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"On the Solution of the Two-Sex Mixing Problem"

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ON THE SOLUTION OF THE TWO-SEX MIXING PROBLEM[1]

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Abstract

In this paper we describe an axiomatic framework that allows for the general incorporation of sexual structure into two-sex pair-formation models for sexually-transmitted diseases. This formulation can also be used to describe the dynamics of vector-transmitted diseases. A representation theorem describing all solutions to this mixing framework as perturbations of particular solutions is proved. Two-sex age-structured demographic and age-structured epidemiological models that make use of our framework, and are therefore capable of describing the dynamics of individuals and/or pairs of individuals are formulated.

1. Introduction

[redacted] The modeling of sexual transmission diseases can be said to have its genesis in the work of Sir Ronald Ross. Several ideas introduced in his modeling work on malaria have proved to be very useful in the development of a mixing framework for social/sexual interactions as well as in the development of models for the spread of venereal diseases. For example, the ~~trivial~~

[1]The work described in this paper has been motivated by our work with Kenneth Cooke. Ken has used his considerable experience in the modeling and analysis of models for STD's, and most recently in the development of models that may help our fight against AIDS. Many of the ideas discussed in this article arose out of our study of Ken's work, our discussions with him, and our collaborative efforts with Ken over the years. We dedicate this paper to him as we celebrate his 65th birthday.

recognition that there must be a conservation of the number of interactions between individuals involved in a disease transmission process, a fact often ignored by modelers, was already clearly articulated in Ross' work on malaria. For malaria, this meant that the number of bites on humans must equal the number of humans bitten (Ross 1911, p. 666-7). In STD's we recognize this constraint as that on the [redacted] rate sexual partnerships formed between individual human interacting groups (a kind of group reversibility property or a conservation law). The consequences of this constraint will be further discussed later in this paper. Ross also observed that models with fixed and variable sized populations must be treated differently, and may have radically different properties (Ross 1916, pp. 212, 215, 222). The fact that in the study of the dynamics of malaria the sizes of the host and vector populations play a key role in transmission forced him to introduce a special mixing structure given by a linear function of the ratio of the vector to host population sizes. We will show later that all solutions to our two-sex mixing framework are given by multiplicative perturbations of these special solutions.

Models for the spread of STD's (sexually-transmitted diseases) were not systematically studied for over fifty years. In 1973, Cooke and Yorke analyzed and developed the first models for the spread of gonorrhea. These papers re-opened this important area of research which reaches a significant plateau with the application of these new adavances to the problem of gonorrhea dynamics and control. A description of these applications to U.S. data is clearly detailed in the excellent monograph [redacted] by Hethcote and Yorke (1984).

This paper is organized as follows: In Section 2, we formulate a general two-sex model for the spread of gonorrhea. This model allows us to discuss the problem of pair-formation or mixing. In Section 3, we discuss some special mixing solutions and provide a representation theorem for all possible two-sex mixing (pair-formation) solutions. In Section 4 we formulate a two-sex age-structured demographic model and a two-sex age-structured epidemiological model that follow pairs of individuals. Models of this type have been formulated earlier by Fredrickson (1971), McFarland (1972), Dietz (1988), Dietz and Hadeler (1988), Castillo-Chavez (1989), Hadeler (1989a, b), and Castillo-Chavez et al. (1990),. Section 4 begins with an axiomatic description of a two-sex age-structured framework and proceeeds to present our general representation theorem for the two-sex mixing problem in an age-structured population.

2. Two-sex gonorrhea model with variable population size

To provide a context for the sexual interactions of a heterosexual population, we introduce a two-sex model with variable population size for the transmission dynamics of gonorrhea. Traditional gonorrhea models (see Hethcote and Yorke, 1984) have assumed that the mixing subpopulations have constant size. This assumption may be very useful when we deal with the relative evaluation of control strategies (loc. cit.). However, this assumption is not appropriate in situations in which we wish to evaluate the impact of different mixing patterns in disease dynamics. The assumption of interacting populations of constant size leads to time-independent mixing probabilities (i.e. constant contact matrices) and hence to mixing patterns that are valid only for populations that have already reached a steady state.

We consider a population of heterosexually active individuals. This population is divided into classes or subpopulations. Classes can be identified by sex, race, socio-economic background, average degree of sexual activity, etc. Models that incorporate factors such as chronological age, age of infection, variable infectivity, and partnership duration can be found in our earlier work (see Busenberg and Castillo-Chavez, 1989, 1990). We consider N-sexually active populations of females and L-sexually active populations of males. Each population is divided into two epidemiological classes: $S_j^f(t)$ and $S_i^m(t)$ (susceptible females and males, i.e., unifected and sexually-active, at time t); $I_j^f(t)$ and $I_i^m(t)$ (infected females and males, at time t); for $j = 1,...,N$ and $i = 1,...,L$. Hence the sexually-active individuals of each sex and each subpopulation at time t are represented by $T_j^f(t) = S_j^f(t) + I_j^f(t)$ and $T_i^m(t) = S_i^m(t) + I_i^m(t)$.

$B_j^f(t)$ and $B_i^m(t)$ denote the j^{th} and i^{th} incidence rates for females in group j and males in group i at time t, that is, the number of new infective cases in each subpopulation per unit time. $B_j^f(t)$ and $B_i^m(t)$ are complicated functions that depend on the frequency and type of sexual interactions that susceptible females of group j and susceptible males of group i have with all other sexually-active individuals, in this case, of the opposite sex (although this condition can be easily relaxed).

