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# HOMOGENEOUS MODELS FOR SEXUALLY TRANSMITTED DISEASES

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ABSTRACT. A system of eight ordinary differential equations describes birth, death, formation of pairs, separation, and transmission of a sexually transmitted disease. Here, in contrast to an earlier version of the model by Dietz and Hadeler, the recruitment process is coupled to the actual population size. Nevertheless, as in most demographic models, the equations are assumed homogeneous. There is a noninfected exponentially growing persistent solution which is stable (in the sense of the stability theory for homogeneous equations) for low rates of pair formation and low infectivity. If these parameters are increased, this state may lose stability, a stable persistent solution describing an infected population bifurcates. The exact bifurcation thresholds are derived in terms of the epidemiologically relevant parameters.

**1. Introduction.** In several recent publications Dietz and Hadeler [5, 6] have discussed a model for sexually transmitted diseases. (For other recent work in this direction see [1, 4, 7, 14, 15]. In this model the social structure is taken into account. Since a strict pair is practically temporarily immune against infection, in a population with a large number of pairs, the spread of the disease is much slower than in a population with random sexual contacts. In these papers it has been assumed that the process of recruitment of young individuals acts on a much slower time scale than the infection process. Thus it has been assumed that the population is renewed with a constant rate, independent of the actual population size. But in some diseases the time scale of the epidemic process has the same order of magnitude as the demographic processes (see also Anderson et al. [1]), and the spread of the disease has a marked impact on the demographic evolution. In the present work we consider essentially the same model, but we assume that the number of newly recruited individuals is proportional to the actual population size. As in Dietz and Hadeler [6], we obtain a system of eight ordinary differential equations for the different classes of individuals. In this case the right-hand side of the differential system

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is homogeneous of degree 1. Therefore, in general, stationary solutions cannot be expected. As in the theory of age-structured populations (renewal equations), the distinguished solutions of mathematical and biological interest are the persistent solutions. In two recent papers [10, 11], a framework for the discussion of existence and stability of persistent solutions of nonlinear homogeneous differential equations has been developed. The same papers contain a qualitative theory of pair formation models for noninfected populations, which completes the discussion of models of Kendall [12], Keyfitz [13], and others (see Hadeler et al. [11] for further references and Hadeler [11]). We present the results so far as they are needed here.

In the model for sexually transmitted diseases we assume that the demographic parameters are such that a noninfected persistent two-sex population exists. This solution shows constant proportions of male and female singles and of pairs. As a function of time, this solution is exponential. Depending on the demographic parameters, the exponent may be positive or nonpositive. If certain parameters such as the infectivity or the rate of pair formation are increased, this solution may lose its stability and an infected persistent solution bifurcates. In general the bifurcating, stable infected solution has the smaller exponent of growth reflecting the fact that the infected individuals have a higher mortality and lower fertility.

**2. Homogeneous evolution equations.** Assume that the function $f : \mathbf{R}^n \to \mathbf{R}^n$ is Lipschitz continuous, continuously differentiable on $\mathbf{R}^n \setminus \{0\}$, and homogeneous of degree 1, i.e.,

$$f(\alpha x) = \alpha f(x) \quad \text{for} \quad \alpha \in \mathbf{R}. \tag{2.1}$$

Consider the differential equation

$$\dot{x} = f(x). \tag{2.2}$$

Necessarily, $x = 0$ is a stationary point. Hence a solution $x = x(t)$ with $x(0) \neq 0$ satisfies $x(t) \neq 0$ for all $t \in \mathbf{R}$.

Equations of the form (2.1), (2.2), which preserve positivity are of particular importance. Let $\mathbf{R}^n_+$ be the usual cone and assume that the flow of equation (2.2) leaves $\mathbf{R}^n_+$ invariant,

$$x \geq 0, \quad x_i = 0 \Longrightarrow f_i(x) \geq 0. \tag{2.3}$$

Then one can introduce the variable

$$z = \frac{x}{e^* x} \qquad \text{for} \qquad x \in \mathbf{R}^n_+ \backslash \{0\}, \tag{2.4}$$

where $e^* = (1, \ldots, 1)$. If $x$ is a solution of equation (2.2) on $\mathbf{R}^n_+ \backslash \{0\}$, then $z$ satisfies

$$\dot{z} = f(z) - e^* f(z) z \tag{2.5}$$

on the simplex

$$S = \{z \geq 0, e^* z = 1\}. \tag{2.6}$$

If $z$ is a solution of equation (2.5), then the corresponding solutions of equation (2.2) are

$$x(t) = z(t) \exp \left\{ \int_0^t e^* f(z(s))\, ds \right\} e^* x(0). \tag{2.7}$$

Suppose $\overline{z} \in S$ is a stationary solution of equation (2.5). Then $\overline{z}$ is a solution of the nonlinear eigenvalue problem

$$f(\overline{z}) = \hat{\lambda} \overline{z}, \tag{2.8}$$

where

$$\hat{\lambda} = e^* f(\overline{z}). \tag{2.9}$$

The corresponding solutions of equation (2.2) are exponential solutions of the form

$$x(t) = \overline{z} e^{\hat{\lambda} t} e^* x(0). \tag{2.10}$$

Next we discuss the stability of the stationary points of the system (2.5). The Jacobian of the vector field (2.5) at any point $z$ is

$$J(z) = f'(z) - z e^* f'(z) - e^* f(z) I. \tag{2.11}$$

Let $\overline{z}$ be a stationary point. From (2.8) and (2.1) it follows that

$$f'(\overline{z}) \overline{z} = \hat{\lambda} \overline{z} \tag{2.12}$$

and furthermore

$$J(\overline{z}) = f'(\overline{z}) - \overline{z}e^* f'(\overline{z}) - \hat{\lambda}I. \tag{2.13}$$

The stationary point is linearly stable if all eigenvalues of the Jacobian are located in the left half-plane. This property of the Jacobian can be traced back to the eigenvalues of $f'(\overline{z})$. In Hadeler, Waldstätter, Wörz-Busekros [11] the following has been shown: If the eigenvalues of $f'(\overline{z})$ are numbered $\lambda_1 = \hat{\lambda}, \lambda_2, \ldots, \lambda_n$, multiplicities counted, then $\overline{z}$ is a linearly stable stationary point of (2.5) if the numbers $\lambda_i - \hat{\lambda}, i = 2, \ldots, n$, are located in the left half-plane. Hence the eigenvalues of $J(\overline{z})$ which determine stability with respect to the flow on $S$ are just the numbers $\lambda - \hat{\lambda}$, where $\lambda$ runs over the eigenvalues $\lambda_2, \ldots, \lambda_n$ of $f'(\overline{z})$.

