MATHEMATISCHES FORSCHUNGSINSTITUT OBERWOLFACH

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Mathematical Models for Infectious Diseases

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In the past twenty years the mathematical theory of epidemics and infectious diseases has evolved as an independent and important field parallel to the growth and in close interaction with Mathematical Biology. Here we understand 'epidemics' indeed as the theory of infectious diseases rather than just as epidemiology of diseases of any kind. As Mathematical Biology in general, the Theory of Epidemics uses differential equations, integral equations, stochastic processes to model the outbreak and spread of infectious diseases. In addition statistical methods are widely used. Due to the special features of the problems, most data are field observations rather than experimental data.

In the early years much attention has been paid to viral and bacterial diseases (smallpox, measles, rubella, typhoid fever), as well as malaria, in the seventies and eighties also tropical helminthic diseases (e.g. schistosomiasis) have been investigated. Naturally at present much interest is concentrated on sexually transmitted diseases, mainly related to the spread of the HIV infection.

The Mathematical Research Institute has recognized the relative importance of this field and has organized this meeting with assistance of K. Dietz (Tübingen), K.P. Hadeler (Tübingen), H. Hethcote (University of Iowa).

One reason to have this meeting exactly in 1989 is related to recent historical research of Klaus Dietz on the work of the Russian medical scientist En'ko who in 1889 in St. Petersburg (Leningrad) developed the first mathematical models for infectious diseases, several decades earlier than the wellknown references in the field. In an introductory lecture Klaus Dietz gave a survey on this early research. Professor Ivannikov from the USSR federal health authorities in Leningrad has been able to attend the meeting.

The 42 participants were mainly mathematicians and statisticians, some working in medical and biological institutions. The major topics were qualitative behaviour of classical models (stability of the infected state, onset of oscillations in autonomous models, forced oscillations, subharmonic bifurcations), relations between epidemic models and ecology (parasite-predator-prey interaction), statistical analysis of disease data, populations structured by age and social parameters and the spread of

disease in such populations, hybrid models and stochastic models for macroparasitic infections. A rather large proportion of lectures and much of the discussions were devoted to the HIV infection: data collection, estimation of incubation periods, stochastic and deterministic models, structured populations, demographic impact.

The organizers had to deal with the well known problem of finding a proper balance between formal presentations and informal discussions and cooperations. The participants solved this problem by agreeing to a schedule of only five lectures per day and informal evening presentations and a general discussion.

The general discussions revealed some rather important problems for future research: 1. The basic reproduction ratio as the number of secondary cases caused by one infected individual is a mathematical quantity with an obvious epidemiological interpretation. For many critical parameters in epidemiological models it has not been shown that they are in fact the basic reproduction ratio. This question is related to the problem of giving a valid stochastic interpretation to deterministic models. 2. The appropriate modeling of heterogeneity. The description of contacts, infections, formation of pairs in heterogeneous populations is a difficult task which can be approached from different sides, e.g. using subdivided populations or random graphs. 3. The investigation of the HIV infection is the most challenging problem both from a practical point of view (e.g. data collection, definition of disease state, estimates of contact rates and incubation periods) as well as in mathematical modeling.

Several participants started joint work at this conference. Many new contacts have been established. The organizers feel that the aims of the conference have been achieved. The participants including the organizers express their thanks to the Mathematical Research Center staff in Freiburg and Oberwolfach for the effective administration and good care.

Although the organizers failed to invite some gifted piano players the music room did not remain unused. One of the senior participants, otherwise known for his excellent lectures, introduced the audience into the intricacies of an ancient English musical instrument.

Vortragsauszüge

Joan L. Aron

Multiple Attractors in Response to a Vaccination Program in a Seasonal SEIR Model

Though it is well known that multiple attractors may co-exist in the SEIR (susceptible/exposed/infective/recovered) epidemic model with vital dynamics and seasonally forced oscillations in transmission, the epidemiological significance of multiple attractors has been subject to debate. I show that the co-existence of attractors is relevant in using the model to study a program of vaccinating a fraction of all newborn susceptibles. When vaccination is introduced, the system may

be attracted to different periodic orbits. The exact timing of the introduction and the basic reproductive number determine which orbit is the attractor.

