Data Driven Network Models for the Spread of Infectious Disease

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Summary

Infectious diseases spread by person-to-person contact may be strongly channeled by patterns of selective (or 'non-random') social mixing. The more intimate and extended the contact needed for disease transmission, the more impact selective mixing will have on the speed and direction of spread. Patterns of selective mixing at the population level are in turn the outcome of the heterogeneity in individual contact networks. This paper will provide an overview of the empirical and theoretical issues that such networks raise for epidemiological modeling, and some examples of the impact that networks can have on disease transmission dynamics. While network models have recently been an active area of research in mathematical epidemiology, the link between models and data has often been neglected. In keeping with the spirit of this volume, the focus here will be on the implications of alternative models for data collection and analysis.

1 Modeling Networks

A 'network' can be defined as a set of nodes connected by a set of links, and network analysis is generally concerned with specifying the probability of a link between two nodes. For infectious disease networks, the nodes are persons (or animals and vectors), and the links represent the relation needed for disease transmission, for example physical proximity, touching, or exchange of bodily fluids. The probability of a link is typically modeled as a function of nodal attributes, e.g. sex, age, or more abstractly 'degree', and sometimes also of higher-order properties such as transitivity or triad bias (if A knows B and B knows C then C is likely to know A, cf., Harary *et al.* (1965), Holland and Leinhardt (1970)).

There are two approaches that have been taken in analyzing such networks cf., Pattison (1993). The first has its roots in graph theory, and is based on a complete enumeration of all the nodes (and nodal attributes) and all the links in a network (Figure 1a). In epidemiology, this graph-theoretic approach has been shown to be consistent with the stochastic formulations of the Reed-Frost model (Mollison and Barbour 1989), and has been adopted by several

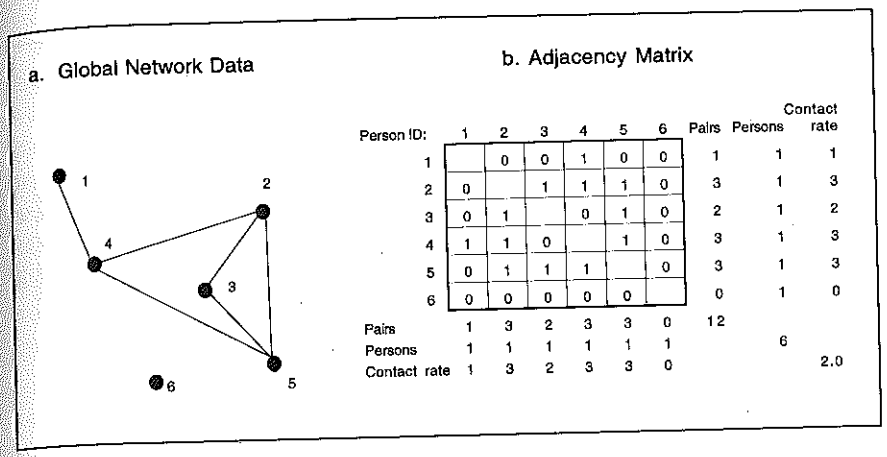

Figure 1: Global network data. For a bounded network, all nodes and links are enumerated (panel (a)), and the data can be displayed in a socio- or adjacency matrix (panel (b)). The zeros and ones in the matrix represent the presence or absence of a link between two modes; the margins represent the total number of partnerships for each group ('pairs'), the number of persons in the group ('persons') and the average number of partnerships per per unit time ('contact group').

authors (Altmann 1993, Blanchard *et al.* 1988, Kretzschmar *et al.* 1993). In sociology, this approach is called global or 'sociocentric' network analysis, as the unit of analysis is the social group. Its origins are usually traced to the early work of Rapoport (Rapoport 1952, 1957, 1980), and it remains the dominant approach in network analysis; for overviews, see Berkowitz (1982), Burt and Minor (1983), Leinhardt (1977), Wasserman and Faust (1994).

The second approach is based on a sampling nodes from a network (Figure 2a). Here information is collected on the attributes of and links from the respondent node, and the respondent is also asked to report on the attributes of the nodes to which they are directly linked. This approach is called local or 'egocentric' network analysis in sociology, because the unit of analysis is 'ego', the respondent; see Burt and Minor (1983), Marsden (1981).

In epidemiology, this approach is most often used in conjunction with (though not limited to) deterministic compartmental modeling, and contact matrices (or their algebraic equivalents) have been used in these models by many analysts; see Anderson *et al.* (1990), Castillo-Chavez and Blythe (1989), Hethcote and Yorke (1984), Hyman and Stanley (1988), Jacquez *et al.* (1989), Sattenspiel (1987).

