CHAPTER 4

MATHEMATICAL ANALYSIS OF THE MODEL FOR HOMOSEXUAL MEN

For systems of linear differential and difference equations, it is possible to find explicit solutions (see introductory differential and difference equations textbooks). The difference equations in Figure 3.2 are nonlinear because the incidences involve products of susceptible fractions and the numbers of infectives . For systems of nonlinear differential and difference equations, it is not generally possible to find explicit solutions, but it is possible to find numerical solutions as a function of time. The numerical solutions of the system of nonlinear difference equations in Figure 3.2 are called the simulations of the HIV transmission dynamics model in Figure 3.1.

The value of the threshold quantity in an epidemiological model determines whether the disease persists or dies out. For single population models the threshold quantity is usually the *contact number*, which is the average number of adequate contacts of an infective during the infectious period (Hethcote, 1976; 1989a). This contact number is also called a *reproduction number* since it gives the number of secondary cases "reproduced" by a typical infective during the infectious period in a population in which everyone is susceptible (Anderson and May, 1991). For models in which the population is subdivided into groups with contacts between the groups given by a matrix, the threshold quantity is the *stability modulus* (i.e., the largest real part of an eigenvalue) of the contact matrix (Lajmanovich and Yorke, 1976; Hethcote, 1978; Hethcote and Yorke, 1984). The disease dies out if the stability modulus is below zero and the disease persists if the stability modulus is above zero. This threshold condition is equivalent to the *spectral radius* (i.e., the maximum absolute value of an eigenvalue) of a transmission matrix being less than one or greater than one (Hethcote and Van Ark, 1987). A general formulation of the reproduction number as a spectral radius has been applied to many models by Diekmann et al. (1990).

Even though explicit solutions of the nonlinear differential or difference equations corresponding to the model in Figure 3.1 cannot be found, it is possible to determine the threshold quantity as the *spectral radius* of a certain matrix. For the differential or difference equations for a simplification of the model in Figure 3.1 in which there is only one sexual activity level, the threshold can be found explicitly. The explicit expression for the *contact number* σ (the threshold quantity) given in equation (4.7) is useful because one can see how each parameter affects the threshold and hence affects whether the disease persists or dies out. In the mathematical analysis of an epidemiological model, often the goals are to determine the threshold quantity, to prove rigorously that *below the threshold* the disease prevalence goes to zero, and that *above the threshold* there is a unique, positive *equilibrium state* and the disease prevalence approaches this positive (endemic) equilibrium state (see Hethcote, 1976, 1989a). In this chapter we obtain some of these results for HIV dynamics models related to Figure 3.1. Those interested primarily in the application of the model to HIV/AIDS and not interested in the mathematical analysis may go directly to Chapter 5.

The *equilibria* of the model are the points with the property that solutions starting at these points stay there. First a differential equations analog of the difference equations model formulated in Chapter 3 for homosexual men is analyzed mathematically by finding the equilibria and their stability. This model can have both a *disease–free* equilibrium (DFE) and a unique *endemic* equilibrium (EE). Threshold results are obtained for this model which determine whether the disease dies out (approaches the DFE) or remains endemic (approaches the EE). This differential equations model analyzed in Sections 4.1 to 4.3 has one sexual activity level. In Section 4.4 it is shown that the threshold results obtained for the differential equations model also hold for the difference equations model with one sexual activity level. Although the thresholds and stability for the models with two sexual activity levels cannot be determined explicitly, the Jacobian is found in Section 4.5 for the difference equations model with two sexual activity levels corresponding to Figure 3.1. For the parameter sets occurring in Section 6.2, the eigenvalues of this Jacobian are found numerically in order to determine the stability of the DFE by finding the value of the *spectral radius* relative to the threshold one.

Another HIV/AIDS model with multiple groups has been studied by Jacquez et al. (1988; 1989), Sattenspiel and Simon (1988), Koopman et al. (1989), Lin (1991), and Simon and Jacquez (1992). Their differential equations model is similar to the model considered in Section 4.1, but their model has constant recruitment into each group and the group population sizes can vary. In contrast to our model, their model does not have transfers between the groups, their waiting times are the same in all stages, and people with AIDS are assumed to be sexually inactive. The model in Section 3.1 has constant recruitment into the two activity groups at a rate proportional to the group sizes and the sizes of the active and very active groups are constant; this also leaves a variable number of people still active in the population. Other multiple–group models for HIV/AIDS have been considered by Hyman and Stanley (1989), May and Anderson (1989), Blythe and Castillo–Chavez (1989), Castillo–Chavez et al. (1989) and Kaplan et al. (1989). See the survey papers of Isham (1987) and Schwager et al. (1989) for more details and references.

4.1 Equilibria for the Differential–Equations Model with One Sexual Activity Level.

The first model considered is a differential equations analog of the difference–equations models in Chapter 3. This model is for a homogeneous population with only one activity level. Let Y_k represent the number of people in stage k where stage 0 people are susceptible (not HIV–infected), stage 1 people are in the first infectious stage (see Chapter 2), $\cdots$, stage m people have AIDS, and stage $m+1$ people have died after having AIDS. Therefore, with N being the (constant) number of people in the population, the variables satisfy $Y_0+\cdots+Y_{m+1} = N$. Define λ_j, $j = 1,2, \cdots, m$ to be the average number of sexual contacts that a person in infectious stage j has with all people that are sufficient to cause HIV infection in susceptible persons. This value is a composite of several parameters defined for the model in Chapter 3.