Viggo Andreasen, Freddy B. Christiansen

Threshold conditions for the persistence of an infectious disease in a heterogeneous population

We derive necessary and sufficient conditions for disease persistence in a subdivided population where intergroup transmission is described by proportionate mixing while intragroup transmission may correspond to preferred mixing, proportionate mixing among subgroups, or mixing between social and non-social subgroups. The disease persists if and only if one of the following conditions is satisfied: i) The disease can persist within at least one group through intragroup contacts. ii) The intergroup transmission is sufficiently high. Here the contribution from each group is weighted according to its activity level squared and to the total number of cases caused by intragroup transmission.

Frank Ball

Coupling, Epidemics and Confidence Intervals

We present four applications of stochastic coupling to the general stochastic epidemic. The first application (Ball 1986) provided a new proof of a result of Daniels (1967), enabling us to derive the triangular set of linear equations for the total size distribution, first given by Whittle (1955). In the second application (Ball 1983) we construct a sequence of epidemics, indexed by initial susceptible population size, from a birth-and-death process. This enables us to show almost sure convergence of the total size of the epidemic processes to that of a birth-and-death process, and consequently provide a new proof of the stochastic epidemic threshold theorem. In the third application (Ball 1985) we show that varying the susceptibilities of individuals to the disease slows down the spread of the epidemic. In the final application we use a coupled family of Barnard Monte Carlo hypothesis tests to provide a Monte Carlo confidence interval for the relative removal rate, based upon the observed total size of an epidemic. The resulting confidence interval is rather wide and an alternative (shorter) interval is presented.

References:

Ball, F.G. (1983): The threshold behaviour of epidemic models. J.Appl.Prob. 20, 227-241.

Ball, F.G. (1985): Deterministic and stochastic epidemics with several types of susceptibles. Adv.Appl.Prob. 17, 1-22.

Ball, F.G. (1986): A note on the total size distribution of epidemic models. J.Appl.Prob. 23, 832-836.

Daniels H.E. (1967): The distribution of the total size of an epidemic. Proc. 5th Berkeley Symp.Math.Statist.Prob. 4, 281-293.
Whittle, P. (1955): The outcome of a stochastic epidemic - a note on Bailey's paper. Biometrika 42, 116-122.

Niels Becker

Analysis of the Infection Rate

Epidemic data typically consists of the times at which individuals show symptoms. On such data one can perform a regression analysis based on a generalized linear model, when one assumes that the latent and infectious periods are of constant durations. This provides an effective way of determining whether variables such as age, sex, number of infections present, etc. affect the risk of infection taking place.
It is important to determine whether the infection rate varies with calendar time as this can point to the presence of heterogeneity among susceptibles.
Variation in the infection rate over time can also be explored by nonparametric estimations using the method of Aalen. This can provide additional insights. These ideas are illustrated with reference to data from an epidemic of smallpox.

Lynne Billard

Incubation Period for AIDS Virus, and some Aspects of Mathematical Modelling

The incubation period is defined as the time from acquisition of the AIDS virus until time of diagnosis as having AIDS. This report investigates the distribution of the incubation period for blood-transfusion data. Results include consideration of the influence of age and sex on the incubation period. Problems associated with the analysis of the data are discussed.

Ph. Blanchard

Modeling AIDS on Random Graphs

The individuals of a given society C are considered as vertices of a graph and the edges of the graph are supposed to represent realized sexual contacts. A pair (G, ϕ) consisting of a space G of random graphs and a time ordering of the edges are introduced to model the sexual contact graph of the real life. If we consider only complete graphs or complete $n-$partite graphs, sexual contacts are now realized uniformly. In other words the standard modeling of epidemics using systems of ordinary differential equations appears as a special limiting case. The spread of the epidemic is described as a discrete time stochastic Markov process.