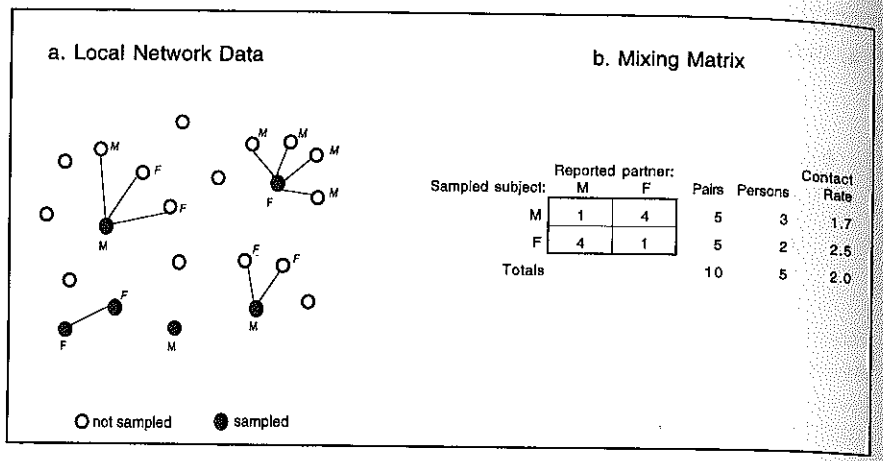

Figure 2: Local network data. For a bounded network, nodes and links are sampled (panel (a)), and the data can be displayed in a mixing or contact matrix (panel (b)). The cell entries of the matrix represent the number of partnerships between respondents in the row category with partners in the column category.

Because the global-local network split has coincided with the stochastic-deterministic split among modelers, a comparison of the two network approaches has been overshadowed by the debate over stochastic and deterministic representations. Local network data can, however, be modeled stochastically (Morris 1991) and there are other issues that determine the relative merits of the two network approaches. The most important of these, from the standpoint of applied epidemiology, are (1) the feasibility of data collection, and (2) the relevance for transmission dynamics.

The first issue for data collection is to identify the appropriate set of nodes. This has been called the 'boundary problem' in network analysis (Laumann, in Burt and Minor 1983). In the context of epidemiology, a reasonable answer would be the people who, by virtue of susceptibility and connectedness, are at risk for an infectious disease. If the life span of the disease agent is very short, or if suscesptibility is rare, this may sometimes be a small group, e.g., an isolated tribe of indigenous peoples. More often, however, the network at risk will be a very large group. With influenza or AIDS, for example, it is probably the majority of the world's population. A complete enumeration of nodes and links for such a network would be impossible. In such cases, the sampling strategy of the local network approach gives it a strong advantage over the global network approach.

Another issue that must be considered is intrusiveness. The global network approach requires that each person in the network identify their contacts, so that each contact can be uniquely matched. If the type of contact is relatively public, e.g., office sharing, there may be little difficulty in obtaining the information from the respondent. If the type of contact is intensely private, e.g., sexual relations, data collection will require questions like 'tell me the names of the people you had sex with in the last six months'. Such questions are likely to be viewed as highly intrusive by the respondent. They raise not only significant issues of privacy, but also of validity and reliability, as intrusive questions may be met with non-disclosure.[1]

By contrast, the local network approach requires a respondent to provide only a list of attributes for each partner, e.g., their age, race, and sex. The partner, otherwise, remains anonymous. While questions about sexual behavior will always be intrusive, the guarantee of partner anonymity reduces intrusiveness and may increase respondent cooperation. Here, again, the local network approach has strong advantages over the global network approach.

The tradeoff is that the local network approach loses information. It is not by virtue of sampling, per se, but rather because it is not possible from egocentric reports to collect specific information on higher order network properties, such as triad bias and chain length. In addition, there is clearly some error introduced by relying on respondent reports of their partners' attributes rather than collecting that information from the partners themselves. How serious these drawbacks are is an open question. The loss of information on higher order network properties is a question that can be explored with simulation. It is an important issue for future research and will be taken up in the conclusion. The magnitude of the measurement error introduced by relying on respondent reports, on the other hand, is an empirical question. There have been studies of the accuracy of such reports in friendship networks (Laumann 1973), which found generally high correlations between the respondent's report and the partner's actual characteristics. Not surprisingly, the degree of accuracy is highest for observable characteristics such as age, where there is about 86% agreement within 12 years, and lower for characteristics such as political party preference (53%). There were no systematic biases observed in the errors that were made, with the exception of political party preference, which respondents were more likely to report as similar to their own. The results of this analysis are encouraging, but not conclusive, because patterns observed for friendship networks may not hold in general.

[1] *Note:* This approach is used now for contact tracing in STD prevention, but non-infected cases are not followed, and among infected cases there is a compelling rationale to provide contact names: they are known to have been exposed and there is treatment available. A global network survey in the service of AIDS research is likely to face much more serious obstacles both at the level of political approval and respondent compliance.

2 Modeling Epidemics on Networks

If networks never changed, then the analysis of epidemic spread on a network would be relatively straightforward. Contact networks, however, are very dynamic. This raises two basic issues for modeling: summarizing the patterns of selective mixing over time, and solving the generalized two-sex problem.

The need for a parsimonious summary of selective mixing parameters can best be appreciated by a simple example of STD transmission. The types of attributes that are likely to influence sexual partner selection include such things as age, sex, race, sexual preference and marital status. Though by no means an exhaustive list, these five simple attributes generate 108 categories for respondents[2], a corresponding number for partners, and a mixing matrix with over ten thousand cells (or a similar number of link-specific probabilities for sociocentric data). Even if it were possible to use the cell counts directly to drive an epidemiological simulation (which it is not unless the vital dynamics and selection patterns are both in equilibrium), it would not be desirable. A model which captures the important selective dynamics in a limited number of parameters is therefore necessary.