If Λ_j^f and Λ_i^m denote the "recruitment" rates (assumed constant), μ_j^f and μ_i^m denote the (constant) removal rates from sexual activity, and γ_j^f and γ_i^m denote the (constant) removal recovery rates from gonorrhea infection, then we can ~~easily~~ write the following model for the transmission dynamics of gonorrhea:

$$\frac{dS_j^f(t)}{dt} = \Lambda_j^f - B_j^f(t) - \mu_j^f S_j^f(t) + \gamma_j^f I_j^f(t), \tag{1}$$

$$\frac{dI_j^f(t)}{dt} = B_j^f(t) - (\gamma_j^f + \mu_j^f) I_j^f(t), \tag{2}$$

$$\frac{dS_i^m(t)}{dt} = \Lambda_i^m - B_i^m(t) - \mu_i^m S_i^m(t) + \gamma_i^m I_i^m(t), \tag{3}$$

$$\frac{dI_i^m(t)}{dt} = B_i^m(t) - (\gamma_i^m + \mu_i^m) I_i^m(t), \tag{4}$$

$i = 1,\dots, L$ and $j = 1,\dots,N$.

Of course, this model is not fully described until we provide explicit expressions for $B_j^f(t)$ and $B_i^m(t)$. The formulae for the incidences will be provided in two steps: first we will provide expressions for the incidences in terms of the set of mixing probabilities $\{p_{ij}(t)$ and $q_{ji}(t)$: $i = 1,\dots,L$ and $j = 1,\dots,N\}$; and secondly, these mixing probabilities will be described (in the next section) in terms of an axiomatic system for sexual interactions.

To describe the formulae for the female and male incidences we need the following definitions:

$p_{ij}(t)$: fraction of partnerships of males in group i with females in group j at time t,

$q_{ji}(t)$: fraction of partnerships of females in group j with males in group i at time t,

$T_i^m(t)$: male population size of group i at time t,

$T_j^f(t)$: female population size of group j at time t.

c_i : average (constant) number of female partners per unit time of males in group i, or the i^{th}-group rate of (male) pair-formation,

b_j : average (constant) number of male partners per unit time of females in group ~~i~~ j, or the j^{th}-group rate of (female) pair-formation,

β_i^m : transmission coefficient (constant) of males in group i,

β_j^f : transmission coefficient (constant) of females in group j.

Using these definitions we obtain the following expressions for the incidence rates:

$$B_i^m(t) = c_i S_i^m(t) \sum_{j=1}^{N} \beta_j^f p_{ij}(t) \frac{I_j^f(t)}{T_j^f(t)}, \tag{5}$$

and

$$B_j^f(t) = c_j S_j^f(t) \sum_{i=1}^{N} \beta_i^m q_{ji}(t) \frac{I_i^m(t)}{T_i^m(t)}. \tag{6}$$

3. Two-sex mixing framework

Special solutions for one-sex mixing populations were obtained by Nold (1980), Hethcote and Yorke (1984), Hyman and Stanley (1988, 1989), Jacquez et al. (1988?, 1989), Blythe and Castillo-Chavez (1989), Castillo-Chavez and Blythe (1989), Gupta et al. (1989), and Anderson et al. (1989). A representation theorem describing all solutions as random perturbations of random (proportionate) mixing, based on the work of Blythe and Castillo-Chavez (op. cits.), was obtained by Busenberg and Castillo-Chavez (1989, 1990). Models that follow pairs of individuals (two-sex models) can be found (in a demographic context) in the works of Kendall (1948), Keyfitz (1972), Parlett (1972), and J. H. Pollard (1973). Formulations of the standard two-sex mixing pair-formation framework are found in the work of Fredrickson (1971) and McFarland (1972). Applications of the Fredrickson-McFarland framework to epidemiological models has been carried out by Dietz (1988), Dietz and Hadeler (1988), Castillo-Chavez (1989), Wäldstatter (1989), Hadeler (1989a, b, 1990), and Castillo-Chavez et al. (1990). In this section we provide an alternative approach to the process of pair formation. This axiomatic framework was introduced in Castillo-Chavez et al. (1990), where some special solutions were found. We use the set of mixing probabilities $\{p_{ij}(t)$ and $q_{ji}(t)$: $i = 1,\ldots,L$ and $j = 1,\ldots,N\}$ to describe the mixing/pair formation in a heterosexually active population through the following set of properties or axioms:

Def $(p_{ij}(t), q_{ji}(t))$ is called a mixing/pair-formation matrix iff it satisfies the following properties (at all times):

(A1) $0 \le p_{ij} \le 1, \quad 0 \le q_{ji} \le 1,$ X

(A2) $\sum_{j=1}^{N} p_{ij} = 1 = \sum_{i=1}^{L} q_{ji}$, whenever $c_i T_i^m \neq 0 \neq b_j T_j^f$.

(A3) $c_i T_i^m p_{ij} = b_j T_j^f q_{ji}, \quad i = 1, \cdots, L, \quad j = 1, \cdots, N.$

(A4) If for some i, $0 \le i \le L$ and/or some j, $0 \le j \le N$ we have that $c_i b_j T_i^m T_j^f = 0$, then we define $p_{ij} \equiv q_{ji} \equiv 0$.

Note that (A3) can be viewed as a conservation of partnerships law or a group reversibility property, while (A4) asserts that the mixing of "non-existing" or non-sexually active subpopulations cannot be arbitrarily defined. For the gonorrhea model, and most deterministic models for STD's, subpopulations that are sexually active do not become extinct and remain sexually active for all time. We now proceed to [redacted] characterize a useful solution, namely Ross's solution. X

[illegible]

Def A two-sex mixing/pair-formation function is called separable iff

$$p_{ij} = p_i p_j \quad \textit{and} \quad q_{ji} = q_j q_i \,.$$

This definition lead us to the following useful characterization of two-sex separable mixing function.