We introduce first the general epidemic process (G, ϕ, x, r) on a space for random graphs and we discuss some special models where the underlying random graphs are generated by independent matchings (pairing of sexual partners). Moreover we study the role and meaning of the reproductive number R as a critical parameter for the existence of an endemic equilibrium state in Random Graph Epidemics. We conclude by discussing some results obtained by computer simulation comparing for the same values of the parameters the spread of the epidemic predicted by the random graph model and by the classical models. Computer simulations show that on the graph the epidemic expands much slower.

G.I. Marchuk, A.A. Romanyukha, G.A. Bocharov

Mathematical Models in Immunology

The defence of a human organism against viral and bacterial infections and the response of the immune system to contamination are the basic problems of clinical medicine. We present three mathematical models of antiviral and antibacterial immune response of the following form:

$$\frac{dy}{dt} = f\Big(y(t), y^{[1]}(t-\tau_1), ..., y^{[m]}(t-\tau_m)\Big), \quad y \in R^N, y^{[i]} \in R^{N_i},$$

$$N_i \leq N, \quad i = 1, 2, ..., m; \quad t_0 \leq t \leq t_0 + T,$$

$$y(t_0) = \varphi^0$$

$$y^{[i]} = \varphi^{[i]}(t), \quad t \in [t_0 - \tau_i, t_0].$$

The simplest mathematical model of an infectious disease was used to investigate the general laws of immune system reaction to an antigen. The mathematical model of the antiviral immune response was used for modeling the acute form of viral hepatitis B. The mathematical models of antiviral and antibacterial immune responses were used for description of biinfections of lungs.

Vincenzo Capasso

Global Stability Results for Epidemic Systems

In Beretta-Capasso (1986), the authors introduced a unified treatment of a wide class of epidemic systems by means of a general ODE system which actually includes many of the models proposed up to now by different authors and analyzed in different "ad hoc" mathematical techniques. Based on the particular structure of the ODE system, sufficient conditions for the global asymptotic stability (hence uniqueness) of the nontrivial equilibrium solution of the system were given.
Here we extend the treatment to include more general structures. The new system describes a larger class of epidemic models, among which continuous time delays and multigroup models are included.

C. Castillo-Chavez

Effects of Social Mixing in the Spread of HIV/AIDS

Two topics are presented. First we report on the formulation and mathematical analysis of single and multiple group models for the sexual spread of the human immunodeficiency virus (HIV) which is the etiological agent for the acquired immunodeficiency syndrome (AIDS). Single group models are shown to be very robust even in the presence of variable infectivity. Multiple group models with variable population size and proportionate mixing are shown to have multiple equilibria. Secondly we present two new general methods for incorporating like-with-like preference into one-sex mixing models in epidemiology. The first is a generalization of the preferred mixing equation, while the second comprises a transformation of a general preference function for partners of similar sexual activity levels. Both methods satisfy the constraints implicit in a mixing model. We then illustrate how the tranformation preference method behaves and compare it with the standard proportionate mixing.

References:

Castillo-Chavez, C.; Cooke, K; Huang, W.; Levin, S.A.: Results on the dynamics for models for the sexual transmission of the human immunodeficieny virus. To appear in Applied Math. Letters.

Blythe, S.P.; Castillo-Chavez, C.: Like-with-like preference and sexual mixing models. To appear in Math. Biosciences.

Castillo-Chavez, C.; Cooke, K.; Huang, W.; Levin, S.A.: On the role of long incubation periods in the dynamics of HIV/AIDS. Part I. Single populations models. J.Math.Biology (in print).