The system of differential equations for this model corresponding to Figure 3.1 is

$$
\begin{aligned}
Y_0' &= (\delta + \mu)(N - Y_0) - \Big(\sum_{j=1}^{m} \lambda_j Y_j\Big)\Big(Y_0 \Big/ \sum_{k=0}^{m} Y_k\Big) , \\
Y_1' &= \Big(\sum_{j=1}^{m} \lambda_j Y_j\Big)\Big(Y_0 \Big/ \sum_{k=0}^{m} Y_k\Big) - (\delta + \mu + \gamma_1) Y_1 , \\
Y_k' &= \gamma_{k-1} Y_{k-1} - (\delta + \mu + \gamma_k) Y_k \ , \ 2 \le k \le m+1
\end{aligned}
\tag{4.1}
$$

where primes denote derivatives with respect to time and $\gamma_{m+1} = 0$. In (4.1) the $-(\delta + \mu)Y_k$ terms represent emigration and natural deaths, while $(\delta + \mu)N$ represents the immigration and other inflow to replace the losses. The *incidence term* is the sum of the contact rates and the numbers infected in the stages times the susceptible fraction. The model (4.1) can be simplified by converting from numbers in the stages to the fractions in the stages. Let $I_j = Y_j/N$ be the *fraction of the population in infectious stage* j, $0 \le j \le m + 1$. The model can then be written

$$
\begin{aligned}
I_1' &= g(I)\, I_0 - \xi_1 I_1 \ , \\
I_k' &= \gamma_{k-1} I_{k-1} - \xi_k I_k \ , \ 2 \le k \le m+1
\end{aligned}
\tag{4.2}
$$

where $g(I) = \big(\sum_{j=1}^{m} \lambda_j I_j\big)/(1 - I_{m+1})$, $\xi_k = (\delta + \mu + \gamma_k)$, $\gamma_{m+1} = 0$, and $I_0 = 1 - \sum_{j=1}^{m+1} I_j$. By examining (4.2) on each face, it can be shown that the region

$$
D = \{(I_1, \cdots, I_{m+1}) \mid 0 \le I_k \le 1; I_1 + \cdots + I_{m+1} \le 1\}
\tag{4.3}
$$

is positively invariant. The right side is Lipschitz continuous for $I_{m+1} < 1$ so that unique solutions of initial value problems exist on a maximal interval which must be $[0, \infty)$ since solutions remain in D (Miller and Michel, 1982). Thus the initial value problem is mathematically well–posed. The system (4.2) is epidemiologically reasonable since solutions remain in $[0, 1]^{m+1}$.

At equilibrium points, the right sides of the system (4.2) are zero. There are two possible equilibrium points for this model: the trivial or disease–free equilibrium (DFE), and an endemic equilibrium (EE) which is explicitly derived below. The DFE, with $I_0 = 1$ and $I_k = 0$ for $1 \le k \le m + 1$, is always in the region D. The EE below is in D when the parameter values satisfy the condition of being *above the threshold*. To obtain the EE, work backwards from the $(m+1)$st equilibrium equation, solving for I_{k-1} in terms of I_k to get:

$$
I_k = \Big[\prod_{j=k}^{m} \xi_{j+1}/\gamma_j\Big] \times I_{m+1} \ , \ 1 \le k \le m .
\tag{4.4}
$$

The $I_1' = 0$ equation gives I_0 in terms of the other I_k values; using (4.4), simplification gives

$$
I_0 = \frac{\xi_1 I_1}{g(I)} = \frac{\big[1 - I_{m+1}\big]}{\sum_{j=1}^{m} \lambda_j I_j}\, \xi_1 I_1 = \frac{\big[1 - I_{m+1}\big] \times I_{m+1}}{\sum_{j=1}^{m} \lambda_j \prod_{k=j}^{m} (\xi_{k+1}/\gamma_k)\, I_{m+1}} \frac{\Big[\prod_{j=1}^{m+1} \xi_j\Big]}{\Big[\prod_{j=1}^{m} \gamma_j\Big]} ,
$$

$$
I_0 = \Big[1 - I_{m+1}\Big] \div \Big[\sum_{j=1}^{m} \Big[\prod_{k=1}^{j-1} (\gamma_k/\xi_k)\Big] (\lambda_j/\xi_j)\Big]
\tag{4.5}
$$

Using $I_0 + \cdots + I_{m+1} = 1$, the I_{m+1} term at endemic equilibrium satisfies

$$\mathrm{I}^{e}_{m+1} = \frac{\left[\sum_{j=1}^{m}\left[\prod_{k=1}^{j-1}\frac{\gamma_k}{\xi_k}\right]\frac{\lambda_j}{\xi_j}\right] - 1}{\left\{\left[\left[\sum_{j=1}^{m}\left[\prod_{k=1}^{j-1}\frac{\gamma_k}{\xi_k}\right]\frac{\lambda_j}{\xi_j}\right]\right]\left[\sum_{j=1}^{m}\left[\prod_{k=j}^{m}\frac{\xi_{k+1}}{\gamma_k}\right] + 1\right] - 1\right\}}. \tag{4.6}$$

Using I^{e}_{m+1} given in (4.6), the equilibrium values I^{e}_{k} and I^{e}_{0} are given by (4.4) and (4.5).