Theorem 1: The only separable solution is Ross's solution given by $(p_{ij}, q_{ji}) =$ $(\bar{p}_j, \bar{q}_i)$ where

$$\bar{p}_j = \frac{b_j T_j^f}{\sum_{i=1}^{L} c_i T_i^m}, \qquad \bar{q}_i = \frac{c_i T_i^m}{\sum_{j=1}^{N} b_j T_j^f}; \qquad j = 1, \cdots, N \quad \text{and} \quad i = 1, \cdots, L\,.$$

Proof Using (A2) we get that whenever $c_i b_i T_i^m T_j^f \neq 0$,

$$1 = q_j \sum_{i=1}^{L} q_i = q_j \tfrac{1}{k}, \qquad k \text{ a constant}$$

$$1 = p_i \sum_{j=1}^{N} q_j = p_i \tfrac{1}{\ell}, \qquad \ell \text{ a constant}$$

which implies $q_j = k$ and $p_i = \ell$, hence,

$$q_{ji} = q_j q_i = k\, q_i \equiv \bar{q}_i \tag{7}$$

$$p_{ij} = p_i p_j = \ell\, p_j \equiv \bar{p}_j \tag{8}$$

If (7) and (8) are substituted into (A3) then

$$c_i T_i^m \ell\, p_j = b_j T_j^f k\, q_i \quad \textit{or} \quad c_i T_i^m \bar{p}_j = b_j T_j^f \bar{q}_i\,. \tag{9}$$

Summing over i, we get

$$\bar{p}_j \sum_{i=1}^{L} c_i T_i^m = b_j T_j^f \sum_{i=1}^{L} \bar{q}_i = b_j T_j^f$$

Thus,

$$\boxed{\bar{p}_j = \frac{b_i T_j^f}{\sum_{i=1}^{L} c_i T_i^m} \quad j, 1, \cdots, N.} \tag{10}$$

Summing over j, we have

$$c_i T_i^m \sum_{j=1}^{N} \bar{p}_j = \bar{q}_i \sum_{j=1}^{N} b_j T_j^f \quad \textit{or} \quad c_i T_i^m = \bar{q}_i \sum_{j=1}^{N} b_j T_j^f$$

Thus,

$$\boxed{\bar{q}_i = \frac{c_i T_i^m}{\sum_{j=1}^{n} b_j T_j^f} \quad i = 1, \cdots, L.} \tag{11}$$

It is not immediately clear why (10) and (11) satisfy the mixing axioms; however, starting with the group reversibility property (A3)

$$c_i T_i^m p_{ij} = b_j T_j^f q_{ji}, \qquad i = 1, \cdots, L;\; j = 1, \cdots, N,$$

summing (A3) over j and i

$$c_i T_i^m = \sum_{j=1}^{N} b_j T_j^f q_{ji},$$

$$\sum_{i=1}^{L} c_i T_i^m = \sum_{i=1}^{L} \sum_{j=1}^{N} b_j T_j^f q_{ji},$$

and changing the order of summation

$$= \sum_{j=1}^{N} \sum_{i=1}^{L} b_j T_j^f q_{ji} = \sum_{j=1}^{N} b_j T_j^f,$$

we conclude that

$$\boxed{\sum_{i=1}^{L} c_i T_i^m = \sum_{j=1}^{N} b_j T_i^f.} \tag{12}$$

Therefore $(\bar{p}_j, \bar{q}_i)$ satisfies (A1) – (A3), and we note that it vacuously satisfies (A4).

<u>Remark:</u> Note that from (A3) it follows that

$$\frac{p_{ij}}{q_{ji}} = \frac{b_j T_j^f}{c_i T_i^m} = \frac{\bar{p}_j}{\bar{q}_i}, \tag{13}$$

and hence using (A4) we see that the support of any two-sex mixing function is contained in the support of $(\bar{p}_j, \bar{q}_i)$.

We now use Equations (10), (11) and (13), to generate more solutions to axioms (A1)-(A4). We begin by introducing some new terms. Let

$(\phi_{ij}^m) \equiv$ males' structural covariance matrix $(0 \le \phi_{ij}^m)$ denoting the degree of preference (i.e., the deviation from random mixing) that group i-males have ~~from~~ for group j-females, $j = 1, \cdots, N$; $i = 1, \cdots, L$.

$$\ell_i^m \equiv \sum_{k=1}^{N} \bar{p}_k \phi_{ik}^m \equiv \text{weighted average preference of group i males, } i = 1, \cdots, L$$

$$R_i^m \equiv 1 - \ell_i^m, \qquad i = 1, \cdots, L. \tag{14}$$

we require that $R_j^m \geq 0$, and that

$$\sum_{i=1}^{L} \ell_i^m \bar{p}_i = \sum_{i=1}^{L} \sum_{k=1}^{N} \bar{p}_k \phi_{ik}^m \bar{p}_i < 1 . \tag{15}$$

Similarly, let

$(\phi_{ji}^f) \equiv$ females' structure covariance matrix ($0 \leq \phi_{ji}^f$) denoting the degree of preference (i.e., the deviation from random mixing) that group j-females have for group i-males, $j = 1,\cdots,N$, $i = 1,\cdots,L$.

