

A "TEST-BED PROCEDURE FOR EVALUATING  
ONE-SEX MIXING FRAMEWORKS

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Abstract

Recent advances mean that a wide variety of functions describing social/sexual mixing may now be employed in sexually transmitted disease models, as opposed to the random or proportionate mixing assumption which was all that was available even a few years ago. We do not yet, however, have much insight into what effect different mixing structures have on transmission dynamics or the shape of the epidemic curve. We propose a simple SIS model as a test-bed for evaluating proposed mixing functions swiftly and easily. Because the model may be solved analytically for the total sub-population of each group in the population, direct calculation of how the mixing structure evolves throughout the course of an epidemic is trivial. Any standard ordinary differential equation solver can be used quickly to examine the details of the epidemic itself.

Key Words: sexually transmitted disease (STD); mixing function; epidemic.

## Introduction

For any sexually transmitted disease (eg. gonorrhoea, syphilis, HIV/AIDS, hepatitis B) the social/sexual mixing structure of the affected population must play a major part in determining the pattern and magnitude of an epidemic. For example, if there are  $N$  groups in the population and individuals choose partners almost exclusively within their home group, then the epidemic will be very slow to appear, and the disease organism may not persist in the population if activity levels (numbers of partners per unit of time, eg. per year) are low enough. By contrast, if people in all groups mix indiscriminately and at random, then we might expect an epidemic to appear quickly and to be of considerable magnitude. Or again, if there is one group of highly active people in a population of otherwise fairly restrained individuals, the disease may be able to persist in this group for very long periods of time despite quite stringent control measures aimed at the population as a whole (this "core group" concept has been successfully applied to the control of gonorrhoea by Hethcote and Yorke, 1977).

What is missing from the above is any idea of how to quantify these expectations for any but the simplest cases. This is because until recently it was impossible to formulate mathematical models which incorporated anything more complicated than random mixing (called proportionate mixing in the literature (refs)). With the threat of AIDS/HIV transmitted by homosexual and heterosexual intercourse, it has become literally of vital importance to be able to employ much more realistic models of sexually transmitted diseases, entailing (amongst other things) having a comprehensive repertoire of descriptions of human sexual mixing (ie. how many partners and who they are).

Recently, several new descriptions of one-sex (refs) and two-sex mixing (refs) have been found. Further, it has been shown that a general solution exists (refs) so that any mixing description can be written in standard form. The relationships between the various published solutions and the one-sex general solution are set out in Blythe and Castillo-Chavez ( ), and the crucial problem of parameter estimation has begun to receive some attention (Blythe et al. ( ), Casella et al. ( )).

These results are all very new, and as yet we do not have much insight into the detailed (quantifiable) effects of different mixing structures upon STD epidemics. In this paper we introduce a procedure whereby such insight may be systematically obtained. We make use of some useful properties of a simple STD model to produce explicit, analytic expressions for the evolution of the actual mixing structure in a one-sex population infected by a STD. Then, using a standard ordinary differential equation solver, we will illustrate how the course of the epidemic itself is affected by any postulated mixing framework.

The Test-Bed Model

The model should be as simple as possible, but contain as many as possible of the salient features of STD transmission. It should also be chosen so as to minimize the difficulty of evaluating mixing frameworks. The following SIS (susceptible-immune-susceptible) model for a STD in a one-sex, N group population, with a prescribed mixing framework, is ideal as a test-bed.

Let  $S_i(t)$  and  $I_i(t)$  respectively denote the number of susceptibles and infecteds in the  $i^{\text{th}}$  group, at time  $t$ . Let  $\Lambda_i$  denote the rate of influx (recruitment) of new susceptibles to the  $i^{\text{th}}$  group, and let  $1/\mu$  and  $1/\sigma$  be the average duration of a sexual "lifetime" and the average duration of the infected phase, respectively. If  $B_i(t)$  is the incidence rate (of infections) in the  $i^{\text{th}}$  group, then we may write

$$\begin{aligned} \frac{dS_i(t)}{dt} &= \Lambda_i - B_i(t) - \mu S_i(t) + \sigma I_i(t) \\ \frac{dI_i(t)}{dt} &= B_i(t) - (\mu + \sigma) I_i(t) \end{aligned} \tag{1}$$

for  $i = 1, 2, \dots, N$ . We of course require initial conditions  $S_i(0) > 0$ ,  $I_i(0) \geq 0$  for all  $i$ . The incidence rates are given by

$$B_i(t) = S_i(t) \sum_{j=1}^N \beta p_{ij}(t) c_j(t) \frac{I_j(t)}{T_j(t)} \tag{2}$$