**3. Models of pair formation.** Now we describe the model for pair formation introduced in Hadeler et al. [11]. It includes birth and death, formation of pairs and separation. Since age structure is not considered, formally newborns are immediately forming pairs. If this assumption is not appropriate, then "birth" should be interpreted as entering the sexually active phase of life.

The state of the population is described by three variables. Let $x, y$ be the densities of female and male singles, respectively, and let $p$ be the density of pairs.

Let $\kappa_x, \kappa_y$ be the birth rates and $\mu_x, \mu_y$ the death rates of females and males, respectively. Let $\sigma$ be the rate of separation of pairs. These constants are all positive. The formation of pairs is described by a function $\varphi : \mathbf{R}_+^2 \to \mathbf{R}_+$ which satisfies the following conditions:

(1) Preservation of positivity. $\varphi(x, 0) = \varphi(0, y) = 0$ for all $x, y \geq 0$,

(2) Homogeneity. $\varphi(\alpha x, \alpha y) = \alpha\varphi(x, y)$ for $\alpha \geq 0$,

(3) Monotonicity. $u \geq 0, v \geq 0 \Rightarrow \varphi(x + u, y + v) \geq \varphi(x, y)$.

For simplicity we call $\varphi$ the mating function or the marriage function.

The function $\varphi$ is assumed to be locally Lipschitz continuous on $\mathbf{R}_+^2$ and continuously differentiable on $\mathbf{R}_+^2 \setminus \{0\}$. In view of the homogeneity, $\varphi$ is necessarily linear on the diagonal, i.e.,

$$\varphi(x, x) = \rho x, \quad \rho > 0. \tag{3.1}$$

Of special interest is the symmetric case where the rates do not depend on the sex and $\varphi$ is symmetric,

$$\varphi(x,y) = \varphi(y,x) \qquad \text{for all } x, y. \tag{3.2}$$

In the later sections we shall use only the harmonic mean function

$$\varphi(x,y) = \rho \frac{xy}{\beta x + (1-\beta)y}, \tag{3.3}$$

in particular, for $\beta = 1/2$,

$$\varphi(x,y) = 2\rho \frac{xy}{x+y}. \tag{3.4}$$

With these assumptions the model for a two-sex population is given by the following three differential equations:

$$\begin{aligned} \dot{x} &= (\kappa_x + \mu_y + \sigma)p - \mu_x x - \varphi(x,y), \\ \dot{y} &= (\kappa_y + \mu_x + \sigma)p - \mu_y y - \varphi(x,y), \\ \dot{p} &= -(\mu_x + \mu_y + \sigma)p + \varphi(x,y). \end{aligned} \tag{3.5}$$

Thus, "singles" are "produced" by birth, death of a partner and separation; they are removed by mating.

In view of the properties of the function $\varphi$ and the sign of the coefficients the system is homogeneous and the positive cone $\mathbf{R}^3_+$ is positively invariant.

If the system (3.5) is interpreted as a system of the form (2.2), then the corresponding system (2.5) is a dynamical system on the two-dimensional triangle

$$S = \{x \geq 0, y \geq 0, p \geq 0, x + y + p = 1\}, \tag{3.6}$$

$$\begin{aligned} \dot{x} &= (\kappa_x + \mu_y + \sigma)p - \mu_x x - \varphi(x,y) - \phi(x,y,p)x, \\ \dot{y} &= (\kappa_y + \mu_x + \sigma)p - \mu_y y - \varphi(x,y) - \phi(x,y,p)y, \\ \dot{p} &= -(\mu_x + \mu_y + \sigma)p + \varphi(x,y) - \phi(x,y,p)p, \end{aligned} \tag{3.7}$$

where

$$\phi(x,y,p) = (\kappa_x + \kappa_y + \sigma)p - \mu_x x - \mu_y y - \varphi(x,y). \tag{3.8}$$

We shall present our results on the qualitative analysis mainly in terms of this system (3.7).

For the equation (3.5), the nonlinear eigenvalue problem reads

$$\begin{aligned}(\kappa_x+\mu_y+\sigma)\overline{p}-(\mu_x+\lambda)\overline{x}&=\varphi(\overline{x},\overline{y}),\\ (\kappa_y+\mu_x+\sigma)\overline{p}-(\mu_y+\lambda)\overline{y}&=\varphi(\overline{x},\overline{y}),\\ (\mu_x+\mu_y+\sigma+\lambda)\overline{p}&=\varphi(\overline{x},\overline{y}).\end{aligned}\tag{3.9}$$

There are two trivial solutions,

$$(1,0,0)\quad\text{with}\quad\lambda=-\mu_x,\quad(0,1,0)\quad\text{with}\quad\lambda=-\mu_y,\tag{3.10}$$

and at most one two-sex stationary solution. This solution exists if and only if the following condition is satisfied:

$$\mu_y>\mu_x-\frac{\kappa_x\varphi_x(0,1)}{\mu_x+\sigma+\varphi_x(0,1)},\quad \mu_x>\mu_y-\frac{\kappa_y\varphi_y(1,0)}{\mu_y+\sigma+\varphi_y(1,0)}.\tag{3.11}$$

When the two-sex stationary solution exists (in $S$) then it is globally attracting in $S$ (of course with the exception of the two trivial stationary points). In the other case, one of the two trivial stationary states is globally attracting (with the exception of the other trivial stationary state).

Hence, in loose terms, we can state the result as follows: If $\kappa_x,\kappa_y,\sigma$ and $\varphi$ are fixed, then the positive stationary solution exists and is globally attracting in the set $S$ (except the two one-sex points) if $\mu_x$ and $\mu_y$ do not differ too much. If, say, $\mu_x$ becomes large, then the positive stationary state moves towards $(0,1,0)$ and leaves the triangle at that point with an exchange of stability to $(0,1,0)$. Hence, the population approximates an all-male population. The latter dies out since its exponent is $-\mu_y$.