$\ell_j^f \equiv \sum_{k=1}^{L} \bar{q}_k \phi_{jk}^f \equiv$ weighted average preference of group j-females, $j = 1,\cdots,N$

$$R_j^f \equiv 1 - \ell_j^f, \qquad j = 1, \cdots, N. \tag{16}$$

Again, we require that $R_j^f \geq 0$, and that

$$\sum_{j=1}^{N} \ell_j^f \bar{q}_j = \sum_{j=1}^{N} \sum_{k=1}^{L} \bar{q}_k \phi_{jk}^f \bar{q}_j < 1 . \tag{17}$$

With these assumptions and definitions, we observe that a solution to axioms (A1) – (A4) is given (formally) by the following multiplicative perturbations to the separable mixing solution $(\bar{p}_j, \bar{q}_i)$:

$$p_{ij} = \bar{p}_j \left[\frac{R_j^f R_i^m}{\sum_{k=1}^{N} \bar{p}_k R_k^f} + \phi_{ij}^m \right], \qquad i = 1,\cdots,L; \quad j = 1,\cdots,N, \tag{18}$$

$$q_{ji} = \bar{q}_i \left[\frac{R_i^m R_j^f}{\sum_{k=1}^{L} \bar{q}_k R_k^m} + \phi_{ji}^f \right]. \tag{19}$$

We now show that (p_{ij}, q_{ji}), $i = 1,\cdots,L$, $j = 1,\cdots,N$, given by (18) and (19) is a two-sex mixing matrix. Since

$$\sum_{j=1}^{N} p_{ij} = R_i^m \left[\frac{\sum_{j=1}^{N} \bar{p}_j R_j^f}{\sum_{k=1}^{N} \bar{p}_k R_k^f} \right] + \left[\sum_{j=1}^{N} \bar{p}_j \phi_{ij}^m \right]$$

$$= R_i^m + \sum_{j=1}^{N} \bar{p}_j \phi_{ij}^m = R_i^m + (1 - R_i^m) = 1,$$

and

$$\sum_{i=1}^{L} q_{ji} = R_j^f \left[\frac{\sum_{i=1}^{L} \bar{q}_i R_i^m}{\sum_{k=1}^{L} \bar{q}_k R_k^m} \right] + \left[\sum_{i=1}^{L} \bar{q}_i \phi_{ji}^f \right]$$

$$= R_j^f + \ell_j^f = R_j^f + [1 - R_j^f] = 1,$$

Thus ~~so~~ (A1) and (A2) are satisfied.

Note that axiom (A3) is satisfied if

$$c_i\, T_i^m\, \bar{p}_j \left[\frac{R_j^f R_i^m}{\sum_{k=1}^{N} \bar{p}_k R_k^f} + \phi_{ij}^m \right] = b_j T_j^f \bar{q}_i \left[\frac{R_i^m R_j^f}{\sum_{k=1}^{L} \bar{q}_k R_k^m} + \phi_{jij}^f \right]. \tag{20}$$

By observing that $c_i T_i^m \bar{p}_j = b_j T_j^f \bar{q}_i$, due to the fact that $(\bar{p}_j, \bar{q}_i)$ is a two-sex mixing function, we see that (20) holds iff

$$\left[\frac{R_j^f R_i^m}{\sum_{k=1}^{N} \bar{p}_k R_k^f} + \phi_{ij}^m \right] = \left[\frac{R_i^m R_j^f}{\sum_{k=1}^{L} \bar{q}_k R_k^m} + \phi_{ji}^f \right]. \tag{21}$$

Further, (21) holds iff

$$\phi_{ij}^m - \phi_{ji}^f = R_i^m R_j^f \left[\frac{1}{\sum_{k=1}^{L} \bar{q}_k R_k^m} - \frac{1}{\sum_{k=1}^{N} \bar{p}_k R_k^f} \right]$$

$$= R_i^m R_j^f \left[\frac{\sum_{k=1}^{N} \bar{p}_k R_k^f - \sum_{k=1}^{L} \bar{q}_k R_k^m}{\left(\sum_{k=1}^{L} \bar{q}_k R_k^m \right)\left(\sum_{k=1}^{N} \bar{p}_k R_k^f \right)} \right]$$

or equivalently, if

$$= R_i^m R_j^f \left[\frac{\sum_{k=1}^{L} \bar{q}_k \ell_k^m - \sum_{k=1}^{N} \bar{p}_k \ell_k^f}{\left(\sum_{k=1}^{L} \bar{q}_k R_k^m \right)\left(\sum_{k=1}^{N} \bar{p}_k R_k^f \right)} \right]$$

R_k^m

$$\boxed{\phi^m_{ij} = \phi^f_{ji} + R^m_i R^f_j \left[\frac{\sum_{k=1}^{N} \bar{p}_k R^f_k - \sum_{k=1}^{L} \bar{q}_k \cancel{R^f_k}}{\left(\sum_{k=1}^{L} \bar{q}_k R^m_k\right)\left(\sum_{k=1}^{N} \bar{p}_k R^f_k\right)} \right]} \quad . \tag{22}$$

Note that if $\phi^f_{ji} = 0$, [redacted] $\forall$ i, j $\Rightarrow$ $\ell^f_j = 0 \;\forall j \Rightarrow R^f_j = 1 \;\forall j$,

≠here;

$$q_{ji} = \bar{q}_i \left[\frac{R^m_i}{\sum_{k=1}^{L} \bar{q}_k R^m_k} \right], \text{ and}$$

$$\phi^m_{ij} = R^m_i \left[\frac{1 - \sum_{k=1}^{L} \bar{q}_k R^m_k}{\sum_{k=1}^{L} \bar{q}_k R^m_k} \right] = \frac{R^m_i}{\sum_{k=1}^{L} \bar{q}_k R^m_k} - R^m_i$$

⋇ Thus

$$\phi^m_{ij} = R^m_i \left[\frac{1}{\sum_{k=1}^{L} \bar{q}_k R^m_k} - 1 \right], \quad \phi^f_{ji} \equiv 0, \text{ that is,}$$

it is independent of j and therefore females show no preference. Therefore

$$p_{ij} = \bar{p}_j \left[R^m_i + \phi^m_{ij} \right] = \bar{p}_j \frac{R^m_i}{\sum_{k=1}^{L} \bar{q}_k R^m_k},$$

and hence we obtain the following "semi-separable" mixing solution:

$$\boxed{(p_{ij}, q_{ji}) = \frac{R^m_i}{\sum_{k=1}^{L} \bar{q}_k R^m_k} (\bar{p}_j, \bar{q}_i)} \quad ; \quad q_{ji} \text{ independent of j .} \tag{23}$$

Similarly,

$$\phi^m_{ij} \equiv 0, \text{[redacted]} \quad \phi^f_{ji} = R^f_j \left[\frac{1}{\sum_{k=1}^{N} \bar{p}_k R^f_k} - 1 \right],$$

giving the following "semi-separable" mixing solution:

$$\boxed{(p_{ij}, q_{ji}) = \frac{R_j^f}{\sum_{k=1}^{N} \bar{p}_k R_k^f} \; (\bar{p}_j, \bar{q}_i)} \quad ; \tag{24}$$

p_{ij} independent of i, and hence, males show no preference.

