
Mathematics of Infectious Diseases
Modélisation mathématique des maladies infectieuses
(Org: **Abba Gumel** (Manitoba))

CHRISTOPHER BOWMAN, Inst. for Biodiagnostics

FRED BRAUER, University of British Columbia
Epidemic models with heterogeneous mixing

We formulate and analyze an epidemic model in a population with groups having different contact rates and proportionate mixing between groups. We obtain a general expression for the reproduction number and the final size of the epidemic. We are able to carry out these calculations also if treatment of infectives is incorporated into the model.

ELAMIN ELBASHA, Merck Research Laboratories
Global dynamics of an HPV vaccination model

We analyze a simple four-dimensional model of the susceptible, infective, and recovered (SIR) type. The model describes the transmission dynamics of human papillomavirus (HPV) infection following the introduction of a mass vaccination program. By constructing suitable Lyapunov functions, we prove that the global dynamics of this model are determined by the reproduction number R_v . If R_v is less than unity, there is a unique infection-free equilibrium which is globally asymptotically stable. For R_v greater than unity, the infection-free equilibrium is unstable, and there is a unique endemic equilibrium which is globally asymptotically stable. Future extensions of the model will be discussed.

HONGBIN GUO, University of Alberta, 632 CAB University of Alberta, Edmonton, AB, T6G 2G1
Global Dynamics of a Staged Progression Model for Infectious Diseases with Amelioration

A mathematical model for infectious diseases that progress through distinct stages within infected hosts is considered. An example of such diseases is AIDS which results from HIV infection. For a general n -stage stage-progression (SP) model with amelioration, we prove that the global dynamics are completely determined by the basic reproduction number R_0 . If $R_0 \leq 1$, then the disease-free equilibrium P_0 is globally asymptotically stable and the disease always dies out. If $R_0 > 1$, P_0 is unstable, and a unique endemic equilibrium P^* is globally asymptotically stable, and the disease persists at the endemic equilibrium.

This is joint work with Michael Y. Li, Dept. of Mathematical and Statistical Sciences, University of Alberta.

MUDASSAR IMRAN, North Carolina State University
The Pharmacodynamics of Antibiotic Treatment

We derive models of the effects of periodic, discrete dosing or constant dosing of antibiotics on a bacterial population whose growth is checked by nutrient-limitation and possibly by host defenses. Mathematically rigorous results providing sufficient conditions for treatment success, i.e., the elimination of the bacteria, as well as for treatment failure, are obtained. Our models

can exhibit bi-stability where the infection-free state and an infection-state are locally stable when antibiotic dosing is marginal. In this case, treatment success may occur only for sub-threshold level infections.

ZACK JACOBSON, Health Canada

How does vaccination affect transient population dynamics?

The talk focuses on the following question: if disease spread in a population is a dynamic process, how will that be affected by vaccination? By exploring transient dynamics and nonlinearities in disease spread within a population and actions of vaccination as an external impulse or force that modifies population dynamics, it is possible to evaluate the impact of the vaccination program and also to compare different vaccination strategies and schedules. We investigate all these using suitable vaccination models (stochastic and/or deterministic) with an eye on optimizing the impact of vaccination on disease spread. In particular, we seek to determine ways the system can be made to converge to a stable equilibrium point where the number of infected individuals is small or zero. Some pertinent modeling questions associated with the use of pulse vaccination are also enumerated.

This is joint work involving Dragos Calitoiu and Zachary Jacobson, Health Canada.

EDWARD LUNGU, University of Botswana, P. Bag 0022, Gaborone, Botswana

Anti-Tuberculosis resistance in patients co-infected with HIV and TB

Globally, levels of HIV and TB co-infection are high and continue to increase rapidly. UNAIDS and WHO data indicate that one third of all people with HIV have TB co-infection and similarly that up to 70% of TB cases are HIV positive. In sub-Saharan Africa, lack of access to affordable TB screening and treatment and poor referral and follow-up systems are some of the reasons why individuals default on their TB treatment, a situation which can lead to patients developing resistance to TB drugs. Botswana implemented 100% coverage of the DOTS (directly observed therapy short course) strategy in 1986 for all newly infected HIV individuals in all health centers. Two surveys undertaken in Botswana in the 1990's recorded low rates of anti-tuberculosis drug resistance despite a three-fold rise in tuberculosis since 1989. Sputum specimens obtained from patients nationwide in 2002 who also underwent anonymous rapid HIV testing by use of Oraquick showed that of the 2200 sputum smear positive patients and 219 previously treated patients with suspected recurrent tuberculosis, 1457 (60%) were infected with HIV.