which is interpreted as follows. Each individual in group  $i$  has  $c_i(t)$  partners per unit time at time  $t$ . Of these, a fraction  $p_{ij}(t)$  come from group  $j$  ( $j = 1, 2, \dots, N$ ), and of these, a fraction  $I_j(t)/T_j(t)$  are infected at time  $t$  ( $T_j(t) = S_j(t) + I_j(t)$ , ie. the total population of the  $j^{\text{th}}$  group). There is assumed to be a constant probability  $\beta$  of a susceptible person becoming infected during a partnership with an infected person. Thus the summation term on the RHS of Equation (2) is the probability per unit time of a susceptible person in group  $i$  becoming infected at time  $t$ , and hence  $B_i(t)$  is the total rate of new infections occurring in group  $i$  at time  $t$ . In this simplified form, if we prescribe the  $\{p_{ij}(t)\}$ , then we have a complete specification of the STD epidemic model.

Equation (1) has the very useful property that it can be solved explicitly for the total populations of each group, the  $\{T_i(t)\}$ . Adding the equations for  $S_i(t)$  and  $I_i(t)$ , we have

$$\frac{dT_i(t)}{dt} = \Lambda_i - \mu T_i(t), \quad T_i(0) = S_i(0) + I_i(0) \tag{3}$$

for all  $i$ . Equation (3) has the solution

$$T_i(t) = \frac{\Lambda_i}{\mu} - \left( \frac{\Lambda_i}{\mu} - T_i(o) \right) e^{-\mu t}, \quad \text{all } i. \quad (4)$$

We will now show that this property allows us to evaluate the functions  $\{p_{ij}(t)\}$  for all  $t$ , independently of the disease dynamics.

### The Evolving Mixing Structure

All possible allowable choices of the  $\{p_{ij}(t)\}$  may be written in the form (refs)

$$p_{ij}(t) = \bar{p}_j(t) \left[ \frac{R_i(t)R_j(t)}{\sum_{k=1}^N \bar{p}_k(t)R_k(t)} + \phi_{ij}(t) \right] \quad (5)$$

where

$$\bar{p}_i(t) = \frac{c_i(t)T_i(t)}{\sum_{k=1}^N c_k(t)T_k(t)}, \quad \text{all } i \quad (6)$$

and

$$R_i(t) = 1 - \sum_{k=1}^N \bar{p}_k(t)\phi_{ik}(t), \quad \text{all } i. \quad (7)$$

The  $\{\phi_{ij}(t)\}$  are a set of parameters (or functions of time) which are constrained only by being positive, small enough such that all the  $\{R_i(t)\}$  are positive, and subject to

$$\phi_{ij}(t) = \phi_{ji}(t), \quad \text{all } i \text{ and } j. \quad (8)$$

In practice it is usually adequate (and always sufficient) to restrict the  $\phi_{ij}$  by

$$0 < \phi_{ij}(t) < 1, \quad \text{all } i \text{ and } j. \quad (9)$$

Some of the published  $\{p_{ij}(t)\}$  require that the  $\{\phi_{ij}(t)\}$  be time-dependent (Blythe and Castillo-Chavez( )). This is undesirable for three reasons. First, it means that the mixing structure in the population is in some sense always changing its distance from random mixing (op. cit.); second, the simplifying restriction of Equation (9) becomes too restrictive, leading to greater difficulty in understanding the function of the  $\{\phi_{ij}\}$  in the epidemic; and third, inconstant  $\{\phi_{ij}\}$  are intrinsically much more difficult to estimate from survey data (requiring

large scale longitudinal sexual behavior studies (Blythe et al., Casella et al.) and much harder to choose for purposes of evaluation. We will thus restrict ourselves to  $\{\phi_{ij}\}$ , which are a set of constant parameters, and which are subject to Equation (9).

Before proceeding, we are now in a position to suggest some terminology (used throughout this paper) which we believe will reduce confusion in discerning mixing problems

<u>Mixing parameters:</u>	The set of constant $\{\phi_{ij}\}$ used in a model, subject to Equations (7) and (8).
<u>Mixing function:</u>	A specific function of two variables which may be used to generate the mixing parameters.
<u>Mixing framework:</u>	The function of the $\{\bar{p}_i(t)\}$ and $\{\phi_{ij}\}$ given by the RHS of Equation (5).
<u>Mixing structure:</u>	The actual numerical values of the $\{p_{ij}(t)\}$ , at any given time $t$ , for a specific model or population.

Thus we may use some mixing functions to generate a test set of mixing parameters. These specify an equation which is the mixing framework used in our model. Because the  $\{\bar{p}_i(t)\}$  are time-dependent, the observed mixing structure in the model will be seen to evolve with time throughout the course of the epidemic.

