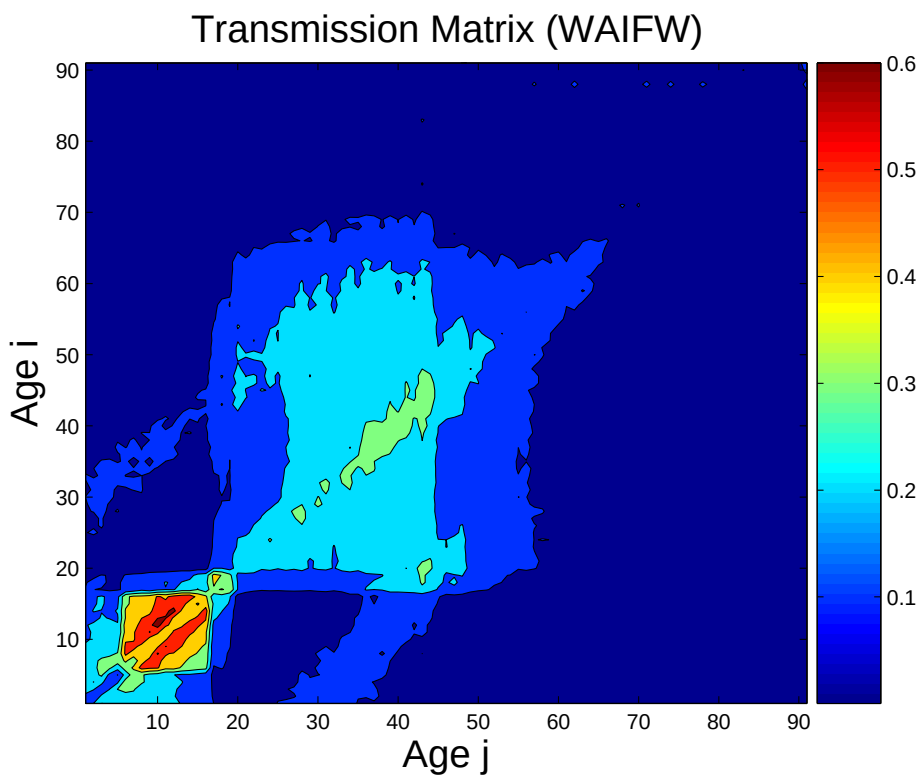

Figure 6: Transmission matrix β_{ij} (WAIFW) for the synthetic population of Portland. Observe that children and teenagers are more likely to acquire infection than the rest of the population.

We now partition the population into 9 categories: 1-10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, and 81-91, and aggregate the elements of each category using the data that generated Figure 6. Table 1 shows the average values for the transmission rates among the aggregated age groups. The transmission rates represent the daily probability that an infected person of age j will transmit the disease to a person in age group i in a fully susceptible population.

The transmission matrix β_{ij} can be used to obtain the forces of infection needed in a mathematical model with age structure. In order to estimate the force of infection for a specific disease using equation (1), one would need to estimate the contact rates (γ_{ij}), the susceptibilities (α_i) for each age group, the infectivities (ξ_{jk}), and the transmissibility parameter (σ) for the disease.

Table 1: Transmission Matrix (WAIFW) of the daily number of adequate contacts per person between the aggregated age groups.

Age	**1-10**	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**	**71-80**	**81-91**
1-10	3.06	2.21	0.63	1.13	0.37	0.10	0.06	0.03	0.01
11-20	2.21	1.54	0.38	0.68	0.68	0.21	0.10	0.04	0.01
21-30	0.63	0.38	0.79	0.81	0.70	0.38	0.18	0.06	0.02
31-40	1.13	0.68	0.81	0.71	0.52	0.26	0.13	0.04	0.01
41-50	0.37	0.68	0.70	0.52	0.50	0.23	0.11	0.03	0.01
51-60	0.10	0.21	0.38	0.26	0.23	0.24	0.10	0.03	0.01
61-70	0.06	0.10	0.18	0.13	0.11	0.10	0.11	0.03	0.01
71-80	0.03	0.04	0.06	0.04	0.03	0.03	0.03	0.06	0.01
81-91	0.01	0.01	0.02	0.01	0.01	0.01	0.01	0.01	0.02

4 Discussion and conclusions

Contact patterns play an important role in determining the progression of epidemics. We have introduced a method for obtaining useful information on the mixing patterns of a social contact network, which might lead to the spread of airborne infections. We argue that mathematical models that use contact matrices based on social networks will be better able to capture age-specific infection patterns of infectious diseases than models that use transmission parameters based on homogeneous mixing or ad-hoc assumptions.

Estimating forces of infection is crucial when using models for specific infectious diseases.

The forces of infection determine the rate of disease transmission and are based on the age-related differences in the degree of mixing and contacts within the population. We used the average number of contacts and a probability distribution based on the average duration per contact to estimate a transmission matrix. With the appropriate specification of disease-related parameters of susceptibility and infectivity, this matrix can be used to estimate age-dependent forces of infection for any disease.

Our results based on EpiSimS data show that in general there are two main blocks of mixing within the population: young individuals (< 20 years) and adults (> 20 years). Furthermore, we observe a weak coupling between children and middle-aged adults, probably due to child-parent contacts. The transmission matrix in Figure 6 shows that school children are more likely to become infected than the rest of the population. This may be due to the longer duration of contacts children have with other children at school. In contrast, adults interact with a wider range of age groups, but their duration of contact is shorter.

Although parameter values for the "sub-location" model were estimated using survey data, there is still uncertainty associated with their values. We found that the average degree is most sensitive to the "sub-location" model. However, the mixing patterns within the population are not sensitive to changes to the "sub-location" model. That is, we observed the same mixing structure (two blocks of mixing) regardless of the parameter values used in the "sub-location" model.

Our study is limited because the current version of EpiSimS does not stratify classrooms by age and therefore the probability of having a contact with any age group in each school is

the same for all children. However, children attending elementary schools mix more in their classrooms with other school children of their own age than with children of other ages. The spread of many childhood diseases is governed by the pattern of contact among children and therefore it is important to incorporate realistic mixing patterns. While recognizing some of the limitations in the current EpiSimS simulation model, EpiSimS represents a potentially powerful resource for estimating mixing pattern parameters in the face of an actual outbreak.

For mathematical models of infectious diseases to be useful in guiding public health policy, they must consider age-dependent forces of infection. Individual behavior is crucial for the spread of infectious diseases and predicting disease spread is difficult. Therefore, new techniques such as the one developed here using social networks are needed as alternative tools when aggregate behavior cannot be applied to the population. The transmission matrix developed here is useful in providing estimates of the age-dependent forces of infection for mathematical models. However, much more needs to be known about the interactions between people that lead to infection before it will be possible to accurately predict an epidemic.

Acknowledgments

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