CHAPTER 3

FORMULATION OF THE SIMULATION MODEL FOR HOMOSEXUAL MEN

Transmissions of HIV have occurred after exposure to people in the pre–antibody period (Peterman et al., 1985). The latent period (i.e., from infection to infectiousness) for HIV infection is short enough to be ignored in a model. The infectious period is unknown, but the virus seems to persist in the host indefinitely since it can be isolated from the blood for many years after the infection (Curran et al., 1988). No evidence to the contrary exists; therefore HIV infectivity is assumed to continue for life. Since individuals are either susceptible to HIV infection or infectious, HIV is an SI (susceptible-infected) disease (Hethcote, 1978, 1989c). In contrast, gonorrhea is an SIS disease since people can recover and return to the susceptible class.

3.1 The Compartmental Model with Two Sexual Activity Levels

In modeling gonorrhea, the population was divided by level of sexual activity (Hethcote et al., 1982; Hethcote and Yorke, 1984). The population considered here consists of homosexual men who change male sex partners frequently, i.e., at least once every few years. This group is subdivided into men who have many different male sex partners (very active) and those who have only a few different partners (active). Although some modelers have used more sexual activity levels or risk groups in theoretical studies (Jacquez et al., 1988; Blythe and Anderson, 1988; Castillo–Chavez et al., 1989; Kaplan and Lee, 1990), the two activity levels used here do not introduce lots of parameters which cannot be estimated and are consistent with the existence of a small fraction of homosexual men who are very active sexually. The mixing structure, sexual activity level and progression to AIDS in a population may depend on the age of the individuals, but there is currently not enough data available to justify the incorporation of age structure into the model; see Busenberg and Castillo–Chavez (1991) for an age–structured HIV/AIDS model.

Consider the flow diagram for homosexual men shown in Figure 3.1. Table 3.1 contains a list of the parameters and variables used in the model. The number m of infectious stages shown in Figure 3.1 is four for simplicity, but in Section 2.1, we found that $m = 6$ or 7 gives best fits to the AIDS incubation data. The population size is Q, the number of very active men is $QV = F \times Q$, and the number of active men is $QA = (1–F) \times Q$. The numbers of susceptible persons are SV and SA for the very active and active groups, respectively. The five compartments X(I) in Figure 3.1 correspond to four stages in the progression to AIDS and death among very active people while the compartments Y(I) are analogous for active people. The sum of the left column of compartments in Figure 3.1 is always QV and the sum of the middle column is QA so that the very active and active population sizes are conserved.

Men in the first three Z(I) compartments are those who have moved from the region after they were infected with HIV. When men in these three Z(I) compartments eventually develop AIDS, they are placed in the ZAIDS compartment. The compartment Z(4) consists of those who emigrated from the region after they had AIDS but who would still be counted as local AIDS cases. The compartments X(5), Y(5) and Z(5) contain men who have died of AIDS, and the