In order to show that every solution of axioms (A1)-(A4) is given by Equations (18)-(19) we proceed as follows. Using property (A4) we observe that $\frac{p_{ij}}{\bar{p}_j}$ and $\frac{q_{ji}}{\bar{q}_i}$ are well defined on the support Δ of $(\bar{p}_j, \bar{q}_i)$, and therefore

$$\frac{p_{ij}}{\bar{p}_j} = \frac{q_{ji}}{\bar{q}_i} \geq 0 \text{ on } \Delta.$$

(imply that the exist

Properties (A1) and (A2) $\cancel{\Rightarrow}$ $\cancel{\exists}$ $\epsilon > 0$ and a set of subset of positive integers $Q \subset Z_+^{\,2} \ni$ $\frac{p_{ij}}{\bar{p}_j} = \frac{q_{ji}}{\bar{q}_i} > \epsilon$

$Q \equiv \left\{(i,j) : \frac{p_{ij}}{\bar{p}_j} > \epsilon\right\}$; and a set related to Q defined as follows:

$\tilde{Q} \equiv \left\{i : (i,j) \in Q \text{ for some } j\right\}$. We now define the following functions

$$R_i^m \equiv \epsilon \, \chi_{\tilde{Q}}(i) \sum_{k=1}^{L} \chi_{\tilde{Q}}(k) \bar{q}_k,$$

$$R_j^f \equiv \epsilon \, \chi_{\tilde{Q}}(j) \sum_{k=1}^{N} \chi_{\tilde{Q}}(k) \bar{p}_k,$$

where χ denotes the characteristic (or indicator function) of a set, and note that

$$\sum_{i=1}^{L} R_i^m \bar{q}_i = \epsilon \left(\sum_{k=1}^{L} \chi_{\tilde{Q}}(k) \bar{q}_k \right)^2, \tag{25}$$

and

$$\sum_{j=1}^{N} R_j^f \bar{p}_j = \epsilon \left(\sum_{k=1}^{N} \chi_{\tilde{Q}}(k) \bar{p}_k \right)^2. \tag{26}$$

Hence

$$\frac{R_j^f R_i^m}{\sum_{k=1}^{N} \bar{p}_k R_k^f} = \epsilon \, \chi_{\tilde{Q}}(i) \chi_{\tilde{Q}}(j) \, \frac{\sum_{k=1}^{L} \chi_{\tilde{Q}}(k) \bar{q}_k}{\sum_{k=1}^{N} \chi_{\tilde{Q}}(k) \bar{p}_k} \tag{27}$$

and

$$\frac{R_j^f R_i^m}{\sum_{k=1}^{L} R_k^m \bar{q}_k} = \epsilon\, \chi_{\tilde{Q}}(i)\chi_{\tilde{Q}}(j)\, \frac{\sum_{k=1}^{N} \chi_{\tilde{Q}}(k)\bar{p}_k}{\sum_{k=1}^{L} \chi_{\tilde{Q}}(k)\bar{q}_k}. \tag{28}$$

Now let

$$\phi_{ij}^m \equiv \frac{p_{ij}}{\bar{p}_j} - \epsilon\, \chi_{\tilde{Q}}(i)\chi_{\tilde{Q}}(j)\, \frac{\sum_{k=1}^{L} \chi_{\tilde{Q}}(k)\bar{q}_k}{\sum_{k=1}^{N} \chi_{\tilde{Q}}(k)\bar{p}_k},$$

and

$$\phi_{ji}^f \equiv \frac{q_{ij}}{\bar{q}_j} - \epsilon\, \chi_{\tilde{Q}}(i)\chi_{\tilde{Q}}(j)\, \frac{\sum_{k=1}^{N} \chi_{\tilde{Q}}(k)\bar{p}_k}{\sum_{k=1}^{L} \chi_{\tilde{Q}}(k)\bar{q}_k}.$$

From the last two expressions we see that

$$\sum_{j=1}^{N} \phi_{ij}^m \bar{p}_j = 1 - \epsilon\, \chi_{\tilde{Q}}(i) \sum_{k=1}^{L} \chi_{\tilde{Q}}(k)\bar{q}_k = l_i^m,$$

and

$$\sum_{j=1}^{L} \phi_{ji}^f \bar{q}_i = 1 - \epsilon\, \chi_{\tilde{Q}}(j) \sum_{k=1}^{N} \chi_{\tilde{Q}}(k)\bar{p}_k = l_j^f .$$

Further, since

$$\phi_{ij}^m - \phi_{ji}^f = \epsilon\, \chi_{\tilde{Q}}(i)\chi_{\tilde{Q}}(j) \left[\frac{\sum_{k=1}^{N} \chi_{\tilde{Q}}(k)\bar{p}_k}{\sum_{k=1}^{L} \chi_{\tilde{Q}}(k)\bar{q}_k} - \frac{\sum_{k=1}^{L} \chi_{\tilde{Q}}(k)\bar{q}_k}{\sum_{k=1}^{N} \chi_{\tilde{Q}}(k)\bar{p}_k} \right],$$

using (25) -(28), we see that Equation (22) is automatically satisfied.

