05w5003 Mathematical Epidemiology
August 20-25, 2005

Abstracts

Speaker: **Linda Allen**
Title: Emerging Infectious Diseases of Wildlife

Abstract:
The emergence of new wildlife diseases and re-emergence of old diseases have been attributed to three processes: (i) ecosystem alterations, (ii) movement of pathogens or vectors and (iii) changes in microbes or in the recognition of them. Emerging infectious diseases (EIDs) of wildlife are often associated with human or domestic animal EIDs. In this lecture, we highlight some of the wildlife EIDs, factors associated with their emergence, and research and modeling efforts in connection with these diseases. We concentrate on two wildlife EIDs, hantavirus infection in rodents and chytrid infection in amphibians. Hantavirus infections in rodents have emerged due to anthropogenic landscape changes and climatic changes that influence the reservoir host. Hantavirus is associated with the human EID hantavirus pulmonary syndrome. Chytridiomycosis is a fungal infection of amphibians. Emergence of this disease may be attributed to human movement of infected amphibians around the world.

Speaker: **Viggo Andreasen**
Title: Influenza A drift-epidemiology

Abstract:
While most viral pathogens depend on host demographic turn-over to produce new susceptible hosts, influenza A virus utilize genetic changes in the virus to circumvent immune protection of its human host thereby allowing the virus to recolonize the same hosts every few years [1]. In this process known as virus drift, high point-mutation rates especially in the gene coding for the hemagglutinin surface protein, cause significant changes in the antigenically active parts of the influenza A surface. Molecular studies show that mutations accumulate at a constant rate along a linear pathway [2].

The antigenic variation confers selective advantage to new viral strains allowing them to partially escape host immunity acquired from previous infections. However, susceptibility to new strains is reduced by the presence of antibodies to related strains. Thus the dynamics of influenza A include two distinct phenomena: co-circulation of cross-immunizing strains and mutation driven drift.

Since strain-interactions as well as the fate of new mutant strains are determined by host immune surveillance, the phenomena are naturally described by extensions of SIR-type epidemic models allowing for multiple strains. Models of cross-reacting strains are rather complicated because it is necessary to keep track of all possible host immune types [3].
In addition virus drift involves frequent introduction of novel strains and coexistence of clusters [4].

I will discuss recent approaches to the modeling of virus drift and in particular models based on annual epidemics as described by the burn-out approximation [5].

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[2] W. M. Fitch et al, *Proc. Natl. Acad. Sci. USA* 94:7712 (1997). D. J. Smith et al, *Science* 305: 371 (2004).

[3] J. R. Gog and J. Swinton, *J. Math. Biol.* 44: 169 (2002). V. Andreasen et al, *J. Math. Biol.* 35: 825 (1997).

[4] J. B. Plotkin et al, *Proc. Natl. Acad. Sci.* USA 99: 6263 (2002).

[5] V. Andreasen, *J. Math. Biol.* 46: 504 (2003). M. F. Boni et al *Theor. Popul. Biol.* 65: 179 (2004). N. M. Ferguson et al, *Nature* 422: 429 (2003). J. R. Gog and B. T. Grenfell, *Proc. Natl. Acad. Sci. USA* 99: 17209 (2002). J. R. Gog et al, *Proc. Natl. Acad. Sci. USA* 100: 11143 (2003).

Speaker: **Chris Bauch**

Title: Game dynamics of vaccinating behaviour for childhood diseases

Abstract:
There exists an interplay between vaccine coverage, disease prevalence and the vaccinating behaviour of individuals. Moreover, because of herd immunity, there is also a strategic interaction between individuals when they are deciding whether or not to vaccinate, because the probability that an individual becomes infected depends upon how many other individuals are vaccinated. To understand this potentially complex interplay, a game dynamic model is developed in which individuals adopt strategies according to an imitation dynamic (a learning process), and base vaccination decisions on disease prevalence and perceived risks of vaccines and disease. The model predicts that oscillations in vaccine uptake are more likely in populations where individuals imitate others more readily or where vaccinating behaviour is more sensitive to changes in disease prevalence. Oscillations are also more likely when the perceived risk of vaccines is high. The model reproduces salient features of the time evolution of vaccine uptake and disease prevalence during the whole-cell pertussis vaccine scare in England and Wales during the 1970s. This suggests that using game theoretical models to predict, and even manage, the population dynamics of vaccinating behaviour may be feasible.

Speaker: **Lora Billings**

Title: Antibody dependent enhancement in multi-strain diseases

Abstract:
As we become more sophisticated in our resources to fight disease, pathogens become more resilient in their means to survive. Antibody dependent enhancement (ADE), a phenomenon in which viral replication is increased rather than decreased by immune sera, has been observed in vitro for a large number of viruses of public health importance, including flaviviruses, coronaviruses, and retroviruses. The most striking in vivo example of ADE in humans is dengue hemorrhagic fever, a disease in which ADE is thought to increase the severity of clinical manifestations of dengue virus infection by increasing virus replication. We examine the epidemiological impact of ADE on the prevalence and persistence of viral serotypes.