In the symmetric case

$$\kappa_x=\kappa_y=\kappa,\quad\mu_x=\mu_y=\mu,\quad\varphi(x,y)=\varphi(y,x),\tag{3.12}$$

the conditions (3.11) are trivially satisfied, and there is a globally attracting positive stationary solution $(\overline{x},\overline{x},\overline{p})$ which is easily obtained from (3.1), i.e., $(\rho=\varphi(1,1))$,

$$\begin{aligned}(\kappa+\mu+\sigma)\overline{p}-(\mu+\lambda)\overline{x}&=\rho\overline{x},\\ (2\mu+\sigma+\lambda)\overline{p}&=\rho\overline{x},\end{aligned}$$

hence

$$\hat{\lambda} = -\frac{3\mu + \sigma + \rho}{2} + \frac{1}{2}[(\mu + \sigma + \rho)^2 + 4\rho\kappa]^{1/2} \tag{3.13}$$

and

$$\frac{\overline{x}}{\overline{p}} = \frac{2\mu + \sigma + \lambda}{\rho}. \tag{3.14}$$

The total population does not decay if the exponent $\hat{\lambda}$ is positive. The exponent is positive if and only if

$$\kappa > \mu + \frac{\mu}{\rho}(\sigma + 2\mu). \tag{3.15}$$

In the case of the harmonic mean function,

$$\varphi_x(0,1) = \frac{\rho}{1-\beta}, \quad \varphi_y(1,0) = \frac{\rho}{\beta}. \tag{3.16}$$

Here the positive stationary solution exists if

$$\begin{aligned} \mu_y &> \mu_x - \frac{\kappa_x \rho}{(1-\beta)(\mu_x + \sigma) + \rho}, \\ \mu_x &> \mu_y - \frac{\kappa_y \rho}{\beta(\mu_y + \sigma) + \rho}. \end{aligned} \tag{3.17}$$

There is no explicit formula for the positive stationary solution. The exponent $\hat{\lambda}$ is a root of the cubic equation

$$\begin{aligned} &\rho(\kappa_x - \mu_x - \lambda)(\kappa_y - \mu_y - \lambda) \\ &\quad = (\mu_x + \mu_y + \sigma + \lambda)[\beta\kappa_x(\mu_y + \lambda) + (1-\beta)\kappa_y(\mu_x + \lambda) \\ &\qquad\qquad - (\mu_x + \lambda)(\mu_y + \lambda)]. \end{aligned}$$

In the symmetric case this equation reduces to

$$\rho(\kappa - \mu - \lambda)^2 = (2\mu + \sigma + \lambda)(\kappa - \mu - \lambda)(\mu + \lambda)$$

which immediately leads to (3.13).

**4. The model for sexually transmitted diseases.** Each individual of the population carries three dichotomous characters: female-male, single-paired, noninfected-infected. Hence there are eight types of individuals. We shall work with the frequencies of pairs rather than with the frequencies of paired individuals:

$$
\begin{aligned}
x_0 &\quad \text{female, single, noninfected,}\\
y_0 &\quad \text{male, single, noninfected,}\\
x_1 &\quad \text{female, single, infected,}\\
y_1 &\quad \text{male, single, infected,}\\
p_{00} &\quad \text{pair, both partners noninfected,}\\
p_{01} &\quad \text{pair, only male infected,}\\
p_{10} &\quad \text{pair, only female infected,}\\
p_{11} &\quad \text{pair, both partners infected.}
\end{aligned}
\tag{4.1}
$$

The sex ratio among the offspring is assumed constant, defined by the parameters $\kappa_x, \kappa_y$. The fertility of a pair depends on the state of infection. Let $\nu_{ij}$ be the relative fertility of a pair $p_{ij}$, $i, j = 0, 1$, $\nu_{00} = 1$. The death rate can depend on sex and state of infection: $\mu_{x0}$ for noninfected females, $\mu_{x1}$ for infected females, $\mu_{y0}$ for noninfected males and $\mu_{y1}$ for infected males.

Pair formation is described by the harmonic mean law of pair formation (3.4) in the form

$$
\varphi_{ij}(x_0, y_0, x_1, y_1) = \frac{2\rho_{ij} x_i y_j}{x_0 + y_0 + x_1 + y_1}, \quad i, j, = 0, 1, \tag{4.2}
$$

which contains only the four constants $\rho_{ij}$, $i, j = 0, 1$. Thus $\varphi_{ij}(x_0, y_0, x_1, y_1)\Delta t + o(\Delta t)$ is the formation rate of pairs of type $p_{ij}$ during a time interval $\Delta t > 0$. The rate of separation of pairs of type $p_{ij}$ is $\sigma_{ij}$, $i, j = 0, 1$. By definition, pair formation starts with *one* sexual contact.

Let $\beta$ be the rate of sexual contacts within a pair. Infection of a partner may occur at pair formation or during the time of existence of a pair. Let $h_x$ be the probability that an infected female infects a susceptible male during one sexual contact, and $h_y$ the corresponding probability for an infected male. Finally, let $\gamma_x$ and $\gamma_y$ be the rates of recovery for an infected female or male, respectively. All parameters are assumed to be nonnegative.