Define the *contact number* σ as

$$\sigma = \left[\sum_{j=1}^{m}\left[\prod_{k=1}^{j-1}\frac{\gamma_k}{\xi_k}\right]\frac{\lambda_j}{\xi_j}\right]. \tag{4.7}$$

In many epidemiological models a contact number serves as the threshold quantity with 1 as the threshold value (Hethcote, 1976; Hethcote and Van Ark, 1987). In the following sections we show that the contact number σ given by (4.7) is the *threshold quantity* which determines whether the disease dies out ($\sigma \leq 1$) or remains endemic ($\sigma > 1$). However, we first give a heuristic interpretation of the contact number σ which explains why it is a reasonable threshold quantity. The quotient $\gamma_k/\xi_k = \gamma_k/(\delta + \mu + \gamma_k)$ is the probability that an infective leaving stage k goes into the next infectious stage $(k+1)$ instead of migrating out of the community or dying. Thus the product of the γ_k/ξ_k up through $(j-1)$ in the expression (4.7) for σ is the probability that an infective reaches stage j. The contact rate of infectives in stage j is λ_j and the mean waiting time in stage j is $1/\xi_j$ so that λ_j/ξ_j is the mean number of adequate contacts (sufficient for transmission of HIV infection) of an infective while in stage j. Thus the summation in the expression (4.7) for σ is the sum over all infectious stages j of the probability of reaching stage j times the mean number of adequate contacts while in stage j. Hence the contact number σ is the average number of adequate contacts of an infective during all of the infectious stages. Since the contact number σ is the average number of new infectives produced by an infective during its infectious stages in a totally susceptible population, it is sometimes called the basic reproductive number (Anderson and May, 1991). It is intuitively reasonable that if $\sigma < 1$, then each infective is replaced with less than one new infective so that the disease dies out (the DFE is asymptotically stable). However, if $\sigma > 1$ so that the average infective in a totally susceptible population is replaced with more than one new infective, then the disease should persist (the DFE is unstable). Below and in the following sections we show that when $\sigma > 1$ the disease persists, there is a unique endemic equilibrium and all solutions approach the endemic equilibrium.

Lemma 4.1 *If $\sigma > 1$, then the endemic equilibrium given by (4.6) and (4.4) is a distinct equilibrium in D and is the only equilibrium in D other than the DFE.*

proof If $\sigma > 1$, then I^{e}_{m+1} given by (4.6) is positive and $1/\mathrm{I}^{e}_{m+1}$ is 1 plus a positive quantity so $\mathrm{I}^{e}_{m+1} < 1$. Thus all of the I^{e}_{k} for $0 \leq k \leq m$ are positive by (4.4) and (4.5). Since the sum of these positive I^{e}_{k} values adds to 1, each of them must be less than one, and this equilibrium is an

EE in D. If $\sigma = 1$, then the EE given by (4.6) and (4.4) is the DFE. If $\sigma < 1$, then I^e_{m+1} is negative, and this equilibrium is not in D.▮

4.2 Stability of the Disease–Free Equilibrium.

The local and global stability of the DFE are now analyzed. Recall that the incidence $\mathcal{I}$ (rate of new infections) is

$$\mathcal{I} = g(I)I_0 = \left[\sum_{j=1}^{m} \lambda_j I_j\right]\left[1-\sum_{k=1}^{m+1} I_k\right](1-I_{m+1})^{-1}.$$

The second and third factors of $\mathcal{I}$ are

$$\left[1-\sum_{k=1}^{m+1} I_k\right]\left[1 + I_{m+1} + I_{m+1}^2 + I_{m+1}^3 + \cdots\right] = \left[1 - \sum_{k=1}^{m} I_k - I_{m+1}\sum_{k=1}^{m} I_k - I_{m+1}^2 \sum_{k=1}^{m} I_k - \cdots\right]$$

so that

$$\mathcal{I} = \sum_{j=1}^{m} \lambda_j I_j - G(\mathbf{I}) \ , \tag{4.8}$$

where $G(\mathbf{I}) = (\sum_{j=1}^{m} \lambda_j I_j)(\sum_{i=1}^{m} I_i)(\sum_{k=0}^{\infty} I_{m+1}^k)$. $G(\mathbf{I})$ is $o(\mathbf{I})$, i.e., $\lim_{\mathbf{I}\to 0} G(\mathbf{I})/|\mathbf{I}| = 0$, so to linearize the model, we replace the incidence term $\mathcal{I}$ by $\mathcal{I}_L = \sum_{j=1}^{m} \lambda_j I_j$. To check for stability by linearization, define $\mathbf{I} = [I_1, I_2, \cdots, I_{m+1}]^T$, $G(\mathbf{I})$ as above, and the $m+1 \times m+1$ matrix A as

$$A = \begin{bmatrix} \lambda_1-\xi_1 & \lambda_2 & \lambda_3 & \cdots & \lambda_m & 0 \\ \gamma_1 & -\xi_2 & 0 & \cdots & 0 & 0 \\ 0 & \gamma_2 & -\xi_3 & \cdots & 0 & 0 \\ \vdots & & & \ddots & & \vdots \\ 0 & 0 & \cdots & & \gamma_m & -\xi_{m+1} \end{bmatrix}$$

The model (4.2) becomes

$$\mathbf{I}' = A\mathbf{I} - [G(\mathbf{I}), 0, \cdots, 0]^T \ . \tag{4.9}$$

The linearization of this is

$$\mathbf{I}' = A\mathbf{I} \ . \tag{4.10}$$

The local stability of the DFE is determined by examining the eigenvalues of A at the DFE.