Using a dynamical system model of n co-circulating dengue serotypes, we study both autonomous and seasonally driven outbreaks in a model containing ADE. For sufficiently small ADE, the number of infectives of each serotype synchronizes, with outbreaks occurring in phase. When the ADE increases past a threshold, the system becomes chaotic, and

infectives of each serotype desynchronize. However, certain groups of the primary and secondary infectives remain synchronized even in the chaotic regime.

We find that ADE may provide a competitive advantage to those serotypes that undergo enhancement compared to those that do not, and that this advantage increases with increasing numbers of co-circulating serotypes. Paradoxically, there are limits to the selective advantage provided by increasing levels of ADE, as greater levels of enhancement induce large amplitude oscillations in incidence of all dengue virus infections, threatening the persistence of both the enhanced and non-enhanced serotypes. Though the models presented here are specifically designed for dengue, our results are applicable to any epidemiological system in which partial immunity increases pathogen replication rates.

Speaker: **Zhilan Feng**
Title: Timely Identification of Control Strategies for Emerging Infectious Diseases

Abstract:
To facilitate intervening effectively early in outbreaks of new diseases, we modeled a generic emerging infectious disease apparently transmitted by close contact, but about which little else is known. The model takes into account various control measures including quarantine, diagnose and isolation. We compute the reproductive number, which is shown to determine the severity of the disease. We present a sensitivity and uncertainty analysis of this reproductive number and the result is used to discuss various control strategies.

Speaker: **John Glasser**
Title: Elucidating varicella-zoster virus transmission and evaluating vaccination strategies for controlling varicella and preventing herpes zoster (with Paul Gargiullo and Dalya Guris)

Abstract:
Varicella persists in the US despite vaccination coverage approaching 80%, with outbreaks increasingly involving modified disease among vaccinated children who may be less infectious (probability of transmission on contact) than ones with typical disease, but have greater contact rates. Our goals are to determine long-term impacts of 1) childhood vaccination on varicella and herpes zoster (HZ) caused by wild-type and vaccine virus, including the role, if any, of internal versus external boosting in maintaining protection against HZ, and 2) adult vaccination on HZ and varicella. We have modeled the transmission and control of varicella-zoster virus in human populations via a system of differential equations. Our model features realistic population dynamics, by virtue of age-specific birth and death rates, seasonal forcing that accounts for such age-dependent and independent effects as the school calendar and temperature, respectively, and hypothetical host-pathogen relations, including progressively less well controlled reactivations of latent virus that results solely in internal boosting initially, but leads eventually to HZ. We will describe parameters estimated from published observations and by fitting our model with different biological assumptions to time-series from active surveillance since before 1995, when vaccination began, in Antelope Valley, CA, and West Philadelphia, PA. These include estimates of the duration of naturally-acquired and artificially-induced immunity and assessments of the importance of internal and external boosting. Given satisfactory reproduction of historical observations in these rural and urban communities, we will evaluate vaccination policy options.

Speaker: **David Greenhalgh** and Nikolaos Sfikas

Title: Estimation of Basic Reproduction Numbers and Evaluation of Vaccination Programs from Age-Structured Serological Data

Abstract:
For many real diseases, particularly diseases of childhood, the age-structure of the population is an important feature of the spread of the disease. Age-structured models have been shown to better fit the data than non age-structured ones. This talk is concerned with developing mathematical and statistical models to evaluate the basic reproduction number and elimination vaccination programs from age-structured data.

Age-structured serological data are preferred as they are more reliable than, and do not suffer the age-related bias of, case report data. The method is simplest with pre-vaccination data, but can be modified to take into account existing known vaccination programs. A non-parametric maximum likelihood method due to Keiding (1991) is used to estimate the force of infection in the absence of vaccination. Kernel smoothing with a variable smoothing bandwidth is a part of the estimation procedure. The force of infection is used to estimate quantities of statistical interest such as the basic reproduction number under homogeneous, proportional, assortative and symmetric mixing assumptions. Minimum elimination vaccination proportions that vaccinate given proportions of individuals at one or two pre-specified ages are also derived. The sensitivity of the results to different age-class divisions and kernel smoothing bandwidths is also assessed.

Additionally a bootstrap method is used to evaluate confidence and percentile intervals for the estimated statistics such as the basic reproduction number and the minimum elimination vaccination proportions. The results are illustrated with data on mumps and rubella in the U.K. and hepatitis A in Bulgaria.

Speaker: **Junling Ma**
Title: Periodic dynamics caused by antigenic drift

Abstract:
Traditionally, seasonal-force is considered to be the major cause of the seasonal behavior of flu. However, Andreasen (2003) showed that repetitive introductions of new strains can lead to cyclic dynamics as well. Yet his model assumes manually introduction of new strains at the end of each epidemic. In this talk, we study a model that combines a stochastic mutation process with a two-strain competition model that governs the spread of the mutant. The deterministic version of the model, in which mutants are introduced as the expected mutation time, exhibits stable periodic dynamics. If we introduce a small seasonal force to the transmission rate, the average period can be regulated to exactly one year if the period of the unforced dynamics is close to one year. If the unforced system has a period that is much larger than one year, then the forced system may behave chaotically.