In the local network tradition several simple models have been proposed, most focusing on the degree of assortative (Laumann 1973) or disassortative mixing (Gupta and Anderson 1989, Haraldsdottir *et al.* 1992). While the assortative-disassortative axis is likely to be the single most powerful summary of mixing, it is difficult to use such a summary for multiple attributes, e.g., mixing by both race (assortative) and sex (disassortative). For this, a more general modeling framework is needed. Several general frameworks have also been proposed (Blythe *et al.* 1991, Koopman *et al.* 1989, Morris, 1991). There is no consensus as yet on the criteria that should be used to evaluate the relative merits of these alternative frameworks, but some data-related criteria may be suggested.

One important criterion involves the estimation and interpretation of mixing parameters. While parameters can usually be calculated from data, estimation is most reliable when backed by a framework for statistical inference. Only then can one answer the central question of how well the model (with its reduced parameter space) fits the observed patterns. When the estimated parameters are also easy to interpret, they can provide insight into the complex impact of mixing on transmission.

The second criterion concerns the solution of multiple matching constraints over time. The constraints are imposed by the inherent symmetry in contact processes – if A meets B, then B has to meet A – and imply symmetry

[2]This is a conservative figure, calculated assuming 3 age groups, 2 sexes, 3 race categories, 3 sexual preference categories and 2 marital statuses. A full cross-tabulation of these categories produces an index with 108 different groups.

in a socio- or contact matrix. This is a generalized version of the 'two-sex problem' familiar to demographers (see Pollard 1948, Schoen 1982). In the context of disease transmission, the problem arises when the sizes, activity levels, or selection patterns of population subgroups change over time. These three basic factors drive the structure of a network. If one or more changes, the network must be reconfigured, and multiple matching constraints must be satisfied. There is more than one way to achieve this, but all involve changing the activity levels and/or preference patterns of other groups, and the assumptions made will clearly affect the disease projections. For this reason, it is important that the assumptions are explicitly stated.

3 things that can change

In the local network tradition, log-linear models for the contact matrix provide the framework for estimation and inference (Morris 1991), and make it possible to explicitly solve the generalized two-sex problem when one or more of the three network factors changes (Morris 1995). In the global network tradition, estimation is more problematic. Models typically include higher-order effects such as triad bias and chain length which imply a dependence between pairs, i.e., one pair is more likely to be linked if it shares a node with another pair. This dependence among observations violates the assumptions of traditional methods of estimation. In the last 10 years some progress has been made on models for Markov random graphs, where the markovian property is interpreted to mean that two links are independent unless they share a node (Frank and Strauss 1986, Strauss and Ikeda 1990).

To summarize, recent work has generated several alternative approaches to modeling the role of networks in disease transmission. The title of this volume suggests that an important criterion for evaluating alternative models is how well they relate to data. From the standpoint of data collection, feasibility and intrusiveness are important considerations. The local network network approach has many advantages here, which are traded off against a loss of information on higher-order network properties. From the standpoint of data representation, the issues of parsimony, flexibility and goodness-of-fit measures become important criteria. Here, too, the local network approach can take advantage of existing statistical methods for estimation and inference. The tradeoff again is loss of higher-order network effects, but it is precisely such effects, and the dependencies they create among observations, which are problematic in the context of traditional statistical methods.

3 Some Examples

Does selective mixing really matter in the spread of disease? The answer is yes, and this section will present several examples based on the spread of HIV that show the strength and variability of these effects. The examples have been chosen to highlight two dimensions of selective mixing that are

realistic and important for disease transmission dynamics: the assortative-disassortative continuum, and the stability of the attributes on which selection is based. Simulations in all cases use compartmental models for disease transmission and log-linear methods for incorporating local network mixing data. HIV-related biological parameters are the same in all cases: infectivity is varied from 0.01-0.1/partnership for gay and heterosexual populations respectively (Fischl *et al.* 1987, Peterman *et al.* 1988, Wiley *et al.* 1989), and for simplicity is modeled as constant throughout the infectious period (but see Longini *et al.* 1989), the incubation period is 10 years (Taylor *et al.* 1991), and time from AIDS to death is 2 years; both periods are modeled with simple exponential functions. Vital dynamics are included, though set to produce fairly stable populations in the absence of disease-induced mortality. In all but one case, the mixing matrices are based on observed behavioral data. Selective mixing is compared to proportional mixing using a 'prevalence ratio': the ratio of infection generated when the simulation is run using selective mixing to that generated when it is run using proportional mixing. When this ratio is larger than 1, selective mixing generates relatively more infection.

Case 1: Race/Ethnicity-matching among heterosexuals

Stable attributes with loose and variable assortative matching

Rates of HIV infection and clinical AIDS in the heterosexual population are much higher among Blacks and Hispanics in the US than among whites (Centers for Disease Control 1991a,b). Because the original focus of heterosexual infection was among IDUs, there is some question whether the epidemic will continue to spread sexually to non-IDUs, and whether patterns of race and ethnicity matching in sexual behavior are strong enough to decouple the HIV epidemics in the different subgroups. The AIDS in Multi-Ethnic Neighborhoods Survey (AMEN), a random sample of adults in 3 high-risk neighborhoods of San Francisco, has collected sexual network data that make it possible to examine parts of this question (Catania *et al.* 1992). The race and ethnicity mixing matrix of sexual partners from this study is presented in Figure 3. Given the sample neighborhoods, the contact rates here, about 2 new partners/year, are likely to be somewhat higher than in the general population.