Thus the equations assume the following form:

(4.3)
$$\begin{aligned}
\dot{x}_0 &= \kappa_x(\nu_{00}p_{00} + \nu_{01}p_{01} + \nu_{10}p_{10} + \nu_{11}p_{11}) - \mu_{x0}x_0 + \gamma_x x_1 \\
&\quad + (\mu_{y0} + \sigma_{00})p_{00} + (\mu_{y1} + \sigma_{01})p_{01} - (\varphi_{00} + \varphi_{01}) \\
\dot{y}_0 &= \kappa_y(\nu_{00}p_{00} + \nu_{01}p_{01} + \nu_{10}p_{10} + \nu_{11}p_{11}) - \mu_{y0}y_0 + \gamma_y y_1 \\
&\quad + (\mu_{x0} + \sigma_{00})p_{00} + (\mu_{x1} + \sigma_{10})p_{10} - (\varphi_{00} + \varphi_{10}) \\
\dot{x}_1 &= -\mu_{x1}x_1 - \gamma_x x_1 + (\mu_{y0} + \sigma_{10})p_{10} + (\mu_{y1} + \sigma_{11})p_{11} - (\varphi_{10} + \varphi_{11}) \\
\dot{y}_1 &= -\mu_{y_1}y_1 - \gamma_y y_1 + (\mu_{x0} + \sigma_{01})p_{01} + (\mu_{x1} + \sigma_{11})p_{11} - (\varphi_{01} + \varphi_{11}) \\
\dot{p}_{00} &= -(\mu_{x0} + \mu_{y0} + \sigma_{00})p_{00} + \gamma_x p_{10} + \gamma_y p_{01} + \varphi_{00} \\
\dot{p}_{01} &= -(\mu_{x0} + \mu_{y1} + \sigma_{01})p_{01} + \gamma_x p_{11} - \gamma_y p_{01} - h_y\beta p_{01} + (1 - h_y)\varphi_{01} \\
\dot{p}_{10} &= -(\mu_{x1} + \mu_{y0} + \sigma_{10})p_{10} + \gamma_y p_{11} - \gamma_x p_{10} - h_x\beta p_{10} + (1 - h_x)\varphi_{10} \\
\dot{p}_{11} &= -(\mu_{x1} + \mu_{y1} + \sigma_{11})p_{11} - (\gamma_x + \gamma_y)p_{11} + h_y\beta p_{01} + h_x\beta p_{10} \\
&\quad + h_y\varphi_{01} + h_x\varphi_{10} + \varphi_{11}
\end{aligned}$$

The right-hand side is homogeneous of degree 1 since the functions $\varphi_{ij}$ are homogeneous. In order to simplify the mathematical treatment we introduce vector notation. Define the following vectors, matrices, and functions. The state variables are

$$\underline{\mathrm{x}} = \begin{pmatrix} x_0 \\ y_0 \\ x_1 \\ y_1 \end{pmatrix}, \quad \underline{\mathrm{p}} = \begin{pmatrix} p_{00} \\ p_{01} \\ p_{10} \\ p_{11} \end{pmatrix}, \tag{4.4}$$

and

$$s(\underline{\mathrm{x}}) = x_0 + y_0 + x_1 + y_1 \tag{4.5}$$

is the total number of singles. The matrices $A, B, C$, and $L$ contain all parameters for birth, separation, contact, recovery, and death, i.e.,

$$A = \begin{pmatrix} -\mu_{x0} & 0 & \gamma_x & 0 \\ 0 & -\mu_{y0} & 0 & \gamma_y \\ 0 & 0 & -(\mu_{x1} + \gamma_x) & 0 \\ 0 & 0 & 0 & -(\mu_{y1} + \gamma_y) \end{pmatrix}, \tag{4.6}$$

$$B = \begin{pmatrix} \mu_{y0} + \sigma_{00} & \mu_{y1} + \sigma_{01} & 0 & 0 \\ \mu_{x0} + \sigma_{00} & 0 & \mu_{x1} + \sigma_{10} & 0 \\ 0 & 0 & \mu_{y0} + \sigma_{10} & \mu_{y1} + \sigma_{11} \\ 0 & \mu_{x0} + \sigma_{01} & 0 & \mu_{x1} + \sigma_{11} \end{pmatrix}, \tag{4.7}$$

$$C = \begin{pmatrix} -\delta_{00} & \gamma_y & \gamma_x & 0 \\ 0 & -\delta_{01} & 0 & \gamma_x \\ 0 & 0 & -\delta_{10} & \gamma_y \\ 0 & h_y\beta & h_x\beta & -\delta_{11} \end{pmatrix}, \tag{4.8}$$

where

$$\begin{aligned} \delta_{00} &= \mu_{x0} + \mu_{y0} + \sigma_{00}, \\ \delta_{01} &= \mu_{x0} + \mu_{y1} + \sigma_{01} + \gamma_y + h_y\beta, \\ \delta_{10} &= \mu_{x1} + \mu_{y0} + \sigma_{10} + \gamma_x + h_x\beta, \\ \delta_{11} &= \mu_{x1} + \mu_{y1} + \sigma_{11} + \gamma_x + \gamma_y, \end{aligned} \tag{4.9}$$

$$\text{Ł} = \begin{pmatrix} \kappa_x\nu_{00} & \kappa_x\nu_{01} & \kappa_x\nu_{10} & \kappa_x\nu_{11} \\ \kappa_y\nu_{00} & \kappa_y\nu_{01} & \kappa_y\nu_{10} & \kappa_y\nu_{11} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}. \tag{4.10}$$

The functions $F, G$ contain all information about the pairing law, i.e.,

$$F(\underline{\mathrm{x}}) = \frac{2}{s(\underline{\mathrm{x}})} \begin{pmatrix} \rho_{00}x_0y_0 + \rho_{01}x_0y_1 \\ \rho_{00}x_0y_0 + \rho_{10}x_1y_0 \\ \rho_{10}x_1y_0 + \rho_{11}x_1y_1 \\ \rho_{01}x_0y_1 + \rho_{11}x_1y_1 \end{pmatrix}, \tag{4.11}$$

$$G(\underline{\mathrm{x}}) = \frac{2}{s(\underline{\mathrm{x}})} \begin{pmatrix} \rho_{00}x_0y_0 \\ (1-h_y)\rho_{01}x_0y_1 \\ (1-h_x)\rho_{10}x_1y_0 \\ h_y\rho_{01}x_0y_1 + h_x\rho_{10}x_1y_0 + \rho_{11}x_1y_1 \end{pmatrix}. \tag{4.12}$$

Then the system (4.3) assumes the form

$$\begin{aligned} \dot{\underline{\mathrm{x}}} &= A\underline{\mathrm{x}} + L\underline{\mathrm{p}} + B\underline{\mathrm{p}} - F(\underline{\mathrm{x}}), \\ \dot{\underline{\mathrm{p}}} &= C\underline{\mathrm{p}} + G(\underline{\mathrm{x}}). \end{aligned} \tag{4.13}$$