Speaker: **Zhien Ma**
Title: Modeling and study for SARS Spread and control in China

Abstract:
As we know, SARS is a newly discovered infectious disease with high potential for spread to close contacts. In 2003 international travel facilitated its spread. As of June 13, 2003, the cumulative number of SARS cases worldwide reached 8454 with 792 deaths. It was especially serious in China, where the cumulative number of diagnosed cases was 5327 with 343 deaths during about half a year. At the time of peak infection (the middle of May, 2003), there were over 100 new cases per day in Beijing, China. During those days many questions

on SARS spread were asked. How many further infections will be produced per day? How many people will get infected in the future? When will the infection peak arrive and how long will it last? Will the current public health measures be enough to bring SARS under control? When is the suitable time to release the people under strict quarantine?

In order to provide answers of these questions, our group did some modeling of SARS.
We formulated a continuous time model and a discrete time model and estimated the parameters of the models by means of statistical data reported by the Chinese Public Health Ministry. T
he numerical simulations were done on May 18, 2003, and the results matched the realistic situation very well. For example, on May 19 (the new SARS patients in Beijing were still over 100) our report showed that according to the standard of the World Health Organization the travel warning in Beijing could be removed in the last ten-day period of June. It was removed on June 23. The number of cumulative cases diagnosed in mainland China estimated by our two models was 5400 and less than 6000; and it was actually 5327.

This lecture will introduce one of our models with 7 compartments, which consists of susceptible, exposed, infectious and recovered people in the free environment and suspected, diagnosed people and health workers taking care of SARS patients in the quarantined environment. It will show how to determine all of the parameters by means of the data reported by our government; and how to determine the reproduction number and stability of the equilibria. It will give numerical simulations for disease forecast and for different disease control strategies.

Speaker: **Mark Newman**
Title: Disease dynamics on contact networks

Abstract:
Human diseases spread in most cases via individual contacts between pairs of people, and these contacts form a network whose structure is one of the crucial determining factors in how far and how fast a disease will spread. After introducing briefly some of the concepts and theory of epidemiology on contact networks I will describe three recent studies we have performed to probe the relationship between network structure and disease transmission: a study of the spread of SARS in Vancouver, BC; a study of an outbreak of walking pneumonia in a hospital in Evansville, IN; and a study of HIV transmission in Seattle, WA.

Speaker: **Mercedes Pascual** and Juan Aparicio
Title: From networks to populations: modified mean-field models of disease dynamics.

Abstract:
Mean-field models if infectious disease dynamics ignore network structure and assume homogeneous mixing. At the opposite extreme, high-dimensional models that are both individual-based and stochastic incorporate the distributed nature of transmission. In between, moment approximations have been proposed that incorporate the effect of correlations on the dynamics of mean quantities of interest. As an alternative closer to traditional epidemiological models, we present here results on `modified mean-field equations' for disease dynamics, in which only mean quantities are followed and the effect of heterogeneous mixing is incorporated implicitly. We illustrate the idea of formulating these equations from the basic reproductive number of the disease, and illustrate the approach with

SIR dynamics in random and small world networks. We ask how much detail is needed on the transmission network to predict the population course of disease dynamics. A second approach relies on power-law relationships between global and local densities. We argue that future work should couple aspects of these two approaches to better capture the effects of heterogeneous mixing.

Speaker: **Shigui Ruan**
Title: Nonlocal Epidemic Models

Abstract:
In this talk, we first propose a host-vector model for a disease without immunity in which the current density of infectious vectors is related to the number of infectious hosts at earlier times. Spatial spread in a region is modeled in the partial integro-differential equation by a diffusion term. For the general model, we first study the stability of the steady states using the contracting convex sets technique. When the spatial variable is one-dimensional and the delay kernel assumes some special form, we establish the existence of traveling wave solutions by using the linear chain trick and the geometric singular perturbation method. We will also use a multi-compartment model to describe the nonlocal spread of SARS. The effect of global travel on the transmission of the disease will be discussed.

Speaker: **James Yorke**
Title: The trajectory of HIV in Africa and India

Abstract:
This talk will be presented jointly with Brandy Rapatski. One key to understanding the dynamics of HIV spread is the determination of when infected individuals transmit the infection, that is, how long have they been infected. The literature has emphasized the importance of transmission in the “primary stage”, the first couple of months of infections. But what about the “symptomatic” stage individuals? These individuals have typically been infected 7 or more years, and while they are symptomatic, they are often not terribly sick yet. They individually may be much more infectious than primary stage individuals, but are greatly outnumbered by primary stage individuals. If the epidemic is doubling each year as apparently has been the case in India, after seven population doublings, the individuals in their first year of infection are 128 times as numerous as those in their eighth year. On the other hand when the epidemic eventually begins to level off, the late stage individuals become the dominant force in maintaining the epidemic. There has been excellent recent news from Africa that indicates that when one person in a marital relationship is infected and both partners know about this and both know the other knows, transmission in the symptomatic stage can be quite low. But when the infected individual is unaware of being infected, the results can be quite different.