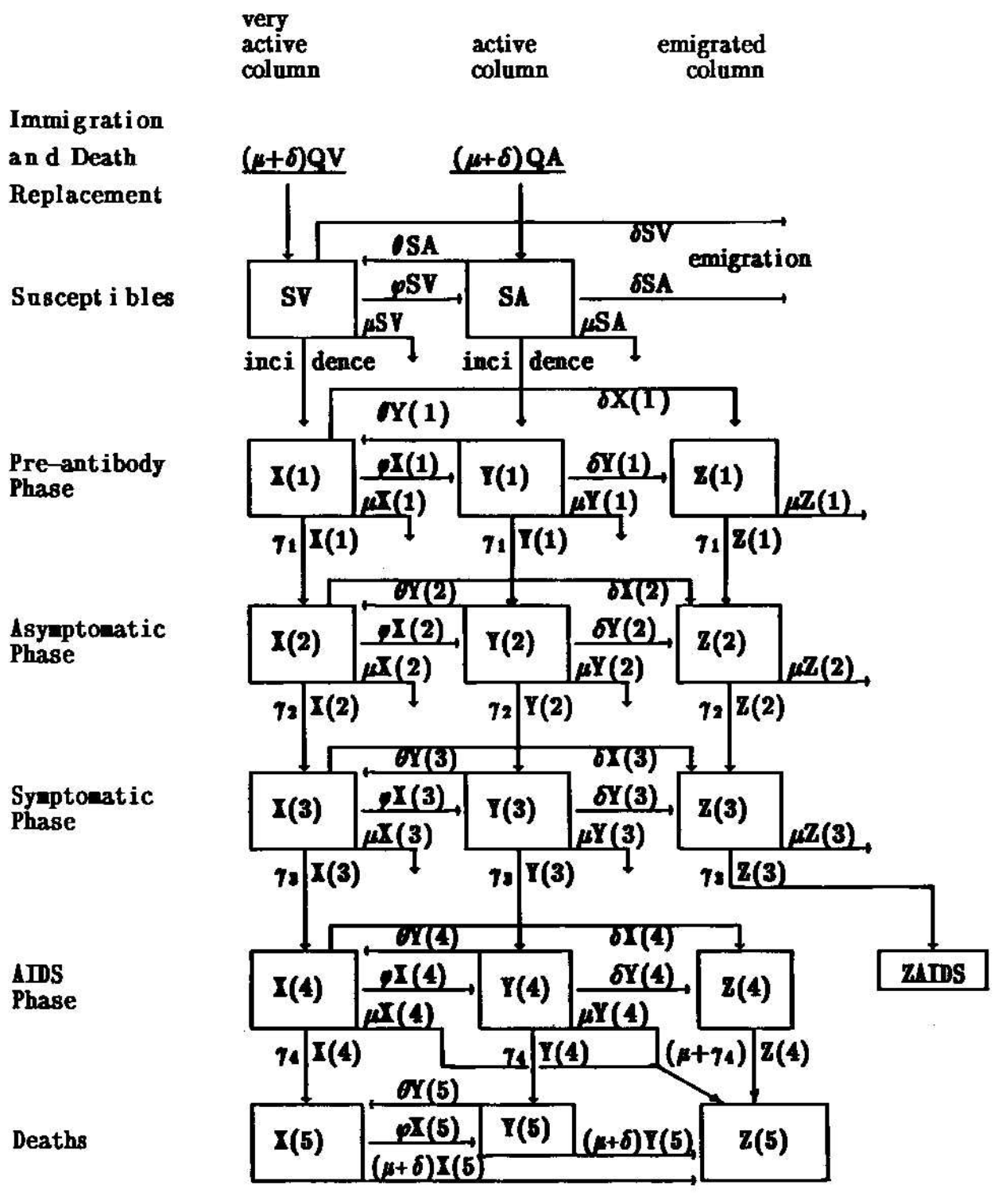

Figure 3.1. Diagram with compartments and transfers in the simulation model.

transfers between these compartments are merely to balance the flows so that the total very active and active populations remain constant. Since men who have died of AIDS are included in the total very active and active population sizes, the fraction of these populations which are still alive and sexually active will decrease as more men in those populations die.

Natural deaths (not related to HIV infection) occur in each compartment with rate constant μ with balancing inflows μQV and μQA into the susceptible compartments. Let δ be the turnover rate constant corresponding to the normal migration of sexually active

Table 3.1. List of parameters and variables.

Population Size and Turnover Rate Constants.

Q = total population size
F = fraction of population who are sexually very active
R = ratio of partnership rates for very active and active men
μ = natural mortality rate constant
δ = migration rate constant
ϕ = transfer rate constant from very active to active states

Stages of the Infection

m = number of infectious stages
γ_k = rate constant for progression from stage k to stage k+1
ω_k = relative infectivity of stage k men compared with asymptomatic men
ρ_k = relative sexual activity of stage k men compared with asymptomatic men

Sexual Activity

STD = starting date of the epidemic
QH = probability of transmission to partners by infected asymptomatic men
PAS = average number of partners per month at start
STR = starting date for reduction in average number of partners per month
STP = stopping date for reductions
RDN = yearly reduction factor
η = fraction of new partnerships distributed by proportionate mixing

Variables (functions of time)

SV = number of susceptible very active men
SA = number of susceptible active men
X(k) = number of very active men in stage k
Y(k) = number of active men in stage k
Z(k) = number of emigrated men in stage k

homosexual men. The emigrations from the very active and active groups are balanced by immigration δQV and δQA into the very active and active susceptibles. In addition to geographic migration, the turnover could also be due to initiation or cessation of homosexual activity. The transfer rate constant φ corresponds to the natural movement of homosexual men from sexually very active status to active status. There are balancing transfers from the active to the very active compartments with a transfer rate constant of $\theta = \phi \times$ QV/QA.