Huang, W.; Castillo-Chavez, C.; Cooke, K.; Levin, S.A.: Multiple group models for the spread of HIV/AIDS with multiple endemic equilibria. In: Mathematical and statistical approaches to AIDS epidemiology. (C. Castillo-Chavez, ed.) Lecture Notes in Biomathematics, Springer-Verlag (volume in preparation).

H.E. Daniels

Perturbation and Saddlepoint Approximations for Simple Epidemics

The saddlepoint approximation for the probabilities of the number of infectives in a simple epidemic is highly accurate for quite small populations. This enables the accuracy of perturbation approximations to the mean and variance to be evaluated for various kinds of simple epidemics and gives some guidance on what to expect of perturbation approximations for more general epidemics where saddlepoint approximations are not available.

Odo Diekmann

On the Definition and the Computation of R_o

The basic reproductive number R_o is by definition the expected number of secondary cases produced by a typical infected individual during its entire period of infectiousness, when introduced in a population which is in a steady demographic state with all individuals susceptible. Mathematically it is the dominant eigenvalue of the (linearized) next generation operator

$$(K(S)\phi)(\xi) = S(\xi) \int_\Omega \int_0^\infty A(\tau, \xi, \eta) d\tau \phi(\eta) d\eta$$

on $L_1(\Omega)$. Here the variable ξ accounts for heterogeneity, S gives the steady distribution of susceptibles and A describes the infectivity towards susceptibles in state ξ of infectives which were infected τ units of time ago while having state η. Under certain conditions (proportionate mixing and variants thereof) one can compute or estimate the dominant eigenvalue. Some examples involving discrete groups, age or propensity to make sexual contacts will be presented.

Klaus Dietz

Historical Aspects of the Mathematical Theory of Infectious Diseases

The first chain binomial model was constructed and fitted to data of measles epidemics by P.D. En'ko, a physician at the Academy for the Daughters of the Middle-Class of the Smolnyi in St. Petersburg and published in 1889 in the weekly medical journal Vrach more than sixty years before the Reed-Frost model was applied to data (see K. Dietz, Austral.J.Stat., 30A, 1988, 56-65). The so called catalytic model of Muench (1959) is to be found in D. Bernoulli (1760) and Ross (1916). The so called Kermack-McKendrick (1927) model for the SIR epidemic was analysed by Ross and Hudson (1916) and the SIR endemic was first formulated by Martini (1921) and studied by Lotka (1923).

H.I. Freedman

Predator-Prey Population with Parasitic Infection

Models of predator-prey systems are considered where both populations are infected by a parasite. In the case where all predators are infected, the prey population is separated into a susceptible and an infected class, each with different functional responses. Criteria are obtained for persistence of the predator population in the presence of parasites when extinction would have occurred otherwise. Criteria leading to a technique for global asymptotic stability of a positive equilibrium are also derived. In the case that both populations consist of infecteds and

noninfecteds, a threshold of infection is shown, below which the infected populations cannot survive. As well, it is shown that above the threshold, the dynamics could demonstrate either Hopf or pitchfork bifurcations.

J.P. Gabriel

A Remark on Global Behavior

The purpose of the talk was the exposition of an elementary method to discuss the asymptotic behavior of some two-dimensional models in parasitology. It can be easily applied to a class containing Ross' model for malaria. It also provides us with a simple proof of the main result of monotone system theory for differential systems in the plane.