The results of simulating the sexual transmission of HIV in this population are presented in the four panels of Figure 4. Simulations based on an infectivity of 0.01/partnership do not sustain the epidemic in this population (panels (a) and (b)). In order to raise the reproductive rate above threshold, infectivity would have to be on the order of 0.1/partnership (panels c and d). At this level, the effects of mixing can be clearly seen. Assortative mixing lowers overall seroprevalence (panel c) but it turns out this is largely a composition effect, as it lowers prevalence among whites, the largest group. At the subgroup level, the effects of the assortative bias vary strongly, interacting with other characteristics of the transmission process (panel d). The initial effects depend on initial prevalence. Where initial prevalence is high, as among whites here, assortative mixing acts to intensify within-group spread, increasing rates of infection relative to proportional mixing. Where initial seroprevalence is low, as it is among blacks here, assortative mixing helps to keep it low. These initial effects may be transient, however. If the group has a relatively lower contact rate, as whites do here, transmission is reduced by within-group selection and eventually leads to lower levels of infection. If the group has a relatively higher contact rate, as Blacks do here, within-group selection amplifies transmission, leading to higher levels of infection. Where both initial prevalence and activity level are low, and the assortative bias is relatively strong, selective mixing always leads to lower levels of infection. This pattern can be seen in the Latin subgroup.

These simulations show that even when the effects of selective mixing are small at the aggregate level, they may be quite pronounced at the subgroup level. While overall seroprevalence is reduced by about 5%, subgroup prevalence may be as much as 20-40% higher (or lower).

Case 2: Sexual preference matching

Stable attributes, strong assortative and disassortative matching

One of the most frequently asked questions about the future of HIV trans-

Men:	Women: Black	Latina	White	Other	Pairs	Contact Rate
Black	506	32	69	26	633	2.61
Latino	23	308	114	38	483	1.61
White	26	46	599	68	739	2.01
Other	10	14	47	32	103	1.56
Pairs	565	400	829	164	1958	
Contact rate	1.58	2.00	2.53	2.73	2.07	2.04
Initial prevalence:						
males:	1.8%	2.4%	3.7%	2.2%		
females:	0.5%	0.7%	0.3%	0.0%		

Black	Latina	White	Other	Margins
36.23				1.00
	8.24			3.16
		3.97		5.70
			1.75	12.24
1.00	1.21	1.36	2.32	0.31

Figure 3: Race and ethnicity matching among heterosexuals. The first table presents the mixing matrix observed in the AMEN study and the race and sex-specific seroprevalence, the second table schematically presents the exponentiated coefficients from the best fitting log-linear model.

why would the lower/higher contact rate in a group reduce transmission? Does this assume that their contact rate would go up if they mix with a different group?