As in Chapter 2, the parameters γ_1, γ_2, γ_3 and γ_4 in Figure 3.1 govern the movement through the stages of HIV infection to AIDS and death due to AIDS. These transfer rate constants correspond to negative exponential waiting times in the compartments with mean waiting times equal to $1/\gamma_1$, $1/\gamma_2$, $1/\gamma_3$ and $1/\gamma_4$, respectively.

The monthly change in the number of people in a compartment in Figure 3.1 is equal to the monthly inflows minus the monthly outflows. Thus the model consists of simultaneous nonlinear difference equations given in Figure 3.2, which correspond to the compartments in

$$\frac{\Delta SV}{\Delta t} = (\delta+\mu)(QV-SV) - V_{incidence} - \varphi SV + \theta SA$$

$$\frac{\Delta SA}{\Delta t} = (\delta+\mu)(QA-SA) - A_{incidence} + \varphi SV - \theta SA$$

$$\frac{\Delta X(1)}{\Delta t} = V_{incidence} - (\gamma_1+\mu+\delta+\varphi)X(1) + \theta Y(1)$$

$$\frac{\Delta Y(1)}{\Delta t} = A_{incidence} - (\gamma_1+\mu+\delta+\theta)Y(1) + \varphi X(1)$$

$$\frac{\Delta Z(1)}{\Delta t} = \delta(X(1)+Y(1)) - (\gamma_1+\mu)Z(1)$$

$$\frac{\Delta X(2)}{\Delta t} = \gamma_1 X(1) + \theta Y(2) - (\gamma_2+\mu+\delta+\varphi)X(2)$$

$$\frac{\Delta Y(2)}{\Delta t} = \gamma_1 Y(1) + \varphi X(2) - (\gamma_2+\mu+\delta+\theta)Y(2)$$

$$\frac{\Delta Z(2)}{\Delta t} = \delta(X(2)+Y(2)) + \gamma_1 Z(1) - (\gamma_2+\mu)Z(2)$$

$$\frac{\Delta X(3)}{\Delta t} = \gamma_2 X(2) + \theta Y(3) - (\gamma_3+\mu+\delta+\varphi)X(3)$$

$$\frac{\Delta Y(3)}{\Delta t} = \gamma_2 Y(2) + \varphi X(3) - (\gamma_3+\mu+\delta+\theta)Y(3)$$

$$\frac{\Delta Z(3)}{\Delta t} = \delta(X(3)+Y(3)) + \gamma_2 Z(2) - (\gamma_3+\mu)Z(3)$$

$$\frac{\Delta ZAIDS}{\Delta t} = \gamma_3 Z(3)$$

$$\frac{\Delta X(4)}{\Delta t} = \gamma_3 X(3) + \theta Y(4) - (\gamma_4+\mu+\delta+\varphi)X(4)$$

$$\frac{\Delta Y(4)}{\Delta t} = \gamma_3 Y(3) + \varphi X(4) - (\gamma_4+\mu+\delta+\theta)Y(4)$$

$$\frac{\Delta Z(4)}{\Delta t} = \delta(X(4)+Y(4)) - (\gamma_4+\mu)Z(4)$$

$$\frac{\Delta X(5)}{\Delta t} = \gamma_4 X(4) + \theta Y(5) - (\mu+\delta+\varphi)X(5)$$

$$\frac{\Delta Y(5)}{\Delta t} = \gamma_4 Y(4) + \varphi X(5) - (\mu+\delta+\theta)Y(5)$$

$$\frac{\Delta Z(5)}{\Delta t} = \delta(X(5)+Y(5)) + (\gamma_4+\mu)Z(4) + \mu(X(4)+Y(4)+X(5)-Y(5))$$

Figure 3.2 The difference equations for the model in Figure 3.1.

Figure 3.1. The HIV epidemic starts with one infected person entering the very active pre–antibody compartment on the starting date STD and then progresses in one–month time steps.