It is with respect to this last point that the test-bed model proves so useful. Because we are able to calculate the  $\{T_i(t)\}$  at all times using Equation (4), we may, when the activity levels  $\{c_i(t)\}$  are specified, also calculate the  $\{\bar{p}_{ij}(t)\}$  terms of Equation (6) directly. As the  $\{\phi_{ij}\}$  are also then prescribed, we can evaluate the mixing structure  $\{p_{ij}(t)\}$  for the model for all time  $t$ , independently of the details of the epidemic.

This means that we can study the impact of different mixing frameworks on the observed mixing structure of a model population algebraically (ie. without recourse to solving differential equations). Of course if we wish to study disease dynamics directly, then we need to solve Equation (1), but this is not a difficult task with any standard ODE solving package.

It is now time to choose a particular mixing framework, and illustrate our evaluation procedure by example.

### An Example Mixing Framework

We choose to use a simple (2 value) but reasonably general example, where the mixing parameters are generated by

$$\phi_{ij} = \begin{cases} a, & i = j \\ b, & i \neq j \end{cases} \quad (10)$$

for  $i, j = 1, 2, \dots, N$ , with  $0 \leq b \leq a \leq 1$ . This example has the suggestion of some preference for taking partners in the home group ( $a > b$ ) (Blythe et al. ( )). The mixing framework is the RHS of

$$p_{ij}(t) = \bar{p}_j(t) \left[ \frac{[1-b+(a-b)\bar{p}_i(t)][1-b+(a-b)\bar{p}_j(t)]}{1-b+(a-b)\sum_{k=1}^N \bar{p}_k(t)^2} + \delta_{ij} a + (1-\delta_{ij}) b \right] \quad (11)$$

for all  $i$  and  $j$ . The symbol  $\delta_{ij}$  is the convenient Kronecker delta function,

$$\delta_{ij} = \begin{cases} 1 & i = j \\ 0 & i \neq j \end{cases} \quad (12)$$

Equation (11) illustrates a number of points about mixing frameworks. Let us define

$$e = \phi_{\max} - \phi_{\min} = a - b \quad (13)$$

as a (rough) measure of the distance of the framework from that of random mixing (where the framework is given by  $p_{ij}(t) = \bar{p}_j(t)$ , and all  $i$  and  $j$  (ref)). If  $a = b$  (any value between zero and one), then Equation (11) reduces to random mixing, and accordingly  $e = 0$ . The maximum distance from random mixing is achieved when  $a = 1$  and  $b = 0$  ( $p = 1$ ), ie. the matrix of mixing parameters has ones along the diagonal and zeroes elsewhere.

Table I lists the model parameters used in the evaluation of this mixing framework, and Table II is a key to the various combinations of  $a$  and  $b$  values we used.

We first consider the evolution of the mixing structure for a few alternative  $a$  and  $b$  values. Figures ??? to ??? show surfaces of the  $\{p_{ij}(t)\}$  at a variety of times: at  $L = 0$ ; at the peak of the epidemic; and for large  $t$  when an equilibrium has been reached. We see...???

Finally, we evaluate the impact of the mixing framework on the epidemic itself. Figures ??? to ??? show how the distance from random mixing (R) alters the timing and magnitude of the epidemic curve. In particular we see that ...???

## Conclusions

We have suggested a test-bed procedure for quickly and easily evaluating proposed mixing frameworks (and some hopefully useful terminology) in the context of a simple SIS epidemic model for a one-sex population. Using a particular (but reasonably general) choice of framework, Equation (11), we have seen how the observed mixing structure of the population,  $\{p_{ij}(t)\}$ , evolves with time throughout the epidemic, and how this observable structure depends on the (constant) distance of the framework from that of random or proportionate mixing. We have also indicated how the details of the epidemic itself depend on the assumed mixing framework.

The results of this exercise, and similar ones using alternative mixing frameworks, should be directly applicable as they stand to any one-sex STD epidemic where the SIS model (Equation 11) is even approximately appropriate. Although this is not the case for HIV/AIDS transmission dynamics (where there is loss from the population due to disease related mortality and the non-participation of AIDS patients in the mixing ???, rather than recovery and return to the susceptible pool), we may still expect to gain some useful insights into the consequences of non-random mixing in heterogeneous populations, which may aid our understanding of the AIDS/HIV epidemic (for example, by using data on diseases where Equation (1) is appropriate to devise the mixing parameters). We are at present exploring such possibilities, and are trying to extend the procedure outlined here to the more complicated two-sex problem.