K.P. Hadeler

Homogeneous Evolution Equations for Sexually Transmitted Diseases

A model system of eight differential equations for noninfected and infected singles of either sex and for the four types of pairs formed of such individuals describes the major demographic features such as birth, death, pair formation and separation as well as the transmission of a sexually transmitted disease. The vector field is homogeneous of degree one. Hence there is a related system on the unit sphere and stationary solutions of the latter correspond to exponential solutions of the original problem. This correspondence leads to a concept of stability of exponential solutions (of homogeneous systems). In the present case there is a noninfected exponential solution with an exponent (the "demographic eigenvalue") $\hat{\lambda}$. The Jacobian of the vector field at this solution determines a threshold ("the epidemic eigenvalue") λ_o. The noninfected solution is stable iff $\hat{\lambda} > \lambda_o$.
References:
Hadeler, K.P.; Waldstätter, R.; Wörz-Busekros, A. (1988): Models for pair formation in bisexual populations, J.Math.Biol. 26/6, 635-649.
Hadeler, K.P.; Ngoma, K.: Homogeneous models for sexually transmitted diseases, G.F. Butler Memorial Conference on Differential Equations and Mathematical Biology, Edmonton 1988, Rocky Mtn.Math.J. Special Volume (in print).

Herbert W. Hethcote

Modeling HIV transmission and AIDS in San Francisco

In the simulation model describing the spread of HIV in the homosexual/bisexual population, infected individuals progress through stages to AIDS and death. Parameter values are obtained so that HIV prevalences and AIDS incidences correspond to the observed values from 1978 to 1987. The model also incorporates

changes in sexual behavior which are consistent with changes found in surveys. The patterns of the projections into the future are similar for all parameter sets which lead to a fit of the data.

M. Iannelli

Global Behaviour of SIS Epidemics in an Age-Structured Population

A SIS model, which incorporates age-structure, is presented and results on the asymptotic behaviour of the solution are reported. Namely the following equation is studied:

$$\begin{cases} \frac{\partial i}{\partial t} + \frac{\partial i}{\partial a} + \mu(a)i(a,t) = \lambda(t,a)[p_\infty(a) - i(a,t)] - \gamma(a)i(a,t), \\ u(0,t) = q\int_0^\infty \beta(a)u(a,t)da, \\ u(a,0) = u_0(a). \end{cases}$$

Here $i(a,t)$ denotes age-density of infectives at time t; $\beta(a)$ and $\mu(a)$ denote age-specific fertility and mortality; $p_\infty(a)$ is the distribution of the total population (stationary); $\gamma(a)$ is the age-specific recovery rate; $q \in [0,1]$ is the vertical transmission parameter and $\lambda(t,a)$ is the force of infection. The problem is studied in both the limiting cases and pure INTRACOHORT transmission:

$$\lambda(t,a) = K(a)i(a,t)$$

and of pure INTERCOHORT transmission:

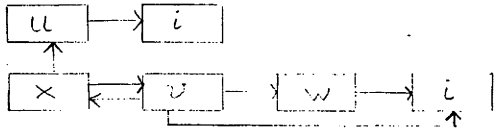
$$\lambda(t,a) = K(a)\int_0^\infty i(a,t)da.$$

In both cases the existence of a threshold parameter is proved which discriminates existence of a non-trivial endemic equilibrium. When this non-trivial endemic state exists, then it attracts any "non-trivial" solution, otherwise the epidemics go to extinction.
While in the intracohort case the method of analysis rests upon reduction to a Volterra integral equation, the intercohort case requires the use of monotonicity techniques within the framework of semi-linear abstract evolution equations.
All these results have been stated in joint papers with S. Busenberg, K. Cooke and H. Thieme.

Yu.G. Ivannikov

The Mathematical Modelling of Spreading of Influenza Viruses which are Resistant to a Chemical Drug

Rvachev's generalized mathematical model of a local influenza epidemic for a single city was used according to the following graph:



where x-susceptible; v and u - infected with drug-sensitive strain whom a drug is (or is not) administered; w - infected with drug-resistant strain; i - immune.
Using a system with discrete time 160 experimental epidemics have been simulated with parameters of the influenza epidemic in Moscow 1969, and have been studied for varied parameters of quota of population using a drug, of effectiveness of a drug and of frequency of virus mutation.
Results: For small effectiveness of the antiinfluenza chemical drugs their unlimited usage does not influence considerably the evolution of resistance of influenza viruses. During application of a drug having high effectiveness the selection of the resistant influenza viruses is highly probable and only reasonable limitation of drug administration does not result in the substitution of the drug-susceptible influenza virus variant by the drug resistant one.