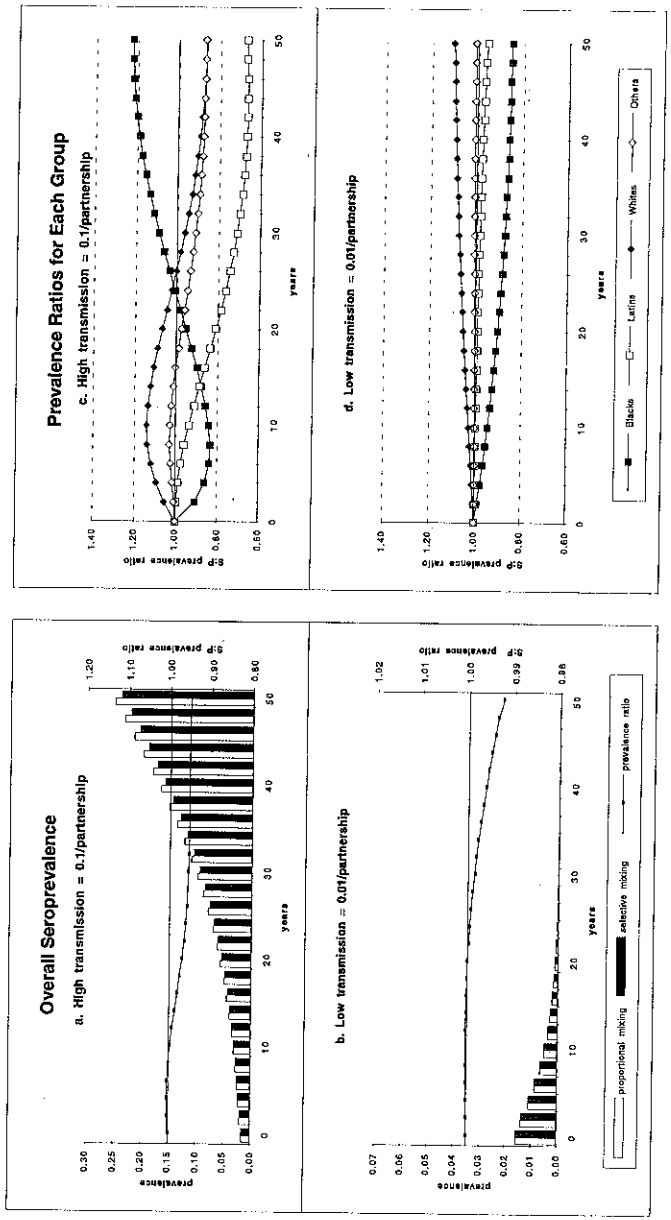

Figure 4: Effects of race and ethnicity matching on seroprevalence. Panels (a) and (b) display the overall seroprevalence in the population under different mixing and contact scenarios in the bars, and the ratio of selective to proportional mixing in the dashed line. Panels (c) and (d) display the four group-specific prevalence ratios for high and low infectivity scenarios. When infectivity is low, the epidemic dies out. When infectivity is high enough to sustain the epidemic, assortative mixing lowers overall seroprevalance, but either raises or lowers group-specific prevalence, depending on contact rates, the strength of the assortative bias, and initial levels of seroprevalence.

Subject:	Partner: He Male	He Female	Bi Male	Ho Male	Pairs	Contact rate
He Male	0	8256	0	0	8256	2.06
Female	8256	0	1140	0	9396	1.88
Bi Male	0	1140	144	1248	2532	5.05
Ho Male	0	0	1248	11268	12516	25.04
					32700	
						5.17
Initial prevalence	0	0	0	10%		

He Male	Female	Bi Male	Ho Male	Margins
0		0	0	1.00
	0		0	.91
				1.10
			1.0	9.97
				4.53

Figure 5: Sexual preference matching (simulated data). The first table presents the mixing matrix of simulated data on sex and sexual preference matching for the high-activity, no assortative bias scenario. Initial prevalence was set at 10% of the homosexual male population. The second table schematically presents the exponentiated coefficients from the log-linear model used to produce the mixing matrix. The shaded cells indicate this is a model of symmetry, so the lower triangle and margins have the same parameters as the upper.

mission in the US is whether the epidemic will spread from gay males to the heterosexual population. The potential for this spread is a function of two things: the size and mixing patterns of the bisexual bridge population and the contact rates for the different subgroups. While some data exist on group-specific contact rates, there are no data on the prevalence and mixing patterns of bisexuals, making simulated data the only way to address this question. The example here uses a log-linear model to generate simulated contact matrices under various mixing and activity level conditions. Four conditions were simulated: high and low levels of activity among homosexual men (25 and 2 new partners/year) and two levels of mixing with bisexuals, regulated by setting the odds-ratio of the bottom right quadrant of the matrix. When this odds-ratio is 1, there is no assortative bias among homosexual and bisexual males. Figure 5 presents the contact matrix for the high activity, no assortative bias condition, and the corresponding exponentiated log-linear parameters.

The effects of the activity and mixing assumptions can be seen in Figure 6.

The activity effects dominate in this set of simulations, with the lower level generating substantially lower seroprevalence (panels a and b). Selective mixing, however, also has strong effects, as the heterosexual population

Figure 6: Effects of sexual preference mixing on seroprevalence. Panels (a) and (b) display the overall seroprevalence in the population under different mixing and contact scenarios in the bars, and the ratio of selective to 'proportional' mixing in the dashed line. Panels (c) and (d) display the four group-specific prevalence ratios for high and low contact scenarios. When contact rates are high, selective mixing reduces transmission from the initially infected group to the other three groups, but this shielding declines over time, especially for heterosexuals. When contact is low, there is little spread beyond the seeded group, and the shielding effect of selective mixing slightly increases over time.

is not infected under any of the four scenarios. Even in the high-contact simulations (panels c and d), which generate 50-70% infection rates among the homosexual and bisexual men, the combination of a limited bridge population and lower transmission in the heterosexual population prevents the epidemic from spreading further. When contact rates are low, assortative mixing displays the same patterns as in the race-matching example, raising within-group transmission among the initially infected group by about 50%, and shielding the other three groups, lowering their prevalence by around 90%. When contact rates are high, the story is a bit more complicated. Assortative mixing reduces overall prevalence, but these effects diminish over time. Among the individual subgroups, the assortative shielding effect is strongest for bisexuals. This effect is also initially strong for heterosexuals, but then, counterintutively, it rises over time and actually becomes larger than 1 for females. The reason is because assortative homosexual mixing here increases bisexual-female contacts by more than it reduces the bisexual infection rate. Under assortative mixing, bisexual contacts with females rise by a factor of 3.7. Part of this is due to the mixing bias (46%), and part to the lower infection, and thus lower AIDS-related population depletion, for bisexuals (54%). The bisexual infection rate is roughly 1/3 lower under assortative mixing. As a result, the increase in contacts outweighs the decrease in prevalence, and there is eventually more spread from bisexuals to heterosexuals under the assortative mixing scenario. In neither case, however, does the prevalence among heterosexuals rise above 1%. Thus, the existence of a bridge population does not in itself guarantee that the epidemic will spread. If the level of activity in the uninfected population is below reproductive threshold, the infections transmitted by the bridge population will not be sustained.

In sum, selective mixing based on stable characteristics permits group isolation. It allows the disease to spread pervasively some groups without ever gaining a foothold elsewhere. One implication of this is that resources should be focused where they will have the most impact, not on a flank where the fear may be high but the the risk is demonstrably low.