Hence, we have established the following results:

Theorem 2. Let $\{\phi_{ij}^m\}$ and $\{\phi_{ji}^f\}$ be two nonegative matrices. Let $\ell_i^m \equiv \sum_{k=1}^{N} \bar{p}_k \phi_{ik}^m$ and $\ell_j^f \equiv \sum_{k=1}^{L} \bar{q}_k \phi_{jk}^f$ where $\{(\bar{p}_j,\bar{q}_i)\ j = 1,\ldots,N \text{ and } i = 1,\ldots,L\ \}$ denotes the set composed of Ross's solutions. We also let $R_i^m \equiv 1 - \ell_i^m,\ i = 1, \cdots, L$ and $R_j^f \equiv 1 - \ell_j^f,\ j = 1, \cdots, N$, and assume that ϕ_{ij}^m and ϕ_{ji}^f are chosen in such a way that R_i^m and R_j^f remain nonnegative for all time. We further assume that

$$\sum_{i=1}^{L} \ell_i^m \bar{p}_i = \sum_{i=1}^{L} \sum_{k=1}^{N} \bar{p}_k \phi_{ik}^m \bar{p}_i < 1,$$

and

$$\sum_{j=1}^{N} \ell_j^f \bar{q}_j = \sum_{j=1}^{N} \sum_{k=1}^{L} \bar{q}_k \phi_{jk}^f \bar{q}_j < 1 .$$

Then all the solutions to axioms (A1)-(A4) are given by Equations (18) and (19).

<u>Remark</u>: ϕ_{ij}^m and ϕ_{ji}^f can always be chosen in such a way that R_i^m and R_j^f remain nonnegative for all time (i.e., let them be in the interval [0,1]). However, there is no recipe for specifying necessary conditions for the nonnegativity of R_i^m and R_j^f because their values are intimately connected to the time-dependent values of Ross's solutions, and hence to the dynamical system.

<u>Corollary:</u> If either $\phi_{ij}^m = \alpha$, $0 \leq \alpha < 1$, $\forall$ i, j or if $\phi_{ji}^f = \beta$, $0 \leq \beta < 1$, $\forall$ i, j then Equations (23) and (24) provide one-sex preferential solutions.

<u>Remarks:</u> 1. In the one-sex framework, the only separable solution is proportionate mixing. Here, solutions can be separable in one sex and not the other. These solutions, where one sex chooses while the other does not, are applicable to models for vector-transmitted diseases in which the vector exhibits strong host preference, while the host is just a "moving" target.

2. Several other one-sex special solutions have been discussed in the literature. These include "preferred" mixing, like-with-like mixing, etc. (see Nold 1980, Hethcote and Yorke 1984, Blythe and Castillo-Chavez 1989, Castillo-Chavez and Blythe 1989, Jacquez et al. 1988, 1989, Hyman and Stanley 1989, Gupta et al. 1989, Blythe et al. 1989, etc.). Blythe and Castillo-Chavez (1990a) have established explicitly that all these solutions are special cases of the general solution found in Busenberg and Castillo-Chavez (1989, 1990).

3. The gonorrhea model found in this section, but for one-sex populations, was introduced (along with some generalizations) by Castillo-Chavez and Blythe (1990) as a simple device to

easily test mixing patterns. A thorough numerical analysis of these mixing matrices (one-sex framework) is found in Blythe and Castillo-Chavez (1990b). A discussion of methods for estimating the mixing matrices (one-sex framework) from data can be found in Blythe et al. (1990).

4. Two-sex age-structured models

We formulate two-sex models of the SI type with age-structur[redacted]. [redacted]. Extensions to models for other diseases such as AIDS or gonorrhea that require a different epidemiological and compartmental structure can be easily formulated following the approach found in Busenberg and Castillo-Chavez (1989, 1990) and Castillo-Chavez et al. (1990). To formulate these models, we need a description of mixing functions that incorporate age (risk can be easily incorporated, see loc. cits.). Pairing is defined through the mixing functions:

$p(a,a',t)$ = proportion of partnerships of males of age a with females of age a' at time t,

$q(a,a',t)$ = proportion of partnerships of females of age a' with males of age a at time t,

and we let

$C(a,t)$ = expected or average number of partners of a male of age a at time t per unit time,

$D(a',t)$ = expected or average number of partners of a female of age a' at time t per unit time,

The following natural conditions characterize these mixing functions:

(B1) $p, q \geq 0$,

(B2) $\int_0^\infty p(a, a', t)da = \int_0^\infty q(a', a, t)da = 1$, if $C(a,t)T^m(a,t) \neq 0$

(B3) $p(a,a', t)C(a,t)T^m(a,t) = q(a',a,t)D(a',t)T^f(a',t)$,

(B4) $C(a,t)T^m(a,t)\,D(a',t)T^f(a',t) = 0 \Rightarrow p(a,a',t) = q(a',a,t) = 0$,

Condition (B2) is due to p and q being proportions. Condition (B3) simply states that the total number of pairs of males of age a with females of age a′ equals the total number of pairs of females of age a′ with males of age a (all per unit time and age). Condition (B4) says that there is no mixing in the age and activity levels where there are no active individuals; i.e., on the set $\mathcal{S}(t) = \{(a,a',t): C(a,t)T^m(a,t)D(a',t)T^f(a',t) = 0\}$. This last condition is usually <u>vacuously</u> satisfied in most applications. The need to state it derives from the proof of Representation Theorem (Theorem 2).