John A. Jacquez, Carl P. Simon

Modeling and Analysis of HIV Transmission. The Effect of Contact Patterns.

A compartmental model is developed for the spread of HIV in a homosexual population divided into subgroups by degree of sexual activity. The model includes constant recruitment rates for the susceptibles in the subgroups. It incorporates stages for the infectious period and so allows one to vary the infectiousness over the infectious period. A new pattern of mixing, preferred mixing, is defined in which a fraction of a group's contacts can be reserved for within-group contacts, the remainder being subject to proportional mixing. The main result is that small amounts of mixing between high and low activity groups markedly increases the spread and steady state levels in low activity groups but has only small effects on the rate of spread in high activity groups.
Recently we have developed far more general ways of specifying many different types of non-random mixing that we call structured mixing and selective mixing. These are described but we do not yet have many results using these methods.

Mirjam Kretzschmar

Persistent and Stationary Solutions in some Models for Parasitic Infections

Three closely related models for macroparasitic diseases are discussed, which describe the dynamics of host and parasite populations. In the first model, which is due to Hadeler and Dietz, the host population is structured by age and parasite load. The parasites influence the hosts mortality and fertility. The infection rate depends on the size of host and parasite populations. The second model is a simplification of the first. It is without age structure and there is no influence of the parasite on the hosts fertility. From this model the Anderson & May model is derived. The existence of exponential and stationary solutions is discussed for the different models depending on the exact form of the infection rate as a function of host and parasite population sizes. Anderson's and May's assumption of a negative binomial distribution of the parasites on the host population is compared with results derived for the first model, for which the distribution of parasites can be calculated.

Claude Lefèvre

On the Inter-Individual Dependence in a Non-Linear Death Process

In the standard linear death process, it is assumed that the individuals behave independently and their life times have a constant hazard rate. We consider here two different situations with some structure of dependence between the individual life times. In the first case, each hazard rate is a function of the number of individuals still present. In the second case, these rates depend on the actual state of an exterior stochastic process. Our purpose is then to characterize the nature of the dependencies involved, using the concepts of orthant dependence and association between random variables.

Ira M. Longini, Jr.

The Statistical Analysis of Infectious Disease Data Using Epidemic Models

Infectious disease data present several characteristics which necessitate the use of special statistical methods in their analysis. Such characteristics include dichotomous response, cluster sampling and correlated response within clusters. A probability model of infection transmission is used to analyze such data. The model is centered on households and partitions sources of transmission into those within the household and those from the community at large. Both the infectiousness of infected individuals and the susceptibilitiy of exposed individuals is

taken into account. Under certain circumstances, the model can be expressed in log-linear form. Examples from influenza epidemics are presented.

Marie-Pierre Malice, Richard Kryscio

Some Remarks about the Modeling of the Incubation Period in the AIDS Epidemic

Two stochastic models are constructed to describe and predict the incidence of AIDS among a large group of homosexuals. In both models, the contact rate between susceptibles and infectious individuals is assumed to be time-dependent. The length of the incubation period is modeled using a negative exponential in the first model and a generalized gamma in the second model. Comparisons of the behavior of the epidemic under different assumptions for the distribution of the incubation period are made using the concept of partial ordering between random variables.