Case 3: Age-Matching among Heterosexuals

Changing attributes, strong assortative matching

Among heterosexuals, one of the strongest forms of assortative mixing is age-matching. If this matching were perfect, young cohorts would never become infected by older ones, and the disease would disappear from the population as the infected cohorts eventually died. Age-matching is not perfect, however, and contact rates tend to be higher among younger persons than among older. As in the examples above, assortative bias coupled with higher contact rates might instead raise infection rates for the younger cohorts. The

Men:	Women: 15-24	25-34	35-44	45-54	Pairs	Contact rate
15-24	21080	1536	108	23	22746	2.55
25-34	4162	7541	768	35	12507	1.22
35-44	135	2426	5589	431	8583	0.93
45-54	25	196	1946	4181	6348	1.06
Pairs	25403	11699	8411	4671	50184	
Contact rate	2.98	1.15	0.89	0.75		1.46
Initial prevalence	10%	0.0	0.0	0.0		

	15-24	25-34	35-44	45-54	Margins
15-24	1.28			0.08^d	1.00
25-34		0.67			0.51
35-44		5.96	1.20		0.28
45-54	0.08^d			0.83	0.42
	1.00	0.98	0.88	1.47	1904.55

Figure 7: Age matching among heterosexuals. The first table presents the mixing matrix for heterosexuals constructed from 1991 US Census marriage tables and General Social Survey data on age-specific sexual contact rates. Initial prevalence was set at 10% of the youngest age group for both sexes. The second table schematically presents the exponentiated coefficients from the best fitting log-linear model. The shading identifies cells with the same selection effect, in this case a strong asymmetric bias towards older men-younger women. The distance effect is only shown in the upper right and lower left corners, but it affects all the off-diagonal cells. This effect requires only one parameter, and takes the form of a decrement, $\beta^{|d|}$, where d is the distance from the diagonal. Here, each step off the diagonal reduces the probability of a partnership by 92%.

strength of the assortative bias will therefore determine the degree of infection in younger cohorts and the future of the disease. There is one survey that has collected sexual network data on age-matching in the US adult population, but was is not publicly available when this analysis was performed. What is used as a proxy here comes from the US Census crosstabulations of age of husbands and wives (United States Bureau of the Census, 1991), supplemented by data from the General Social Survey on age-specific sexual contact rates (Davis and Smith 1992, Smith 1991, 1992). The resulting mixing matrix is presented in Figure 7.

The effects of age-matching on the epidemic can be seen in Figure 8. Here, as in the previous example, the contact rates are too low to support an epidemic when infectivity is at 0.01/partnership. The reproductive threshold occurs at around 0.05/partnership, and a sustained epidemic in the youngest group requires infectivity closer to 0.1/partnership. The results in Figure 8 are based on the 0.1 level. The effects of mixing are similar for each level of infectivity, but easier to see at higher levels.

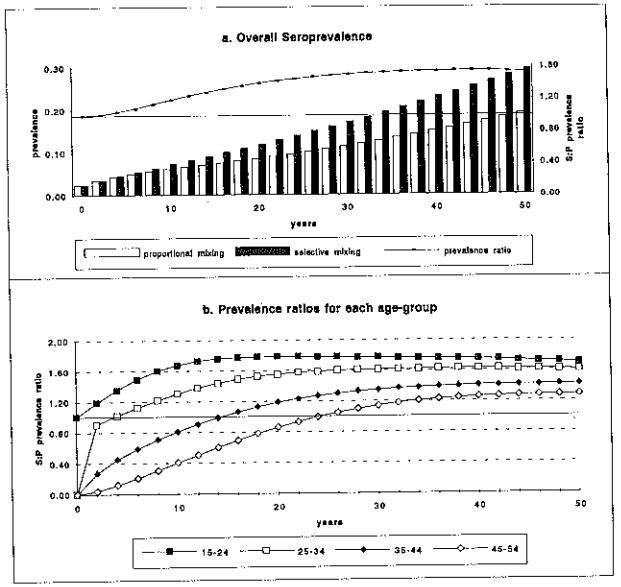

Figure 8: Effects of heterosexual age matching on seroprevalence. Panel (a) displays the overall seroprevalance in the population under proportional and selective mixing scenarios in the bars, and the prevalence ratio in the dashed line. Panel (b) displays the age-group specific prevalence ratios. Here assortative mixing raises seroprevalence in every age group.

In contrast to the two previous examples, selective mixing here increases overall seroprevalence by about 60% (panel a), and eventually increases the prevalence in every age group as well (panel b). The assortative bias generates higher levels of infection among the youngest group from the start, due, as in the previous examples, to the combination of assortative bias and higher contact rates. At its peak, assortative mixing raises prevalence by 80% over proportional mixing. The older groups, with lower contact rates and initially lower prevalence, are shielded by the assortative bias at first. But this effect is transitory because age, unlike race or sexual preference, is an attribute that changes over time. As a result, the infections are sent up the age chain in two ways: through sexual contacts between age groups, and by the aging process. While assortative mixing reduces the contacts between groups, it does not affect the aging process, so the higher prevalence it generates among the youngest group becomes, as they age, higher prevalence among the older groups.