<u>*Lemma 4.2.*</u> *For the above matrix* A, *the eigenvalue with largest real part is an algebraically simple real eigenvalue.*

proof Let E_k be the $k \times k$ identity matrix. Then the characteristic equation of A is $|\alpha E_{m+1} - A| = (\alpha + \xi_{m+1})|\alpha E_m - A_m|$, where A_m is the $m \times m$ matrix obtained by crossing off the last row and column of A, i.e., expanding around the last column of A. The eigenvalue already obtained is $\alpha = -\xi_{m+1} = -(\delta + \mu) < 0$, and the remaining m eigenvalues of A are the eigenvalues of A_m. Define the *stability modulus* $s(A)$ to be the maximum of the real parts of the eigenvalues of A and the *spectral radius* $\rho(A)$ to be the maximum of the absolute values of the eigenvalues of A. Let $\tau = \max\{\xi_1-\lambda_1, \xi_2, \xi_3, \cdots, \xi_m\} + 1 > 0$, and $B = A_m + \tau E_m$. Therefore, B is a non–negative matrix with eigenvalues $\beta_k = (a_k + \tau)$, $k = 1, \cdots, m$, where $\{a_1, a_2, \cdots, a_m\}$ are the eigenvalues of A_m. Since infection in any stage I_k can spread the infection throughout the population, the matrix A_m (hence the matrix B also) is *irreducible* [Hethcote, 1978]. Since B is irreducible and nonnegative, $\rho(B) = s(B)$ is an eigenvalue of B which is real and geometrically and algebraically simple, and there exists a positive eigenvector ω for $s(B)$ [Horn and Johnson, 1985, p 508]. Therefore, $s(A_m) = (s(B) - \tau)$ is a real, simple eigenvalue of A.█

By a similar approach [Horn and Johnson, 1985, p 492] we find bounds on $s(A_m)$ given by

$$\min_{1\leq k\leq m} \{\lambda_k-\delta-\mu\} \leq s(A_m) \leq \max_{1\leq k\leq m} \{\lambda_k-\delta-\mu\}.$$

Lemma 4.3. *The eigenvalues of the matrix* A_m *above are the roots of the characteristic equation* $p_m(a) = det[aE_m - A_m]$, *where*

$$p_m(a) = \prod_{j=1}^{m}(\xi_j + a) - \sum_{k=1}^{m} \left[\prod_{j=1}^{k-1}\gamma_j\right](\lambda_k)\left[\prod_{i=k+1}^{m}(\xi_i + a)\right]$$

$$= \left[\prod_{j=1}^{m}(\xi_j + a)\right]\left[1 - \sum_{k=1}^{m}\left[\prod_{i=1}^{k-1}\frac{\gamma_i}{\xi_i+a}\right]\frac{\lambda_k}{\xi_k+a}\right], \tag{4.11}$$

(*with* $\prod_{j=m+1}^{m}(\cdot) = 1$).

proof The proof is by induction on m. Observe that

$$|\alpha E_2 - A_2| = \begin{vmatrix} a+\xi_1-\lambda_1 & -\lambda_2 \\ -\gamma_1 & a+\xi_2 \end{vmatrix} = (a+\xi_1)(a+\xi_2) - \lambda_1(a+\xi_2) - \lambda_2\gamma_2,$$

so (4.11) is true for $m = 2$.

Assume that the induction hypothesis is true for m. Note that

$$|\alpha E_{m+1} - A_{m+1}| = \begin{vmatrix} \alpha+\xi_1-\lambda_1 & -\lambda_2 & -\lambda_3 & & \cdots & -\lambda_{m+1} \\ -\gamma_1 & a+\xi_2 & 0 & 0 & \cdots & 0 \\ 0 & -\gamma_2 & a+\xi_3 & 0 & \cdots & 0 \\ \\ 0 & \cdots & & -\gamma_{m-1} & a+\xi_m & 0 \\ 0 & \cdots & & 0 & -\gamma_m & a+\xi_{m+1} \end{vmatrix}$$

Expanding around the last column gives

$$|\alpha E_{m+1} - A_{m+1}| = (-1)^{m+1}\lambda_{m+1}\prod_{j=1}^{m}(-\gamma_j) + (a+\xi_{m+1})p_m(a)$$

$$= -\left[\prod_{j=1}^{m}\gamma_j\right]\lambda_{m+1} + \prod_{j=1}^{m+1}(\xi_j+a) - \sum_{k=1}^{m}\left[\prod_{j=1}^{k-1}\gamma_j\right](\lambda_k)\left[\prod_{i=k+1}^{m+1}(\xi_i+a)\right]$$

$$= \prod_{j=1}^{m+1}(\xi_j+a) - \sum_{k=1}^{m+1}\left[\prod_{j=1}^{k-1}\gamma_j\right](\lambda_k)\left[\prod_{i=k+1}^{m+1}(\xi_i+a)\right] = p_{m+1}(a).█$$