The pair (p,q) is called a *two-sex mixing function* iff it satisfies axioms (B1-B4). Further, a two-sex mixing function is called *separable* iff

$$p(a,a',t) = p_1(a,t)\, p_2(a',t) \quad \text{and} \quad q(a,a',t) = q_1(a,t)\, q_2(a',t)\,.$$

If we let

$$h_p(a,t) = C(a,t)T^m(a,t) \tag{29}$$

and

$$h_q(a',t) = D(a',t)T^f(a',t) \tag{30}$$

then, omitting t to simplify the notation, we establish the following result:

<u>Theorem</u> 3: The only two-sex Ross's (separable) mixing function satisfying conditions (B1-B4) is given by $(\overline{p},\overline{q})$, where

$$\overline{p}(a') = \frac{h_q(a')}{\int_0^\infty h_p(u)du}, \tag{31}$$

$$\overline{q}(a) = \frac{h_p(a)}{\int_0^\infty h_q(u)du} . \tag{32}$$

The proof is found in Castillo-Chavez et al. (1990). X

If we now let m(a,t) denote the density of (uninfected) males of age a who are not in pairs at time t, and let f(a′,t) denote the density of (uninfected) females of age a′ who are not in pairs at time t. If we assume that D and C (as defined above) and μ_m and μ_f are functions of age (the mortality rates for males and females), σ denotes the constant rate of separation, and we assume that w(a,a′,t) denotes the age-specific density of heterosexual (uninfected) pairs (where a denotes the age of the male and a′ the age of the female). Using the two-sex mixing functions p and q, we arrive at the following demographic model for heterosexual (uninfected) populations:

$$\frac{\partial m}{\partial t} + \frac{\partial m}{\partial a} = -C(a)m(a,t) \int_0^\infty p(a,a',t)da'$$

$$- \mu_m(a)m(a,t) + \int_0^\infty [\mu_f(a') + \sigma]w(a,a',t)da' , \tag{33}$$

$$\frac{\partial f}{\partial t} + \frac{\partial f}{\partial a'} = -D(a')f(a',t) \int_0^\infty q(a',a,t)da$$

$$- \mu_f(a')f(a',t) + \int_0^\infty [\mu_m(a) + \sigma]w(a,a',t)da , \tag{34}$$

$$\frac{\partial w}{\partial t} + \frac{\partial w}{\partial a} + \frac{\partial w}{\partial a'} = D(a')f(a',t)q(a,a',t)$$

$$- [\mu_f(a') + \mu_m(a) + \sigma]w(a,a',t) . \tag{35}$$

To complete this model we need to specify the initial and boundary conditions. To this effect we let λ_m and λ_f denote the female age- and sex-specific fertility rates, and let m_o, f_o, and w_o denote the intial age densities. Hence, the initial and boundary conditions are given by

$$m(0,t) = \int_0^\infty \lambda_m(a')w(a,a',t)da' , \tag{36}$$

$$f(0,t) = \int_0^\infty \lambda_f(a')w(a,a',t)da' , \tag{37}$$

$$w(0,0,t) = 0 \tag{38}$$

$$f(a,0) = f_o(a), \;\; m(a,0) = m_o(a), \;\; w(a,a',0) = w_o(a,a'). \tag{39}$$

A preliminary analysis of this demographic model is found in Castillo-Chavez et al. (1990). If we let $\sigma \to \infty$ then (formally) the above system approaches the classical MacKendrick/Von Foerster model (see loc. cit.). This demographic model, in conjunction with the MacKendrick/Von Foerster model, will be used to formulate epidemiological models through the usual creation of the appropriate epidemiological compartments (see Hoppensteadt 1974, Dietz 1988, Dietz and Hadeler 1988, Castillo-Chavez 1989).

We begin by letting $T^m(a,t)$ and $T^f(a',t)$ denote, respectively, the male and female densities of single infected individuals. Hence, the densitities for heterosexual pairs are denoted by: $w_{mf}(a,a',t)$, $w_{Mf}(a,a',t)$, $w_{mF}(a,a',t)$, and $w_{MF}(a,a',t)$. If we use the earlier notation with the <u>appropriate indexing</u> (that is, f, m, F, or M), we then arrive at the following epidemiological model that follows pairs:

Y ∧

$$\frac{\partial m(a,t)}{\partial t} + \frac{\partial m(a,t)}{\partial a} = - C_{mf}(a,t)m(a,t) \int_0^\infty p_{mf}(a,a',t)da'$$

$$- C_{mF}(a,t)m(a,t) \int_0^\infty p_{mF}(a,a',t)da' - \mu_m(a)m(a,t)$$

$$+ \int_0^\infty \left[\mu_f(a') + \sigma(a',a)\right] w_{mf}(a,a',t)da' + \int_0^\infty \left[\mu_F(a') + \sigma(a',a)\right] w_{mF}(a,a',t)da', \tag{40}$$

X a

$$\frac{\partial f(a',t)}{\partial t} + \frac{\partial f(a',t)}{\partial a'} = - D_{fm}(a',t)f(a',t) \int_0^\infty q_{fm}(a',a,t)da$$

$$- D_{fM}(a',t)f(a',t) \int_0^\infty q_{fM}(a',a,t)da - \mu_f(a')f(a',t) +$$

$$\int_0^\infty \left[\mu_m(a) + \sigma(a',a)\right] w_{mf}(a,a',t)da + \int_0^\infty \left[\mu_M(a) + \sigma(a',a)\right] w_{Mf}(a,a',t)da, \tag{41}$$

$$\frac{\partial M(a,t)}{\partial t} + \frac{\partial M(a,t)}{\partial a} = - C_{Mf}(a,t)M(a,t) \int_0^\infty p_{Mf}(a,a',t)da'$$

$$- C_{MF}(a,t)M(a,t) \int_0^\infty p_{MF}(a,a',t)da' - \mu_M(a)M(a,t)$$

$$+ \int_0^\infty \left[\mu_f(a') + \sigma(a,a)\right] w_{Mf}(a,a',t)da' + \int_0^\infty \left[\mu_F(a') + \sigma(a',a)\right] w_{MF}(a,a',t)da', \tag{42}$$