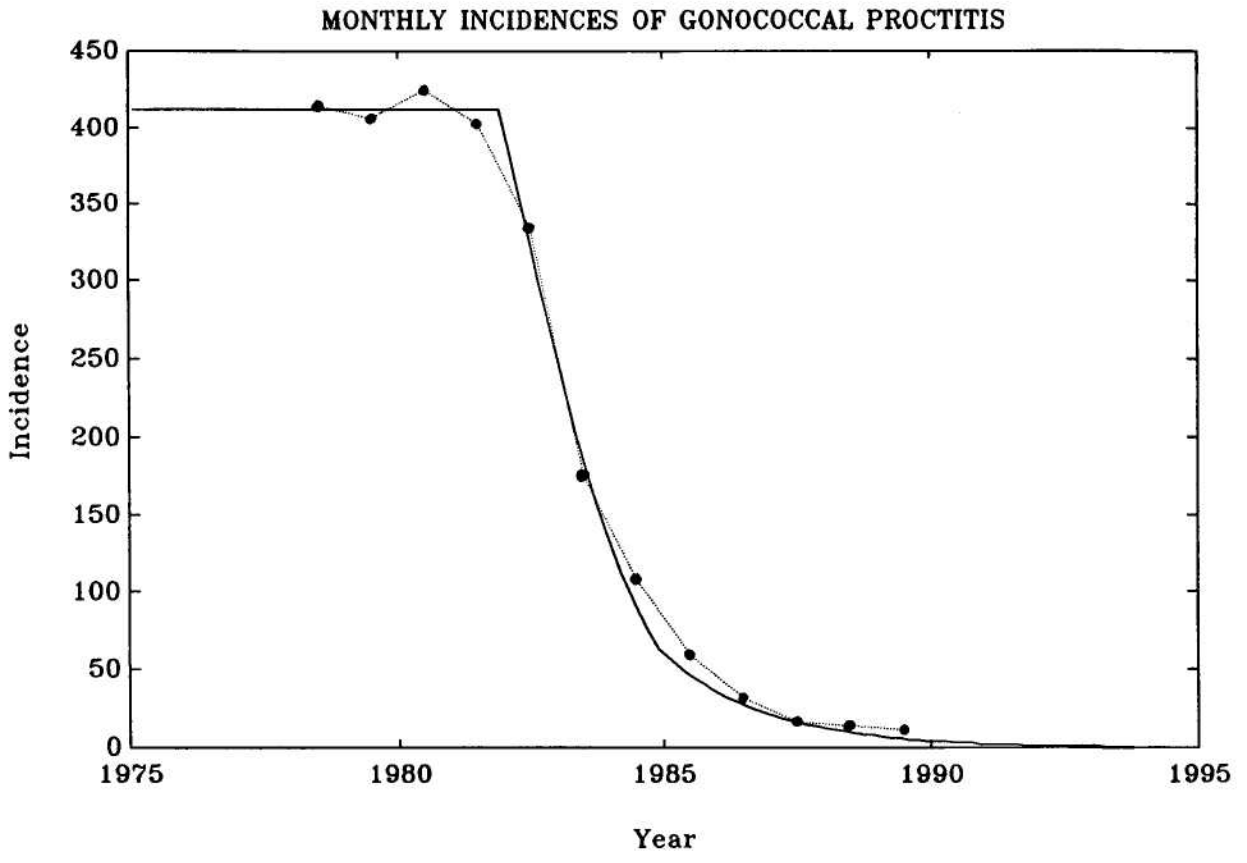

Figure 3.3. The curve with • symbols indicates the incidence of gonococcal proctitis in San Francisco, and the solid curve is the incidence in the gonorrhea simulation.

3.2 Modeling the Incidence of HIV Infection

Individuals in some phases cease sexual activity or adopt protective measures when they learn of their HIV status because of a desire to avoid infecting others; others cease sexual activity because they are ill due to HIV–related symptoms. Let PA be the average number of partners per month for asymptomatic infected men. Let ρ_k be the relative sexual activity of those in stage k compared to asymptomatic infected men, so $\rho_k PA$ is the average number of homosexual partners per month for stage k infected men.