This eight-dimensional system has a three-dimensional subsystem which describes a noninfected population. Of course this system is equivalent to the system (3.5) with the rates specified by

$$\begin{aligned} \dot{x}_0 &= (\kappa_{x0}\nu_{00} + \mu_{y0} + \sigma_{00})p_{00} - \mu_{x0}x_0 - \varphi(x_0, y_0), \\ \dot{y}_0 &= (\kappa_{y0}\nu_{00} + \mu_{x0} + \sigma_{00})p_{00} - \mu_{y0}y_0 - \varphi(x_0, y_0), \\ \dot{p}_{00} &= -(\mu_{x0} + \mu_{y0} + \sigma_{00})p_{00} + \varphi(x_0, y_0). \end{aligned} \tag{4.14}$$

We assume that all solutions of this system approach the two-sex persistent solution. Hence the system (4.13) has the noninfected persistent solution

$$(\underline{\mathrm{x}}_0, \underline{\mathrm{p}}_0) = (\overline{x}_0, \overline{y}_0, 0, 0, \overline{p}_{00}, 0, 0, 0)^* \exp(\hat{\lambda} t), \tag{4.15}$$

and this solution satisfies the equations

$$\begin{aligned} A\underline{\mathrm{x}}_0 + L\underline{\mathrm{p}}_0 + B\underline{\mathrm{p}}_0 - F(\underline{\mathrm{x}}_0) &= \hat{\lambda}\underline{\mathrm{x}}_0, \\ C\underline{\mathrm{p}}_0 + G(\underline{\mathrm{x}}_0) &= \hat{\lambda}\underline{\mathrm{p}}_0. \end{aligned} \tag{4.16}$$

We expect that, for certain values of the parameters, the noninfected persistent solution loses stability and an infected persistent solution bifurcates. For the stability analysis we compute the Jacobian at the noninfected solution which is a block matrix,

$$J = \begin{pmatrix} A & B \\ 0 & C \end{pmatrix} + \begin{pmatrix} D & 0 \\ E & 0 \end{pmatrix}, \tag{4.17}$$

where $A, B, C$ are defined above and the additional blocks are given by

$$D = 2\begin{pmatrix} -\rho_{00}\overline{y}^2 & -\rho_{00}\overline{x}^2 & \rho_{00}\overline{xy} & \rho_{00}\overline{xy} - \rho_{01}\overline{x} \\ -\rho_{00}\overline{y}^2 & -\rho_{00}\overline{x}^2 & \rho_{00}\overline{xy} - \rho_{01}\overline{y} & \rho_{00}\overline{xy} \\ 0 & 0 & -\rho_{10}\overline{y} & 0 \\ 0 & 0 & 0 & -\rho_{01}\overline{x} \end{pmatrix}, \tag{4.18}$$

$$E = 2\begin{pmatrix} \rho_{00}\overline{y} & \rho_{00}\overline{x} & 0 & 0 \\ 0 & 0 & 0 & (1-h_y)\rho_{01}\overline{x} \\ 0 & 0 & (1-h_x)\rho_{10}\overline{y} & 0 \\ 0 & 0 & h_x\rho_{10}\overline{y} & h_y\rho_{01}\overline{x} \end{pmatrix}. \tag{4.19}$$

Here

$$\overline{x} = \frac{x_0}{x_0 + y_0}, \quad \overline{y} = \frac{y_0}{x_0 + y_0}. \tag{4.21}$$

The matrix $J$ must have a three-dimensional invariant subspace corresponding to a noninfected population. If one reorders the variables according to

$$(x_0, y_0, p_{00}, x_1, y_1, p_{01}, p_{10}, p_{11}) \tag{4.22}$$

and performs the corresponding permutation of rows and columns of the matrix, then one obtains the block triangular matrix

$$\tilde{J} = \begin{pmatrix} \tilde{A} & \tilde{B} \\ 0 & \tilde{C} \end{pmatrix}, \tag{4.23}$$

where

$$\tilde{A} = \begin{pmatrix} -\mu_{x0} - 2\rho_{00}\overline{y}^2 & -2\rho_{00}\overline{x}^2 & \mu_{y0} + \sigma_{00} + \kappa_x\nu_{00} \\ -2\rho_{00}\overline{y}^2 & -\mu_{y0} - 2\rho_{00}\overline{x}^2 & \mu_{x0} + \sigma_{00} + \kappa_y\nu_{00} \\ 2\rho_{00}\overline{y}^2 & 2\rho_{00}\overline{x}^2 & -\delta_{00} \end{pmatrix}, \tag{4.24}$$

(4.25)

$$\tilde{B} = \begin{pmatrix} \gamma_x+2\rho_{00}\overline{xy} & 2\rho_{00}\overline{xy}-2\rho_{01}\overline{x} & \mu_{y1}+\sigma_{01}+\kappa_x\nu_{01} & \kappa_x\nu_{10} & \kappa_x\nu_{11} \\ 2\rho_{00}\overline{xy}-2\rho_{10}\overline{y} & \gamma_y+2\rho_{00}\overline{xy} & \kappa_y\nu_{01} & \mu_{x1}+\sigma_{10}+\kappa_y\nu_{10} & \kappa_y\nu_{11} \\ 0 & 0 & \gamma_y & \gamma_x & 0 \end{pmatrix},$$

$$\tilde{C} = \begin{pmatrix} -\mu_{x1}-\gamma_x-2\rho_{10}\overline{y} & 0 & 0 & \mu_{y0}+\sigma_{10} & \mu_{y1}+\sigma_{11} \\ 0 & -\mu_{y1}-\gamma_y-2\rho_{01}\overline{x} & \mu_{x0}+\sigma_{01} & 0 & \mu_{x1}+\sigma_{11} \\ 0 & 2(1-h_y)\rho_{01}\overline{x} & -\delta_{01} & 0 & \gamma_x \\ 2(1-h_x)\rho_{10}\overline{y} & 0 & 0 & -\delta_{10} & \gamma_y \\ 2h_x\rho_{10}\overline{y} & 2h_y\rho_{01}\overline{x} & h_y\beta & h_x\beta & -\delta_{11} \end{pmatrix}. \tag{4.26}$$

The matrix $\tilde{A}$ is the Jacobian of the pair formation model for a noninfected population. It depends on the parameter $\nu_{00}$. On the other hand, the matrix $\tilde{C}$ does not depend on the parameters $\nu_{ij}$.