Notice that $p_m(0) = \prod_{j=1}^{m}(\xi_j) - \sum_{k=1}^{m}\left[\prod_{j=1}^{k-1}\gamma_j\right](\lambda_k)\left[\prod_{i=k+1}^{m}(\xi_i)\right]$, and $|A_m| = (-1)^m p_m(0)$.

By Lemma 4.1, s(A) is the real simple eigenvalue with largest positive (or least negative) real root for $p(a) = 0$, so if $s(A) < 0$, then all eigenvalues of A have negative real parts, and if $s(A) > 0$, at least one eigenvalue of A has positive real part. In the former case, the DFE is locally asymptotically stable, and in the latter case, it is unstable. The Theorem below gives a threshold condition on this property. The following Lemma will be used in the proof of the Theorem.

Lemma 4.4. Let $p_m(a)$ be given by (4.11) and σ be as in (4.7). Then $\sigma < 1$ implies that $p_m(a)$ has no nonnegative real roots.

proof Notice that

$$p_n(a) = (\xi_n + a)p_{n-1}(a) - \lambda_n \prod_{j=1}^{n-1}\gamma_j\,, \tag{4.12}$$

so that $p_n' = p_{n-1} + (\xi_n + a)p_{n-1}'$. The proof is by induction on $p_n(0) > 0$ and $p_n'(a) > 0$ for $a > 0$ with $1 \le n \le m$. For $n = 1$, $\sigma < 1$ implies that $\lambda_1 - \xi_1 < 0$. Then $p_1(0) = -\lambda_1 + \xi_1 > 0$, and p_1' is $1 > 0$, so the induction hypothesis is true for $n = 1$.

Now assume that the induction hypothesis is true for all $n \le m - 1$. Now $\sigma < 1$ for $n + 1$ implies

$$p_{n+1}(0) = \left[\prod_{j=1}^{n+1}(\xi_j)\right]\left[1 - \sum_{k=1}^{n+1}\left[\prod_{j=1}^{k-1}\frac{\gamma_j}{\xi_j}\right]\frac{\lambda_k}{\xi_k}\right] > 0.$$

Also $p_{n+1}'(a) = p_n(a) + (\xi_{n+1} + a)p_n'(a) > 0$ for $a > 0$, since $p_n(a) > 0$ and $p_n'(a) > 0$ for $a > 0$. Thus the induction hypothesis is true for m so that $p_m(a)$ has no nonnegative real roots.█

Theorem 4.5. Let σ be given by *(4.7). Then the* DFE *for the model (4.2) is locally asymptotically stable if $\sigma < 1$, and the* DFE *is unstable if $\sigma > 1$.*

proof The characteristic polynomial is $|\alpha E - A| = (\xi_{m+1} + a)p_m(a) = 0$. Notice that $|\alpha E - A|$ is a polynomial in a with leading coefficient +1, so that as $a \to \infty$, $|\alpha E - A| \to +\infty$.

Evaluating $|\alpha E - A|$ at $a = 0$ yields $\prod_{j=1}^{m+1}(\xi_j)(1-\sigma)$, which has the same sign as $1 - \sigma$. Therefore, if $1 - \sigma < 0$ there exists $\hat{a} > 0$ such that $|\hat{\alpha}E - A| = 0$, so that $\hat{a}$ is a real eigenvalue of A, and the DFE is unstable. On the other hand, if $\sigma < 1$, Lemma 4.4 implies that $p_m(a)$ has no real roots for $a \ge 0$, and the remaining root is $-\xi_{m+1} = -(\delta + \mu) < 0$. Since Lemma 4.2 proves that s(A), the eigenvalue of A with largest real part, is real, the argument above proves that $s(A) < 0$, so that the DFE is locally asymptotically stable [Miller and Michel, 1982, p 261].█

Theorem 4.6. For $\sigma \le 1$, the DFE for the model (4.2) is globally asymptotically stable.

proof The transpose A^T of the matrix A in (4.9) is irreducible with nonnegative off–diagonal elements, so it has a positive eigenvector ω corresponding to the eigenvalue $s(A) = s(A^T)$ (Hethcote, 1978). Note from the proof of Theorem 4.5 that $\sigma \le 1$ is equivalent to $s(A) \le 0$. As in Lajmanovich and Yorke [1976] or Hethcote [1978], consider the Liapunov function $V = \omega \cdot I$ with derivative given by

$$V' = \omega \cdot I' = \omega \cdot (AI - [G(I), 0, \cdots, 0]^T) = A^T \omega \cdot I - \omega_1 G(I) = s(A)\omega \cdot I - \omega_1 G(I) \le 0.$$

By Liapunov theory [Miller and Michel, 1982, p 227], all solutions approach the largest invariant subset of the set M in which $V' = 0$. For the Liapunov function V above, this subset M is the origin, so all solutions approach the DFE where the I_k are zero for $1 \le k \le m + 1$.∎

4.3 Stability of the Endemic Equilibrium.

The local stability of the endemic equilibrium (EE) given by (4.4) and (4.6) is proved by methods similar to those in the previous Section.