The relative impact of aging and sexual transmission can be observed by comparing these results to models run without any sexual transmission (i.e., models where the infectivity is set to 0). The effects of aging are larger for the groups closer to the initially seeded group, as might be expected. Aging

accounts for about 50% of the infections among the 25–34 year olds, 16% among the 35–44 year olds, and 6% among the 45–54 year olds. These effects are slightly stronger under selective mixing, as the assortative bias reduces the extent of sexual transmission between groups. When infectivity is too low to sustain the epidemic over time, the infection moves like a bulge through the age chain, and the highest rates of infection are eventually found among the older groups.

When the attributes that define mixing groups change over time, therefore, mixing may not isolate infection in groups but spread it more effectively. This has strong implications for the way in which HIV may spread in minority communities in the US. While race and ethnicity-matching may serve to decouple the epidemics, age-matching within racial and ethnic subgroups may serve to amplify within-group spread.

Case 4: Age-Matching among Gay Men

Changing attributes, loose assortative matching

As in the example above, the future of HIV among gay men in the US will be determined largely by the rates of new infection among its younger cohort. Age-matching again might be expected to provide a partial shield against the transmission of HIV from the higher prevalence older cohorts. The assortative bias is likely to be looser among gay men than among heterosexuals, however, and surveys suggest that young gay men continue to practice unsafe sex at higher rates than their older peers (Ekstrand and Coates 1990, Hays *et al.* 1990). Whether the interaction between mixing and contact rates is sufficient to sustain the epidemic in this population is thus an open question. Data from the Longitudinal AIDS Impact Project (LAIP), one of the few studies of gay men to collect any form of network data, will be used to examine this question. LAIP is a 7-year cohort study based on a stratified convenience sample of gay men in New York City (Martin and Dean 1990). The age-matching matrix for insertive and receptive anal intercourse partners from this study is presented below in Figure 9.

The infection is seeded into the 35–54 year olds (groups 3 and 4 in the matrix). Contact rates change over the simulation period from about 13/year to about 1/yr, based on LAIP data. Initial simulations were calibrated against AIDS surveillance data in New York City for the risk group 'men who have sex with men' to ensure that early patterns in the epidemic were matched. The calibrated model suggests that the current patterns of behavior are just on the boundary of reducing the epidemic spread below the reproductive threshold. If these data on behavior are accurate, and the patterns are maintained in the future, then the disease would eventually die out in the absence of other sources of infection (e.g., links with IDUs). If, on the other hand, respondents

I don't understand this table and what determines which cells (and why) are grey or blank

	Receptive: 18-24	25-34	35-44	45-54	Pairs	Contact rate
Insertive: 18-24	55	161	51	14	281	8.78
25-34	206	1873	1360	292	3732	11.01
35-44	85	1373	2474	483	4416	16.17
45-54	12	229	371	171	783	9.67
Pairs	359	3636	4257	960	9212	
Contact rate	11.21	10.73	15.59	11.86		12.71
Initial prevalence	0.0	0.0	0.01	0.01		

	18-24	25-34	35-44	45-54	Margins
18-24	6.14		0.48		1.00
25-34		0.51			1.65
35-44			1.11		1.58
45-54				2.13	1.15
	1.00	2.22	2.17	1.21	6.34

Figure 9: Age-matching among gay men. The first table presents the age-mixing matrix observed in the LAIP study for 1981, and initial age-specific prevalence is set for both insertive and receptive groups as shown. The second table schematically presents the exponentiated coefficients from the best fitting log-linear model. The shading represents cells with the same selection effect, here a 'blocking' effect that reduces the probability of a partnership by 52% in the off-diagonal quadrants.

have under-reported the number of new partners they have, the result could be quite different. With about two new partners per year (instead of the one reported), the disease would instead become endemic, with seroprevalence levels of about 50% among the exposed population in the oldest group, and about 25% among the youngest.

The mixing effects can be seen in Figure 10. In contrast to the previous example, age-matching here initially raises seroprevalence, but eventually lowers it (panel a). This pattern is reproduced for each age-group (panel b), but the reasons are fairly complicated.

For the initially seeded groups, the assortative bias raises within-group contacts by 25–100%, leading to faster within-group spread at first. Within five years, however, the higher infection rates begin to lead to greater population depletion in these two groups. This translates into fewer infections passed down the age chain, and, by virtue of the aging process, eventually leads to lower seroprevalence among these older groups.

The key to the rest is what happens to the second group, the 25–34 year olds. The assortative bias here lowers contacts with the older two groups by 20–25%, but the 40–60% higher infection rates in the older groups offset the contact reduction, and the net result is 20–30% more infections transmitted to this group. During the first five years, while contact rates are still high, the assortative bias amplifies the higher rates of infection entering the group,