Next we discuss the symmetric special case where all parameters are independent of sex. We introduce symmetric and antisymmetric variables,

$$\Big(\frac{(x_0+y_0)}{2}, p_{00}, \frac{(x_0-y_0)}{2}, \frac{(x_1+y_1)}{2}, \frac{(p_{01}+p_{10})}{2}, p_{11}, \frac{(x_1-y_1)}{2}, \frac{(p_{01}-p_{10})}{2}\Big). \tag{4.27}$$

With respect to these variables the Jacobian has the form

$$\hat{J} = \begin{bmatrix} \hat{A}_1 & 0 & & \hat{B} & \\ 0 & \hat{A}_2 & & & \\ & & \hat{C}_1 & & 0 \\ & 0 & & & \\ & & 0 & & \hat{C}_2 \end{bmatrix}. \tag{4.28}$$

Here the diagonal blocks are the symmetric part

$$\hat{A}_1 = \begin{pmatrix} -(\mu_0 + \rho_{00}) & \mu_0 + \sigma_{00} + \kappa\nu_{00} \\ \rho_{00} & -(2\mu_0 + \sigma_{00}) \end{pmatrix} \tag{4.29}$$

and the antisymmetric part

$$\hat{A}_2 = (-\mu_0) \tag{4.30}$$

of the matrix $\hat{A}$ and the symmetric part

$$\hat{C}_1 = \begin{pmatrix} -(\mu_1 + \gamma + \rho_{10}) & \mu_0 + \sigma_{10} & \mu_1 + \sigma_{11} \\ (1-h)\rho_{10} & -\delta_{01} & \gamma \\ 2h\rho_{10} & 2h\beta & -\delta_{11} \end{pmatrix} \tag{4.31}$$

and the antisymmetric part

$$\hat{C}_2 = \begin{pmatrix} -(\mu_1 + \gamma + \rho_{10}) & -(\mu_0 + \sigma_{10}) \\ (1-h)\rho_{10} & -\delta_{10} \end{pmatrix} \tag{4.32}$$

of the matrix $\hat{C}$. The off-diagonal block $\hat{B}$ is not of interest for a linear stability analysis. The Perron root of the matrix $\hat{A}_1$ is the exponent $\hat{\lambda}_d$ of the noninfected persistent solution

$$\hat{\lambda}_d = -\frac{1}{2}(3\mu_0 + \sigma_{00} + \rho_{00}) + \frac{1}{2}[(\mu_0 + \sigma_{00} + \rho_{00})^2 + 4\rho_{00}\kappa\nu_{00}]^{1/2}. \tag{4.33}$$

If the product $\kappa\nu_{00}$ increases from 0 to $+\infty$, then $\hat{\lambda}_d$ increases from $-\mu_0$ to $+\infty$. The noninfected persistent solution is stable in the sense of Section 2 if and only if $\det(\hat{C}_1 - \hat{\lambda}_d I) < 0$. In this general case it is not helpful to expand the determinant into a sum of terms.

For a more detailed discussion we restrict ourselves to the special case where all rates are independent of sex and the state of infection and where $\gamma = 0$. We omit subscripts from now on. Thus we have to discuss the cubic

(4.34)

$$\begin{aligned} \mathcal{D}(\lambda) = \det(\hat{C}_1 - \lambda I) = &-(2\mu + \sigma + h\beta + \lambda)(2\mu + \sigma + \lambda)(\mu + \rho + \lambda) \\ &+ (2\mu + \sigma + h\beta + \lambda)(\mu + \sigma)2h\rho \\ &+ (2\mu + \sigma + \lambda)(\mu + \sigma)(1-h)\rho \\ &+ (\mu + \sigma)(1-h)2h\beta\rho. \end{aligned}$$

One easily finds

$$\begin{aligned}\mathcal{D}(-\mu) &= h\rho(\mu+\sigma)[\mu+\sigma+\beta] > 0,\\ \mathcal{D}'(-\mu) &= -(\mu+\sigma)[(\mu+\sigma)+(1-h)\rho+h\varphi] - h\rho\beta < 0,\\ \mathcal{D}''(-\mu) &= 2[2(\mu+\sigma)+\rho+h\beta] < 0.\end{aligned}$$

Hence, in the interval $(-\mu,\infty)$, the cubic $\mathcal{D}(\lambda)$ has exactly one root $\lambda_0$ and

$$\begin{aligned}\mathcal{D}(\lambda) &> 0 \qquad \text{for} \qquad -\mu \le \lambda < \lambda_0,\\ \mathcal{D}(\lambda) &< 0 \qquad \text{for} \qquad \lambda_0 < \mu < +\infty.\end{aligned}$$

If the product $\kappa\nu$ runs from 0 to $+\infty$, then $\hat{\lambda}_d$ runs from $-\mu$ to $+\infty$. The noninfected persistent solution is stable if and only if $\mathcal{D}(\hat{\lambda}_d) < 0$. Hence we have the following result.

THEOREM. *The noninfected persistent solution is stable if and only if* $\hat{\lambda}_d > \lambda_0$.

*In biological terms we can express this statement as follows*: *The noninfected solution is stable if the demographic eigenvalue* $\hat{\lambda}_d$ *exceeds the epidemic eigenvalue* $\lambda_0$.

We believe that this theorem is also valid in the general case (see note added in proof).

**5. Dependence on epidemiological parameters.** Next we clarify how the stability of the noninfected persistent solution is related to the *infection rate* $h$. We rearrange the terms in the expression for $\mathcal{D}$,

(5.1)

$$\begin{aligned}\mathcal{D}(\lambda) &= h\mathcal{D}_1(\lambda) - \mathcal{D}_2(\lambda),\\ \mathcal{D}_1(\lambda) &= (2\mu+\sigma+\lambda)(\mu+\sigma)\rho - (2\mu+\sigma+\lambda)(\mu+\lambda)\beta - \rho(\lambda-\sigma)\beta,\\ \mathcal{D}_2(\lambda) &= (2\mu+\sigma+\lambda)(\mu+\lambda)(2\mu+\sigma+\rho+\lambda).\end{aligned}$$

Obviously the cubic $\mathcal{D}_2$ is positive for $\lambda > -\mu$. In the interval $\lambda > -\mu$ the quadratic function $\mathcal{D}_1(\lambda)$ has one zero $\lambda_1$ with a sign change from positive to negative. Hence there are two cases.