J.A.J. Metz

Applying the Diekmann-Thieme Model for the Spatial Spread of Epidemics

The *DT* model is a spatial extension, along the lines pioneered by David Kendall and Denis Mollison for the ODE or locally Markovian case, of the Kermack-McKendrick functional differential equation model for the development of an epidemic. For this model Diekmann und Thieme independently proved the existence of an asymptotic speed of radial expansion. To apply the Diekmann-Thieme model in practice one has to devise well fitting parameter sparse submodels for the integral kernel and corresponding parameters estimation procedures. My talk described the results of a cooperation project to this end by Frank van den Bosch (ITB Leiden), Jan Carel Zadoks (Agricultural University Wagingen) and myself. The agreement between the observed and predicted rate of focus expansion turned out to be surprisingly good. I furthermore discussed some approximation formulas for calculating the speed and possible extensions of the *DT* results to nonrotationally-symmetric space kernels and to more general types of density dependence (necessary extensions if one wishes to study the large scale spread of plant epidemics) which have been considered on a heuristic level by Frank van den Bosch, Odo Diekmann and me. As a second example I considered the spread of rabies as this shows how the simplest approximation formula combined with some elementary insights into fox behaviour can lead to strong biological results.

Denis Mollison

Random Graphs and Heterogeneous Epidemics

The themes of the talk are: The sensitivity of results to assumptions, and hence the value of looking carefully at their dependence, not only on parameters but also on the structure of the model (for instance *deterministic/stochastic, discrete/continuous time, homogeneous/heterogeneous mixing)*; and the importance of keeping models clear and simple, as far as possible, and of expressing them in terms of basic ecological parameters, such as the *basic reproduction ratio* and the *generation gap* of disease. These themes were illustrated by discussion of a 'pre-model', differential and difference equations, and spatial stochastic models for the spread of rabies (Mollison 1986, Cox and Durrett 1988).

A third, rather different, theme was the possibility of making use of the detailed structure of stochastic models. The distinction was made between the minimal 'surface description' of a process, and more detailed 'internal descriptions', whose extra detail may at first seem purely decorative, but which can often yield insights not otherwise easily obtainable; as for instance with the use of the random graph $G(n,p)$ as an internal description of the Reed-Frost chain-binomial epidemic in a population of n individuals (Barbour and Mollison 1989). It is also often possible to use internal descriptions to *couple* two or more different processes (see e.g. Ball 1989).

One of the results for the Reed-Frost epidemic which follows immediately from its relation to $G(n,p)$ is that the probability of a large outbreak is equal to the proportion of the populations affected if a large outbreak occurs. This extends to provide insights into the spread of similar epidemic processes in grouped populations. More general random graph models were discussed briefly, including the idea of characterising the contact graph by 'triangle' probabilities; for instance, if 'ab' denotes that a has an infectious link to b,

$$\text{Prob}[ac \text{ given } ab \text{ and } bc]/\text{Prob}[ac] = 1$$

for $G(n,p)$, but $= O(n)$ for a model with spatially local contacts; graphs with intermediate behaviour, which might be appropriate for human diseases, can be constructed using simulations with annealing.

Ball, F. (1989): Coupling, epidemics and confidence intervals (this meeting).

Barbour, A., Mollison, D. (1989): Epidemics and random graphs, in: Stochastic Theory of Epidemic Models (eds. Gabriel, J.-P; Lefèvfre, C.; Picard, Ph.) (to appear).

Cox, J.T., Durrett, R. (1988): Limit theorems for the spread of epidemics and forest fires, Stoch.Procs.Applics. 30, 171-191.

Mollison, D. (1986): Modelling biological invasions: Chance, explanation, prediction, Phil.Tans.Roy.Soc. B314, 675- 693.

Ingemar Nåsell

Estimation of Malaria Infection and Recovery Rates

A Markov chain model for malaria infection of human hosts is established. The model allows for superinfection, relapses and false negatives. The superinfection is assumed to be limited, Nåsell [1986]. For fixed number of superinfections the host is in one of three states, i.e. newly infected, relapsed or latent. Two additional states are introduced to allow for the possibility that a newly infected or relapsed host is falsely observed as not patent. The parameters in the model are estimated using the maximum likelihood method. The estimation is based on longitudinal parasitological data from the Garki project and estimates of misclassification probabilities by Nedelman [1988]. The results are used to test the hypothesis that limited superinfection can occur in malaria. Our preliminary results support this hypothesis for all host ages.