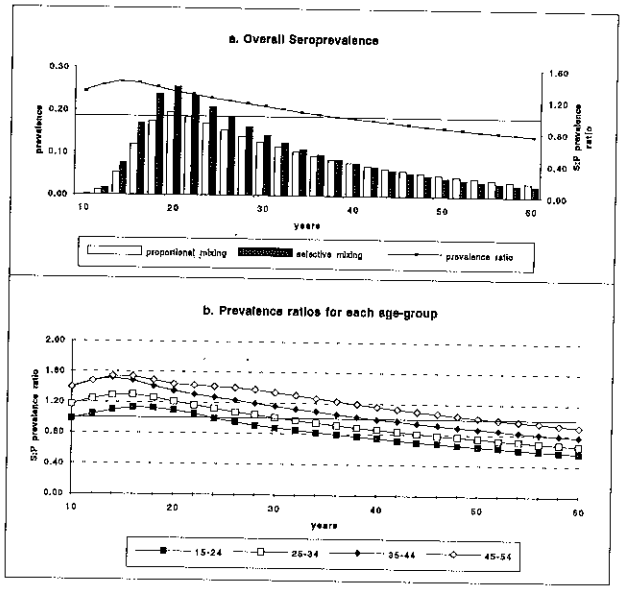

Figure 10: Effects of homosexual age matching on seroprevalence. Panel (a) displays the overall seroprevalance in the population under selective and proportional mixing scenarios in the bars, and the prevalence ratio in the dashed line. Panel (b) displays the age-group specific prevalence ratios. Age-matching again increases prevalence in all groups, but the effect declines over time, and the assortative bias eventually acts as a shield.

and the result is prevalence levels 40% above those found under proportional mixing. Eventually, however, the population depletion in the older two groups reduces the number of contacts sufficiently that the assortative shielding effect begins to dominate, and prevalence is lowered relative to proportional mixing.

The youngest group is initially the least active here, and the assortative bias is strongest for them, so one might have expected selective mixing to lower their prevalence from the beginning. The 'block' effect found in the off-diagonal quadrants of the mixing matrix data, however, is strong enough to raise the number of contacts between this group and their 25–34 year old neighbors by about 25%. Coupled with the 25–30% higher rates of infection among 25–34 year olds, these additional contacts translate into higher rates of infection among the youngest group as well. Once prevalence begins to decline in the 25–34 year olds (due to population depletion in the older groups), it also begins to decline in this group. As in the heterosexual age-matching example, the lower rates of infection for the young eventually work their way up the age chain to become lower rates of infection for older groups, cf. Morris and Dean (1994) for a more complete discussion.

Assortative age-matching can therefore have a shielding effect, but the timing of this effect depends on other parameters of the transmission process. Rates of contact and AIDS-related population depletion determine whether the assortative bias increases or reduces rates of infection over time.

4 Conclusion

These examples make it clear that network structures matter for disease transmission. The type of attributes that define network boundaries also matter, and can channel diffusion into markedly different paths. Where attributes like race and sexual preference form stable mixing groups, the potential for spread from a seeded population depends on bridges, initial seroprevalence, and eventually group-specific contact rates. With a small bridge, infection may remain isolated, even under fairly extreme conditions, provided contact rates in other groups are below the reproductive threshold. Where attributes like age instead form ordinal, fluid mixing groups, the potential for spread is much higher. Here the mixing structure is characterized by a dual transmission regime, with some infections carried up the age ladder along with each cohort, and others passed by sexual contact. This mixing structure makes the epidemic much more likely to spread, even with lower contact rates. Assortative age-matching can provide some shielding effect to younger cohorts, but the strength of this effect depends on the strength of the bias and on other aspects of the transmission process, especially disease-related population depletion.

Given the complicated way that mixing interacts with other factors, it may not be possible to develop simple descriptions of 'mixing effects'. Analytic results should continue to be sought, however, and this is an important area for future research. The initial explorations here suggest that the assortative/disassortative continuum and the stable/changing attributes distinction must be incorporated into any future analytic development.

The importance of stable and changing attributes has a parallel in spatial models: 'nearest neighbor' models can be thought of as forcing nodes to occupy a stable position, while models that permit long jumps allow for some notion of changing position. From this perspective, people can be thought of as inhabiting a multidimensional space. Some of these dimensions describe their coordinates in the physical world, but the remainder describe their position in social terms, and their 'distance' from others. The integration of spatial and social networks is necessary to provide a comprehensive framework for non-random mixing. This is an important goal for future research.

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The Effect of Antigenic Diversity on Endemic Prevalence

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Summary

The rapid rise with age in exposure to *Plasmodium falciparum* malaria has generally been ascribed to its high transmissibility. In this chapter, we propose that this interpretation is only valid for infections that induce lifelong immunity, and thus cannot be applied to malaria. The delay in development of protective immunity to malaria permits a rapid increase in exposure with age for low values of the basic reproductive rate (transmissibility) that are consistent with epidemiological observations, and particularly with realistic measures of the duration of infectiousness. The long period required to develop protective immunity to malaria can be explained by the antigenic diversity of the parasite. We present data on patterns of seroconversion to 5 antigenically distinct isolates of *P. falciparum* in a holoendemic malarious area, showing that exposure to any one serotype rises slowly with age. This indicates that malaria can be seen as a basket of mildly transmissible antigenic types, each of which may induce lifelong serotype-specific immunity. The basic reproductive rate of malaria, as calculated from this data appears to be between 6 and 7, which is an order of magnitude lower than typical previous estimates.

1 Introduction

Plasmodium falciparum malaria is one of the major causes of child mortality and morbidity in tropical and sub-tropical regions. The number of yearly reported cases is in the range of 200 million with more than 2 million deaths (Struchler 1984). The success of global malaria eradication programmes has