*Case* 1. $\hat{\lambda}_d < \lambda_1$. Then $\mathcal{D}_1(\hat{\lambda}_d) > 0$ and the noninfected persistent solution is stable if $\mathcal{D}(\hat{\lambda}_d) < 0$, i.e.,

$$h < \mathcal{D}_2(\hat{\lambda}_d)/\mathcal{D}_1(\hat{\lambda}_d).$$

The biological interpretation is obvious: The noninfected solution is stable, if the infection rate $h$ is sufficiently low.

*Case* 2. $\hat{\lambda}_d > \lambda_1$. Then $\mathcal{D}(\hat{\lambda}_d) < 0$ for all values of $h$. The noninfected solution remains stable, however large the parameter $h$ is. In this case population growth is so strong that the newly infected always present a negligible portion of the total population.

Finally we investigate the role of the *pair formation rate* $\rho$ in the stability problem. For this purpose we consider the expression $\mathcal{D}(\lambda)$ as a function of $\rho$. Again we decompose this expression into two parts,

$$\begin{aligned} \mathcal{D}(\lambda) &= \rho\mathcal{D}_3(\lambda) - \mathcal{D}_4(\lambda), \\ \mathcal{D}_3(\lambda) &= (2\mu+\sigma+\lambda)[h(\mu+\sigma) - (\mu+\lambda)] - h\beta(\lambda-\sigma), \\ \mathcal{D}_4(\lambda) &= (2\mu+\sigma+\lambda)(\mu+\lambda)(2\mu+\sigma+h\beta+\lambda). \end{aligned} \tag{5.2}$$

The function $\mathcal{D}_4$ is a polynomial of degree 3 with zeros $-(2\mu+\sigma), -\mu$, and $-(2\mu+\sigma+h\beta)$. These are all less than or equal to $-\mu$. Hence, in the interval $(-\mu,\infty)$, the function $\mathcal{D}_4(\lambda)$ is always positive. The quadratic polynomial $\mathcal{D}_3(\lambda)$ has the properties

$$\begin{aligned} \mathcal{D}_3(-\mu) &= h(\mu+\sigma)^2 + h\beta(\mu+\sigma) > 0, \\ \mathcal{D}'_3(\lambda) &= h(\mu+\sigma) - 2(\mu+\sigma+\lambda) - (\mu+\lambda) - h\beta, \end{aligned}$$

and thus

$$\mathcal{D}'_3(-\mu) = h(\mu+\sigma-\beta) - (\mu+\sigma) < -\beta.$$

Finally $\mathcal{D}''_3(\lambda) < 0$. Hence the polynomial $\mathcal{D}_3(\lambda)$ has exactly one zero $\lambda_2$ in the interval $(-\mu,\infty)$, and the sign changes from positive to negative. Again we have two cases.

*Case* 1. $\hat{\lambda}_d < \lambda_2$. Then $\mathcal{D}_3(\hat{\lambda}_d) < 0$. The noninfected persistent solution is stable if and only if $\mathcal{D}(\hat{\lambda}_d) < 0$, i.e., if

$$\rho < \mathcal{D}_4(\hat{\lambda}_d)/\mathcal{D}_3(\hat{\lambda}_d).$$

The noninfected persistent solution is stable if the rate of pair formation is low.

*Case* 2. $\hat{\lambda}_d > \lambda_2$. Then $\mathcal{D}_3(\hat{\lambda}_d) > 0$, and the stability condition is satisfied for all values of $\rho$.

**6. A second look at the bifurcation.** In order to make the bifurcation phenomenon more transparent, we look again at the symmetric case without recovery and with increased mortality and decreased fertility. Then we have a system of five equations for the noninfected single females $x_0$, the infected single females $x_1$, the noninfected pairs $p_0$, the pairs with only the female being infected $p_1$, and the pairs where both partners are infected $p_2$ (by definition, $x_0$ is also the number of noninfected males, etc.):

(6.1)
$$\begin{aligned}
\dot{x}_0 &= \kappa\nu p_0 + \kappa\nu_1(2p_1 + p_2) - \mu x_0 + (\mu + \sigma)p_0 + (\mu_1 + \sigma)p_1 - \rho x_0,\\
\dot{x}_1 &= -\mu_1 x_1 + (\mu + \sigma)p_1 + (\mu_1 + \sigma)p_2 - \rho x_1,\\
\dot{p}_0 &= -(2\mu + \sigma)p_0 + \rho x_0^2/x,\\
\dot{p}_1 &= -(\mu + \mu_1 + \sigma)p_1 - h\beta p_1 + (1-h)\rho x_0 x_1/x,\\
\dot{p}_2 &= -(2\mu_1 + \sigma)p_2 + 2h\beta p_1 + 2h\beta p_1 + 2h\rho x_0 x_1/x + \rho x_1^2/x,
\end{aligned}$$

where $x = x_0 + x_1$. The corresponding nonlinear eigenvalue problem reads

(6.2)
$$\begin{aligned}
(\hat{\lambda} + \mu + \rho)x_0 &= (\kappa\nu + \mu + \sigma)p_0 + (2\kappa\nu_1 + \mu_1 + \sigma)p_1 + \nu_1 p_2,\\
(\hat{\lambda} + \mu + \rho)x_1 &= (\mu + \sigma)p_1 + (\mu_1 + \sigma)p_2,\\
(\hat{\lambda} + 2\mu + \sigma)p_0 &= \rho x_0^2/x,\\
(\hat{\lambda} + \mu + \mu_1 + \sigma + h\beta)p_1 &= (1-h)\rho x_0 x_1/x,\\
(\hat{\lambda} + 2\mu_1 + \sigma)p_2 &= 2h\beta p_1 + 2h\beta p_1 + 2h\rho x_0 x_1/x + \rho x_1^2/x.
\end{aligned}$$