Theorem 4.7. If $\sigma > 1$, then the endemic equilibrium of (4.2) is locally asymptotically stable.

proof The Jacobian of (4.2) evaluated at the EE given by (4.4) and (4.6) is

$$B = \begin{bmatrix} \tau_1 - \xi_1 & \tau_2 & \tau_3 & \cdots & \tau_m & \tau_{m+1} \\ \gamma_1 & -\xi_2 & 0 & \cdots & 0 & 0 \\ 0 & \gamma_2 & -\xi_3 & \cdots & 0 & 0 \\ \vdots & & & \ddots & & \vdots \\ & & & & -\xi_m & 0 \\ 0 & 0 & \cdots & & \gamma_m & -\xi_{m+1} \end{bmatrix} \tag{4.13}$$

where $\tau_i = \lambda_i/\sigma - g(I)$ for $1 \le i \le m$ and $\tau_{m+1} = -(1 - 1/\sigma)g(I)$. From the proof of Lemma 4.3, we find that the characteristic equation corresponding to the matrix B is

$$|\alpha E - B| = q_{m+1}(\alpha) = 0$$

where $q_{m+1}(\alpha)$ is the same as $p_{m+1}(\alpha)$ defined by (4.11) with λ_k replaced by τ_k. The proof is by induction on $q_n(0) > 0$ and $q_n'(\alpha) > 0$ for $\alpha > 0$, with $1 \le n \le m + 1$. For $n = 1$, $q_1(\alpha) = \alpha - \tau_1 + \xi_1$, so $q_1' = 1 > 0$ and $q_1(0) = \xi_1[1 - (\lambda_1/\xi_1)/\sigma + g(I)] > 0$ since $\sigma > \lambda_1/\xi_1$ by (4.7).

Assume that the induction hypothesis is true for $q_n(\alpha)$. If $n < m$, then

$$\begin{aligned} q_{n+1}(0) &= \left[\prod_{j=1}^{n+1}(\xi_j)\right]\left[1 - \sum_{k=1}^{n+1}\left[\prod_{j=1}^{k-1}\frac{\gamma_j}{\xi_j}\right]\frac{\tau_k}{\xi_k}\right] \\ &= \left[\prod_{j=1}^{n+1}(\xi_j)\right]\left[1 - \left[\sum_{k=1}^{n+1}\left[\prod_{j=1}^{k-1}\frac{\gamma_j}{\xi_j}\right]\frac{\lambda_k}{\xi_k}\right]/\sigma + \sum_{k=1}^{n+1}\left[\prod_{j=1}^{k-1}\frac{\gamma_j}{\xi_j}\right]\frac{g(I)}{\xi_k}\right] > 0. \end{aligned}$$

The positivity follows because the denominator σ in the second term is greater than or equal to the numerator. If $n = m$, then

$$q_{m+1}(0) = \left[\prod_{j=1}^{m+1}(\xi_j)\right]\left[\sum_{k=1}^{m}\left[\prod_{j=1}^{k-1}\frac{\gamma_j}{\xi_j}\right]\frac{g(I)}{\xi_k} + \prod_{j=1}^{m}\frac{\gamma_j}{\xi_j}\frac{(1-1/\sigma)g(I)}{\xi_{m+1}}\right] > 0.$$

As in the proof of Lemma 4.4,

$$q'_{n+1}(\alpha) = q_n(\alpha) + (\xi_n + \alpha)q'_n(\alpha) > 0$$

by the induction hypothesis for q_n. Thus $q_{m+1}(0) > 0$ and $q'_{m+1}(\alpha) > 0$ so $q_{m+1}(\alpha) > 0$ for $\alpha \geq 0$, and $q_{m+1}(\alpha)$ has no nonnegative real roots. If $q_{m+1}(\alpha)$ had a complex conjugate pair of roots with nonnegative real parts, then the graph of q_{m+1} would have a local minimum for some nonnegative α. This is impossible since $q'_{m+1}(\alpha) > 0$, so $q_{m+1}(\alpha)$ has no complex roots with nonnegative real part. Thus the endemic equilibrium is locally asymptotically stable.∎

4.4 Stability of the Difference Equations Model with One Sexual Activity Level.

In Sections 4.1 – 4.3 thresholds and stability of equilibria are analyzed for the differential–equations model corresponding to Figure 3.1 with one activity level. The model actually used in the calculations involve difference equations with a one–month time step. Here it is shown that the stability threshold for the differential equations model also works for the difference–equations model.