Resistance to atleast one drug in new patients rose from 3.7% in 1995 to 10.4% in 2002. We construct a model to investigate

- (i) whether the 100% coverage of DOTS is responsible for the rise in TB drug resistance, and
- (ii) whether screening newly infected HIV patients for TB and administering DOTS to those without TB and treating those with TB would reduce the possibility of developing resistance.

TUFAIL MALIK, Arizona State University–Mathematics, P.O. Box 871804, Tempe, AZ 85287-1804

Microbial Quiescence, A Survival Strategy In Environmental Stress

Quiescence, or dormancy, is a strategy for microbial survival through an environmental stress such as lack of a resource. To investigate when quiescence is a beneficial strategy, we quantify and compare fitness of a quiescence-capable population and that of a 'sleepless' quiescence-incapable population under various growth conditions. Fitness is defined as the top Lyapunov exponent of certain non-autonomous linear ordinary differential equations forced by resource availability. Special attention is given to the case of periodic and stochastic resource availability. Nonlinear models are also considered where resource limitation is assumed to trigger transition to and from the quiescent state.

RONALD MICKENS, Clark Atlanta University
SIR Models with \sqrt{SI} Dynamics

We investigate various forms of SIR models where the disease dynamics is modeled by a \sqrt{SI} term in contrast to the standard SI representation. It is shown, for the general case, that two fixed-points exist, one stable, one unstable. The unstable state consists of only susceptible individuals, while the stable fixed-point has both susceptibles and infective individuals. Using nullclines, we construct geometrically, in the 2-dim S-I phase space, the general behavior of the associated trajectories. To obtain numerical solutions, we show the construction of a nonstandard finite difference (NSFD) scheme for this set of SIR differential equations.

The work reported here is supported by a grant from DOE and funds from the MBRS-SCORE Program at Clark Atlanta University.

JEFF MUSGRAVE, UNB – Fredericton
An evaluation of control strategies for the HIV epidemic

Since the discovery of HIV/AIDS there have been numerous mathematical models proposed to explain the epidemic of the disease and to evaluate possible control measures. In particular, several recent studies have looked at the potential impact of condom usage on the epidemic (Greenhalgh 2001, Gumel 2005, Hethcote 2000, Hyman 1999). We propose a model of the effect of condom use and withdrawal on the spread of the virus, similar to that of Gumel et al. (2005), and show that a simple rescaling can be used to broaden the results of a sensitivity and uncertainty analysis. Based on available estimates, we predict a condom preventability of approximately 95% is necessary to ensure control of the epidemic. A further simplification of the model, replacing the standard incidence with a bilinear infection term and assuming the demographic timescale is much slower than the disease timescale, allows an estimate of the peak size of the epidemic.

CHANDRA PODDER, University of Manitoba, 342 Machray Hall, 186 Dysart Road, Winnipeg, R3T 2N2
Mathematical Analysis of a Model for Assessing the Impact of Antiretroviral Therapy, Voluntary Testing and Condom Use in Curtailing HIV

This paper presents a deterministic model for evaluating the impact of several anti-HIV strategies, namely the use of anti-retroviral drugs (ARVs), voluntary HIV testing (using standard antibody test and a new DNA-based test) and condom use. The model is rigorously analysed, showing the existence of a globally-stable disease-free equilibrium whenever a certain epidemiological threshold, known as the *effective reproduction number* (\mathcal{R}_{eff}), is less than unity, an endemic equilibrium whenever $\mathcal{R}_{\text{eff}} > 1$.