This can be reduced to one polynomial equation in $\hat{\lambda}$, but, in this general case, the reduction does not give much insight. However, in the special case where mortality and fertility do not depend on the state of infection,

(6.3)
$$\nu_1 = \nu, \quad \mu_1 = \mu,$$

the reduction is useful. Here the variables $x = x_0 + x_1$ and $p = p_0 + 2p_1 + p_2$ satisfy the two-dimensional system

$$\begin{aligned} \dot{x} &= -(\mu+\rho)x + (\kappa\nu + \mu + \sigma)p, \\ \dot{p} &= \rho x - (2\mu+\sigma)p \end{aligned} \tag{6.4}$$

with the eigenvalue problem

$$\begin{aligned} (\lambda+\mu+\rho)x &= (\kappa\nu+\mu+\sigma)p, \\ (\lambda+2\mu+\sigma)p &= \rho x, \end{aligned} \tag{6.5}$$

from where the demographic eigenvalue

$$\hat{\lambda}_d = -\frac{1}{2}(3\mu+\sigma+\rho) + \frac{1}{2}[(\mu+\sigma+\rho)^2 + 4\rho\kappa\nu]^{1/2} \tag{6.6}$$

and the corresponding eigenvector

$$\overline{x} = \nu + \mu + \sigma, \quad \overline{p} = \hat{\lambda}_d + \mu + \rho. \tag{6.7}$$

Now we return to the eigenvalue problem (6.2) with (6.3) and determine the solution. We know that the exponent of the infected solution is also $\hat{\lambda}_d$. In the fourth equation of (6.2), with $\hat{\lambda} = \hat{\lambda}_d$, we can solve for $p_1$. We can introduce this expression into the fifth equation and solve for $p_2$. Hence $p_1, p_2$ are expressed in terms of $x_0, x_2$, and $\hat{\lambda}$. The results are inserted into the second equation which then reads

$$\begin{aligned} (\hat{\lambda}+\mu+\rho)x_1 = \frac{\mu+\sigma}{x}\Big(&\frac{(1-h)\rho x_0 x_1}{\hat{\lambda}+2\mu+\sigma+h\beta} + \frac{2h\rho x_0 x_1 + \rho x_1^2}{\hat{\lambda}+2\mu+\sigma} \\ &+ \frac{2h\beta(1-h)\rho x_0 x_1}{(\hat{\lambda}+2\mu+\sigma)(\hat{\lambda}+2\mu+\sigma+h\beta)}\Big). \end{aligned} \tag{6.8}$$

The equation has the solution $x_1 = 0$, corresponding to the noninfected exponential solution. For $x_1 \neq 0$, we can divide by $x_1$, multiply by $x = x_0 + x_1$ and collect terms to get

(6.9)

$$\begin{aligned} \Big((\hat{\lambda}+\mu+\rho) &- \frac{(1-h)\rho(\mu+\sigma)}{\hat{\lambda}+2\mu+\sigma+h\beta} \\ &- \frac{2h\rho(\mu+\sigma)}{\hat{\lambda}+2\mu+\sigma} - \frac{2h\beta(1-h)\rho(\mu+\sigma)}{(\hat{\lambda}+2\mu+\sigma)(\hat{\lambda}+2\mu+\sigma+h\beta)}\Big)x_0 \\ &= \Big(\frac{\rho(\mu+\sigma)}{\hat{\lambda}+2\mu+\sigma} - (\hat{\lambda}+\mu+\rho)\Big)x_1. \end{aligned}$$

We can solve for $x_1/x_0$,

$$\frac{x_1}{x_0} = \frac{\mathcal{D}(\hat{\lambda})}{\mathcal{D}_0(\hat{\lambda})}, \tag{6.10}$$

where $\mathcal{D}$ is given by (4.34) and

$$\mathcal{D}_0(\hat{\lambda}) = (\hat{\lambda}+2\mu+\sigma+h\beta)[(\hat{\lambda}+\mu+\rho)(\hat{\lambda}+2\mu+\sigma)-(\mu+\sigma)\rho]. \tag{6.11}$$

Clearly, $\mathcal{D}_0(\lambda) > 0$ for $\lambda > -\mu$. We have seen before that $\mathcal{D}(\lambda)$ has a single zero $\lambda_0$ in $(-\mu, \infty)$ which we have called the epidemic eigenvalue. The noninfected solution is stable if $\lambda_0 < \hat{\lambda}_d$. This result is recovered here. Note that $\lambda_0$ is *not* the exponent of the infected exponential solution.

If $\lambda_0 > \hat{\lambda}_d$, i.e., if the epidemic eigenvalue is greater than the demographic eigenvalue, then the expression

$$\mathcal{D}(\hat{\lambda}_d)/\mathcal{D}_0(\hat{\lambda}_d)$$

is positive and gives the proportion of infected and noninfected singles. Fixing $x_0$ at any value, say $x_0 = 1$, one can obtain $x_1$ from (6.10) and then $p_0, p_1, p_2$ from (6.2). If $\lambda_0 < \hat{\lambda}_d$ then the quotient is negative and the noninfected solution is stable.

In this special case, where the disease has no effect on mortality and fertility, the differential equations (6.1) have two independent solutions with exponent $\hat{\lambda}_d$, the noninfected one given by (6.7), and the infected on given by (6.10).

## NOTES ADDED IN PROOF

1. The matrix $\tilde{C}$ in (4.26) has nonnegative off-diagonal elements. Hence the Perron-Frobenius theorem (continuous version) applies. There is a real eigenvalue $\overset{\lambda}{0}$ with maximal real part and positive eigenvector. From Section 2 it follows that the noninfected solution is stable when it's exposed to larger than $\lambda_0$.

2. For homogeneous systems also see: K.P. Hadeler [1990a], Periodic solutions of homogeneous equations, J. Diff. Eq., in print.

3. For pair formation: K.P. Hadeler [1990b], Homogeneous delay equations and model for pair formation, J. Math. Biol., submitted.

4. For sexually transmitted disease: C. Costillo-Chevez (ed.), Mathematical and Statistical Approaches to AIDS Epidemiology. Lecture Notes in Biomathematics **83**, Springer-Verlag, 1989.

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