The difference equations for the one activity level model are

$$\begin{aligned} Y_0^{n+1} &= Y_0^n + (\delta+\mu)(N - Y_0^n) - \left[\sum_{j=1}^{m}\lambda_j Y_j^n\right]\left[Y_0^n/\sum_{k=0}^{m}Y_k^n\right] \\ Y_1^{n+1} &= Y_1^n + \left[\sum_{j=1}^{m}\lambda_j Y_j^n\right]\left[Y_0^n/\sum_{k=0}^{m}Y_k^n\right] - (\delta+\mu+\gamma_1)Y_1^n \\ Y_k^{n+1} &= Y_k^n + \gamma_{k-1}Y_{k-1}^n - (\delta+\mu+\gamma_k)Y_k^n \text{ for } 2 \leq k \leq m+1\,. \end{aligned} \tag{4.14}$$

As in Section 4.1, let $I_j^n = Y_j^n/N$ be the fraction of the population in stage j so the model (4.14) becomes

$$\begin{aligned} I_1^{n+1} &= I_1^n + g(I^n)I_0^n - \xi_1 I_1^n \\ I_k^{n+1} &= I_k^n + \gamma_{k-1}I_{k-1}^n - \xi_k I_k^n \quad \text{for } 2 \leq k \leq m+1 \end{aligned} \tag{4.15}$$

where $g(I^n) = (\sum_{j=1}^{m}\lambda_j I_j^n)/(1-I_{m+1}^n)$, $\xi_k = (\delta+\mu+\gamma_k)$, $\gamma_{m+1} = 0$, and $I_0^n = 1 - \sum_{j=1}^{m+1}I_j^n$.

The equilibria for the difference–equations model (4.15) are precisely the same as those for the differential–equations model (4.2). The disease–free equilibrium (DFE) is the origin and the endemic equilibrium (EE) is given by (4.4) and (4.6). Lemma 4.1 shows that the EE is a distinct equilibrium if $\sigma > 1$, where σ is the contact number given by (4.7). Let $\mathbf{V}^n$ be the vector of I_k for $1 \leq k \leq m+1$ and $\mathbf{V}^{n+1} = \mathbf{F}(\mathbf{V}^n)$ be the nonlinear difference equations (4.14). The linearization of (4.15) at the DFE is

$$V^{n+1} = TV^{n} = (E + A)V^{n} \tag{4.16}$$

where E is the identity matrix and A is the matrix in (4.9).

The matrix T is irreducible and nonnegative if $\xi_k < 1$ for $1 \le k \le m+1$. This condition that the mean waiting times $1/\xi_k$ are greater than one month is always satisfied for our application of the model for HIV/AIDS. The Perron–Frobenius theory applies to the matrix T so that T has a real simple eigenvalue equal to its stability modulus s(T) and equal to its spectral radius $\rho(T)$, the corresponding eigenvector ω is positive, and any nonnegative eigenvector is a positive multiple of ω. Since $\rho(T) = s(T) = s(A+E) = s(A)+1$, the condition $s(A) < 0$ is equivalent to $\rho(T) < 1$. In Section 4.2 the condition $s(A) < 0$ is shown to be equivalent to $\sigma < 1$ where the contact number σ is given by (4.6). Recall that an equilibrium for a difference equation is locally stable iff the spectral radius of the linearization is less than 1. Thus we have proved the following Theorem, which is analogous to Theorem 4.5.

__Theorem 4.8.__ If $\sigma < 1$, then the DFE for the model (4.15) is locally asymptotically stable. If $\sigma > 1$, the DFE is unstable.

Although the analog of Theorem 4.6 is probably true for the difference–equations model (4.15) so that the endemic equilibrium (EE) is locally asymptotically stable for $\sigma > 1$, the obvious proof method does not quite work. The Jacobian at the EE is $V = E + B$, where B is given by (4.13), and $s(V) = s(E + B) = 1 + s(B)$. From Theorem 4.7 $s(B) < 0$ if $\sigma > 1$, so $s(V) \le 1$ if $\sigma > 1$. But $V = E + B$ is not nonnegative since $\tau_{m+1} = -(1 - 1/\sigma)g(I) < 0$, so that the Perron–Frobenius theory does not guarantee that $\rho(V) = s(V)$. Thus this approach does not quite prove that $\rho(V) < 1$, which is needed for local stability.

4.5 Stability for the Difference–Equations Model with Two Sexual Activity Levels

The stability analyses of the difference–equations model and the differential–equations model corresponding to Figure 3.1 with very active and active groups are analytically intractable. Here the linearization at the DFE is found for the difference–equations model so the spectral radius can be evaluated numerically. This is the model which is used in later chapters in this monograph. Since the spectral radius (the largest absolute value of an eigenvalue) is often used as a measure of the contact number or intrinsic reproduction number [Hethcote and Van Ark, 1987; Diekmann et al., 1988], its size indicates how far above or below the threshold value of one the current parameters for the infectious disease process are.