Philippe Picard

Some Variants of Nåsell's Model for Helminthic Diseases with Concomitant Immunity

Nåsell-Hirsch's models for helminthic infections may be analyzed as the conjunction of two independent stochastic components connected by two deterministic linkages. In getting rid of the stochastic independence and taking one of the stochastic components subordinated to the other (and therefore using only one of the deterministic linkages), it is possible to build more refined models. These new models are much more complicated than Nåsell-Hirsch's ones, but in some way they are more realistic and give valuable information on the adequacy between these classic hybrid models and their fully stochastic counterparts. In a recent paper (to appear in Math.Biosciences) Picard has shown how to study such models in the case where parasites are hermaphroditic. The present talk will consider the still much more complicated case where the definitive hosts develop concomitant immunity. Such generalizations are also worth studying in malaria context.

Stavros Busenberg, Kenneth L. Cooke, Horst R. Thieme

Threshold conditions for HIV to change the growth of a population

A simple model is proposed for studying the interaction of the dynamics of a host population and the spread of a 'directed contact' disease like AIDS:

$$
\begin{aligned}
N_0' &= \beta_1 N_1 + \beta_2 N_2 - (\mu_0 + r_1 + r_2) N_0, \\
N_1' &= r_1 N_0 - \mu_1 N_1, \\
N_2' &= r_2 N_0 - \mu_2 N_2 - \gamma I_2, \\
I_2' &= K(N_2 - I_2) I_2 / N_2 - (\mu_2 + \gamma) I_2.
\end{aligned}
$$

The model includes a rough age structure via a juvenile class N_0 and a rough heterogeneity by splitting the adult population into a non-core N_1 and a core N_2. The model differs from most other epidemic models by allowing the populations to grow exponentially in absence of the disease with an exponential rate λ_0. One of the main results is the following: Let $R_1 = K/(L_0 + \mu_2 + \gamma)$ be the basic net reproductive number of the disease. If $R_1 < 1$, then $I_2(t)/N_2(t) \to 0$ for $t \to \infty$. If $R_1 > 1$, then $I_2(t)/N_2(t)$ is bounded away from zero for all times.

P. van den Driessche

Some Epidemiological Models with Periodic Solutions

Several classes of models have been developed for explaining the periodicity which is observed in data from many diseases. Periodic solutions have been found in various models with constant, nonperiodic coefficients. One such class incorporates a time delay in the removed compartment, and another class assumes a nonlinear incidence rate generalizing the bilinear mass action. These two formulations are considered and models analyzed to determine their equilibria and stability. Some parameter values yield multiple equilibria with the possibility of periodic solutions arising by Hopf bifurcation.
(Joint work with H.W. Hethcote)

Roland Waldstätter

The Effect of Prostitution on Sexually Transmitted Diseases

One-sex models in epidemiology implicitly assume that the numbers of infected males and females are equal and the duration of a partnership is zero. Dietz-Hadeler (1988) developed a two-sex model which takes into account pairs of infected or susceptible individuals. The noninfected individuals cannot be infected as long as the individuals remain together. But the model does not include liasons or prostitutes, which may be an important factor.
To test the liason effect in the Dietz-Hadeler model I consider an additional class of prostitutes who interact only with the male population. The threshold condition for the stability of the noninfected state is derived.

Grace Yang

Obtaining Incubation Information from Reported AIDS Incidence

A joint density of the times of occurrences of the infectives $T_1, ..., T_n$ and their respective times of diagnosis $T_1 + \xi_1, ..., T_n + \xi_n$ is constructed. In the construction we introduce explicitly a contagion function for the disease and a probability distribution for the incubation period ξ_i. This model is used to study the effect of

incubation period on the AIDS epidemic as reported by the monthly incidence of AIDS in San Francisco. Some simulation results are presented.
A special case of this model is the Markovian SIR model. We use this well known model to examine the differences between the system of differential equations for the expected number of susceptibles and infectives and its deterministic counter part.

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