The infectiousness of individuals in the phases leading to AIDS seems to vary. People in the pre–antibody, symptomatic and AIDS phases seem to be more infectious than people in the asymptomatic phase (Longini et al., 1989). If QH is the probability of transmission of HIV infection to a partner by an infected asymptomatic man and ω_k is the relative infectivity of those in stage k, normalized so $\omega_k = 1$ for asymptomatics, then the probability of transmission for infected persons in stage k is $\omega_k QH$. All of the ω_k are equal for men in the symptomatic stages. Since there are many types of sexual interactions in a homosexual partnership, QH is a simplified composite or average of many factors such as the numbers and types (anal, oral, receptive, insertive, unprotected, safer) of contacts per partner. Although very active people may tend to have shorter length partnerships with fewer contacts than active people, the contacts of very active people may have higher risk of transmission. The quantity QH is really the

proportion of partners of infected asymptomatic men who are infected, but it is usually called the probability of transmission.

Data on sexual behavior and gonococcal proctitis for homosexual men in large cities suggest that partnership formation rates for homosexual men have changed (CDC, 1990a, 1990c). A simple way to model this phenomenon is to assume that the average number PA of different partners per month is first constant, then decreases as a geometric sequence, and then is constant again. A geometric sequence is the discrete approximation to a negative exponential decrease in partnership rates suggested by the gonococcal proctitis data in Figure 3.3. In the model, the number of partners per month before reduction starts is PAS, the date at which reduction starts is STR, the date at which reduction stops is STP, and the yearly reduction factor is RDN.

The number of different partners per month is $PH = PA/(1+F(R-1))$ for the fraction $1-F$ of the population which is active and $R \times PH$ for the fraction F which is very active. The monthly effective contact rate is the product of the contact rate (the number of different partners per month) and the proportion of partnerships resulting in transmission.

One method of specifying the contact rates between subpopulations in an epidemiologic model is with proportionate mixing (Hethcote and Yorke, 1984; Nold, 1980; Dietz and Schenzle, 1985b; Hethcote and Van Ark, 1987). In this method each group has a sexual activity level, and the new partners of a person are distributed among the groups in proportion to the activity levels of the groups. Alternatively, a person may be more likely to choose a sexual partner with the same level of sexual activity. This situation occurred in the gonorrhea modeling of Hethcote and Yorke (1984, p.83) in which 20% of the contacts were internal to the activity level groups and 80% were external contacts governed by proportionate mixing. This is now called preferred mixing (Jacquez et al.,1988; Blythe and Castillo-Chavez, 1989).

Since data have not been found on mixing patterns in SF, the more general form of mixing is used here. Let η be the fraction of the new partnerships distributed by proportionate mixing among all groups so that the fraction $1-\eta$ of new partnerships occur internally to each group. Since some of the contacts of a group governed by proportionate mixing are contacts with others in the same group, these proportionate-mixing contacts are really internal to the group, so that not all of the proportionate-mixing contacts are external to the group. Nevertheless, it is convenient to use the term *internal* for the fraction $1-\eta$ of the partnerships which must be within the group and to use the term *external* for the fraction η governed by proportionate mixing. The incidences of HIV infection in the active and very active groups due to the internal mixing in each group are, respectively,

$$\left[\sum_{i=1}^{m} (1-\eta) \times \rho_i \times PH \times \omega_i \times QH \times Y(i)\right] \times \frac{SA}{QA-Y(m+1)},$$

$$\left[\sum_{i=1}^{m} (1-\eta) \times \rho_i \times R \times PH \times \omega_i \times QH \times X(i)\right] \times \frac{SV}{QV-X(m+1)}.$$

Now consider the fraction η of new partnerships distributed by proportionate mixing among all groups (Hethcote and Van Ark, 1987, eq. 6.6). The activity levels for the active and very active subpopulations are the numbers of partners per month, PH and R * PH, respectively. The average number of partnership formations in the population per month is

$$C = PH * (QA - Y(m+1)) + R * PH * (QV - X(m+1))$$

so that the incidences in the active and very active subpopulations due to proportionate mixing are, respectively,

$$\sum_{i=1}^{m} \eta * \rho_i * PH * \omega_i * QH * [R * X(i)+Y(i)] * \frac{PH * SA}{C},$$

$$\sum_{i=1}^{m} \eta * \rho_i * PH * \omega_i * QH * [R * X(i)+Y(i)] * \frac{R * PH * SV}{C}.$$

The total incidences in the active and very active subpopulations are the sums of the internal incidences and the external proportionate mixing incidences.