The difference equations for the very active and active risk groups in the model corresponding to Figure 3.1 are:

$$
\begin{aligned}
X_0^{n+1} &= X_0^n + (\delta+\mu)[fN - X_0^n] - g_1 X_0^n - \phi X_0^n + \theta Y_0^n \\
X_1^{n+1} &= X_1^n + g_1 X_0^n - \xi_1 X_1^n - \phi X_1^n + \theta Y_1^n \\
X_k^{n+1} &= X_k^n + \gamma_{k-1} X_{k-1}^n - \xi_k X_k^n - \phi X_k^n + \theta Y_k^n \quad \text{for } 2 \le k \le m+1 . \\
Y_0^{n+1} &= Y_0^n + (\delta+\mu)[(1-f)N - Y_0^n] - g_2 Y_0^n + \phi X_0^n - \theta Y_0^n \\
Y_1^{n+1} &= Y_1^n + g_2 Y_0^n - \xi_1 Y_1^n + \phi X_1^n - \theta Y_1^n \\
Y_k^{n+1} &= Y_k^n + \gamma_{k-1} Y_{k-1}^n - \xi_k Y_k^n + \phi X_k^n - \theta Y_k^n \quad \text{for } 2 \le k \le m+1 .
\end{aligned}
\tag{4.17}
$$

where $\sum_{j=0}^{m+1} X_j^n = fN$, $\sum_{k=0}^{m+1} Y_k^n = (1-f)N$, $\theta = f\phi/(1-f)$, $\xi_k = (\delta+\mu+\gamma_k)$ for $2 \le k \le m+1$, $\gamma_{m+1} = 0$,

$$g_1 = (1-\eta)\sum_{j=1}^{m} R\lambda_j X_j^n/[fN - X_{m+1}^n] + \eta\sum_{j=1}^{m} R\lambda_j(R\,X_j^n + Y_j^n)/[R(fN - X_{m+1}^n) + (1-f)N - Y_{m+1}^n],$$

$$g_2 = (1-\eta)\sum_{j=1}^{m} \lambda_j Y_j^n/[(1-f)N - Y_{m+1}^n] + \eta\sum_{j=1}^{m} \lambda_j(R\,X_j^n + Y_j^n)/[R(fN - X_{m+1}^n) + (1-f)N - Y_{m+1}^n],$$

and $\lambda_k = \rho_k \times PH \times \omega_k \times QH$.

This system of nonlinear difference equations could be converted to a system for the fractions in each class as in Section 4.4, but this is not necessary here since the eigenvalues and spectral radius will be found numerically. Since there is some redundancy in the system above, the subsystem for X_k^n and Y_k^n with $1 \le k \le m+1$ is considered, where $X_0^n = fN - \sum_{j=1}^{m+1} X_j^n$ and $Y_0^n = (1-f)N - \sum_{k=1}^{m+1} Y_k^n$. The disease–free equilibrium (DFE) for this subsystem is the origin and the matrix for the linearization around this DFE is given by:

$$T = \left[\begin{array}{c|c} T_{11} & T_{12} \\ \hline T_{21} & T_{22} \end{array}\right],$$

where

$$T_{11} = \begin{bmatrix}
1-\xi_1-\phi+\tau_1 & \tau_2 & \tau_3 & \cdots & \tau_m & 0 \\
\gamma_1 & 1-\xi_2-\phi & 0 & & & 0 \\
0 & \gamma_2 & 1-\xi_3-\phi & & & \vdots \\
\vdots & & & & & 0 \\
0 & 0 & \cdots & & \gamma_m & 1-\xi_{m+1}-\phi
\end{bmatrix},$$

$$T_{22} = \begin{bmatrix}
1-\xi_1-\theta+\omega_1 & \omega_2 & \omega_3 & \cdots & \omega_m & 0 \\
\gamma_1 & 1-\xi_2-\theta & 0 & & & 0 \\
0 & \gamma_2 & 1-\xi_3-\theta & & & \vdots \\
\vdots & & & & & 0 \\
0 & 0 & \cdots & & \gamma_m & 1-\xi_{m+1}-\theta
\end{bmatrix},$$

$$
\mathrm{T}_{12} = \begin{bmatrix} \chi_1+\theta & \chi_2 & \chi_3 & \cdots & \chi_m & 0 \\ 0 & \theta & 0 & \cdots & & 0 \\ 0 & & \theta & & & \vdots \\ \vdots & & & & & \vdots \\ & & & & & 0 \\ 0 & 0 & \cdots & & 0 & \theta \end{bmatrix},
$$

$$
\mathrm{T}_{21} = \begin{bmatrix} \nu_1+\phi & \nu_2 & \nu_3 & \cdots & \nu_m & 0 \\ 0 & \phi & 0 & \cdots & & 0 \\ 0 & & \phi & & & \vdots \\ \vdots & & & & & \vdots \\ & & & & & 0 \\ 0 & 0 & \cdots & & 0 & \phi \end{bmatrix},
$$

$$
\tau_k = \left[\frac{(1-\eta)\,R\lambda_k}{fN} + \frac{\eta R\lambda_k R}{RfN+(1-f)N}\right] fN,
$$

$$
\chi_k = \left[\frac{\eta R\lambda_k fN}{RfN+(1-f)N}\right],
$$

$$
\nu_k = \left[\frac{\eta\lambda_k(1-f)N}{RfN+(1-f)N}\right],
$$

$$
\omega_k = \left[\frac{(1-\eta)\,\lambda_k}{(1-f)N} + \frac{\eta\lambda_k R}{RfN+(1-f)N}\right](1-f)N.
$$

The eigenvalues of T above are found numerically for the parameter sets in later Chapters. If the spectral radius satisfies $\rho(\mathrm{T}) < 1$, then the DFE is stable. If $\rho(\mathrm{T}) > 1$, the DFE is unstable, and solutions approach the endemic equilibrium.