$$\frac{\partial F(a',t)}{\partial t} + \frac{\partial F(a',t)}{\partial a'} = - D_{Fm}(a',t)F(a',t) \int_0^\infty q_{Fm}(a,a',t)da$$

$$- D_{FM}(a',t)F(a',t) \int_0^\infty q_{FM}(a,a',t)da - \mu_F(a')F(a',t)$$

$$+ \int_0^\infty \left[\mu_m(a) + \sigma(a',a)\right] w_{mF}(a,a',t)da + \int_0^\infty \left[\mu_M(a) + \sigma(a',a)\right] w_{MF}(a,a',t)da, \tag{43}$$

$$\frac{\partial w_{fm}(a,a',t)}{\partial a} + \frac{\partial w_{fm}}{\partial a'} + \frac{\partial w_{fm}}{\partial t} = D_{fm}(a')f(a',t)q_{fm}(a',a,t) - (\sigma(a',a) + \mu_m(a) + \mu_f(a'))w_{fm}, \tag{44}$$

$$\frac{\partial w_{Fm}(a,a',t)}{\partial a} + \frac{\partial w_{Fm}}{\partial a'} + \frac{\partial w_{Fm}}{\partial t} = D_{Fm}(a')f(a',t)q_{Fm}(a',a,t) - (\sigma(a',a) + \mu_m(a) + \mu_F(a'))w_{Fm}, \tag{45}$$

$$\frac{\partial w_{fM}(a,a',t)}{\partial a} + \frac{\partial w_{fM}}{\partial a'} + \frac{\partial w_{fM}}{\partial t} = D_{fM}(a')f(a',t)q_{fM}(a',a,t) - (\sigma(a',a) + \mu_M(a) + \mu_f(a'))w_{fM}, \tag{46}$$

$$\frac{\partial w_{FM}(a,a',t)}{\partial a} + \frac{\partial w_{FM}}{\partial a'} + \frac{\partial w_{FM}}{\partial t} = D_{FM}(a')f(a',t)q_{FM}(a',a,t) - (\sigma(a',a) + \mu_M(a) + \mu_F(a'))w_{FM}, \tag{47}$$

with apropriate initial and boundary conditions (see Castillo-Chavez 1989). It is important to note that we have used "restricted" mixing functions, that is, mixing functions that deal exclusively with certain "pairs" (namely, mf, fM, Mf, and M F), and hence the mixing axioms (B1)-(B4) have to be re-interpreted in this context (see loc. cit.).

An SI model that does not follow pairs but individuals is therefore given by the following set of equations:

$$\frac{\partial m(a,t)}{\partial t} + \frac{\partial m}{\partial a} = - C_m(a,t)m(a,t) \int_0^\infty \beta_{Fm}(a,a')p_{(m+M)(f+F)}(a,a',t) \, \frac{F(a',t)}{F(a',t) + f(a',t)} \, da' - \mu_m(a)m(a,t), \tag{48}$$

$$\frac{\partial f(a',t)}{\partial t} + \frac{\partial f}{\partial a'} = - D_f(a',t)f(a',t) \int_0^\infty \beta_{Mf}(a,a')q_{(f+F)(m+M)}(a,a',t) \, \frac{M(a,t)}{M(a,t) + m(a,t)} \, da - \mu_m(a)f(a',t), \tag{49}$$

$$\frac{\partial M(a,t)}{\partial t} + \frac{\partial M}{\partial a} = + C_m(a,t)m(a,t) \int_0^\infty \beta_{Fm}(a,a')p_{(m+M)(f+F)}(a,a',t) \, \frac{F(a',t)}{F(a',t) + f(a',t)} \, da' - \mu_M(a)M(a,t), \tag{50}$$

$$\frac{\partial F(a',t)}{\partial t} + \frac{\partial F}{\partial a'} = + D_f(a,t)f(a',t) \int_0^\infty \beta_{Mf}(a,a')q_{(f+F)(m+M)}(a,a',t) \, \frac{M(a,t)}{M(a,t) + m(a,t)} \, da - \mu_F(a')F(a',t) \, , \tag{51}$$

where $\beta_{Fm}(a',a)$ and $\beta_{Mf}(a,a')$ represent the appropriate transmission coefficients. For a detailed derivation of the above model for one-sex populations see Busenberg and Castillo-Chavez (1989, 1990).

and for the determination of the endemic threshold criterion of this model

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5. Conclusion

In this paper we have found a representation theorem for the general solution of the two-sex mixing problem. This representation theorem is based on multiplicative perturbations of Ross's solutions.

Special solutions that allow for one-sex preferential sexual systems were described explicitly. The application of these special solutions to vector-transmitted diseases is being carried out (see Castillo-Chavez and Blythe, 1990). We have also formulated a model of the SIS type for a discrete number of groups that can be easily explored. We outline generalizations to age-structured populations through the introduction of two epidemiological models that incorporate this mixing framework at the level of individual interactions or at the level of pair dynamics. We point out that although models of this type have been formulated before (see Dietz 1988, Dietz and Hadeler 1988, Castillo-Chavez 1989) this is the first time that they have been formulated explicitly under a unified framework.

Finally, we note that S. P. Blythe (1990) has shown that our original solution (Busenberg and Castillo-Chavez, 1989, 1990) provides a representation theorem for the n-sex problem. Nevertheless, the separation of the mixing into two mixing matrices (p and q) provides useful results (such as one-sex preferential solutions, Equations 23 and 24) that are not immediate from our original formulation. This extra information arises from the breaking up of the group reversibility property (Axiom A3) through the use of the connectivity properties of the groups involved (in the version in this paper, for example, individuals of the same sex do not mix, that is, same sex groups are not connnected).

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