Simulations, using plausible parameter values, show that for reasonably small testing and treatment rates, as well as modest condom compliance (70%) and efficacy (87%), the use of condoms is the most effective single intervention for reducing HIV burden, followed by the use of ARVs and then voluntary HIV testing. If the testing and treatment rates are increased (by 10-fold) further, the use of ARVs can offer better long-term benefit than any of the other interventions. It is shown that the combined use of voluntary testing methods and condom use can lead to significant reduction in HIV burden than the singular use of ARV treatment if the testing and treatment rates are low. Although it is shown that the use of ARVs is the most effective control strategy, in the long run, for modestly high treatment and testing rates, the lack of widespread availability of these drugs call for the consideration of other affordable interventions. This study shows that the combined use of voluntary testing and condoms can be a cost-effective means of combatting the global spread of HIV.

TIMOTHY RELUGA, Los Alamos National Laboratory
Population Games for Epidemiology

In recent years, game theory has gained attention as a method to explain behavior and evolution. In this talk, I'll describe how the combination of classic epidemiology models with Markov decision processes can be used to formulate population games and study public health policy problems. Example applications to influenza vaccination and polio will be discussed.

OLUWASEUN SHAROMI, University of Manitoba, 342 Machray Hall, 186 Dysart Road, Winnipeg, R3T 2N2
Mathematical Analysis of the Transmission Dynamics of HIV/TB Co-infection in the Presence of Treatment and Condom Use

This paper addresses the synergistic interaction between HIV and mycobacterium tuberculosis using a deterministic model, which incorporates many of the essential biological and epidemiological features of the two diseases. In the absence of TB infection, the model (*HIV-only model*) is shown to have a globally-asymptotically stable disease-free equilibrium whenever the associated *reproduction number* is less than unity; and has a unique endemic equilibrium whenever this number exceeds unity. On the other hand, it was shown, using Centre Manifold theory, that the model with TB alone (*TB-only model*) undergoes the phenomenon of backward bifurcation, where the stable disease-free equilibrium co-exists with a stable endemic equilibrium when the associated reproduction threshold is less than unity.

The full model, with both HIV and TB, is also rigorously analysed. Its simulation shows that the use of a treatment strategy that targets only one of the two diseases not only results in significant reduction of new cases of the disease being targeted for treatment, but also induces an indirect benefit of reducing the number of new cases of the other disease. Further, although treating individuals with TB only (and those with dual HIV/TB infection treated for TB) always results in more cases of TB prevented than that of HIV, the treatment of people with HIV (including those with dual infection treated for HIV) results in more cases of TB prevented than cases of HIV prevented. Finally, the study shows that the universal treatment of individuals infected with both diseases is more beneficial compared to treating individuals infected with a single disease only.

NAVEEN VAIDYA, York University, 4700 Keele Street, Toronto, ON, M3J 1P3
Modeling, Analysis, and Control of the HIV Epidemics in Far Western Nepal

We present a dynamic transmission model of the HIV epidemics in Far Western Nepal, where high rate of seasonal migration to India has been the most threatening HIV risk factor. In addition to some analytical and simulation results, we discuss the optimal control strategy based on the results of our model.

JAMES WATMOUGH, University of New Brunswick
The final size of an epidemic

The early disease transmission model of Kermack and McKendrick established two main results that are still at the core of most disease transmission models today: the basic reproduction number, \mathcal{R}_o , as a threshold for disease spread in a population; and the final size of an epidemic. As models become more complex, the relationships between disease spread, final size and \mathcal{R}_o are not as clear; yet \mathcal{R}_o remains the main object of study when comparing control measures. In this talk I review the final size relation for a simple epidemic model and discuss its form in more complex models for treatment and control of influenza and HIV.

MATTHIAS WINTER, Brunel University, Mathematical Sciences, Uxbridge UB8 3PH, UK
Spikes for Biological Systems: The Role of Boundary Conditions

We consider the shadow system of the Gierer–Meinhardt system in a smooth bounded domain $\Omega \subset \mathbb{R}^N$:

$$\begin{cases} A_t = \epsilon^2 \Delta A - A + \frac{A^p}{\xi^q}, & x \in \Omega, t > 0, \\ \tau |\Omega| \xi_t = -|\Omega| \xi + \frac{1}{\xi^s} \int_{\Omega} A^r dx, & t > 0 \end{cases}$$

with Robin boundary condition

$$\epsilon \frac{\partial A}{\partial \nu} + a_A A = 0, \quad x \in \partial\Omega,$$

where $a_A > 0$.

The positive reaction rates (p, q, r, s) satisfy

$$1 < \frac{qr}{(s+1)(p-1)} < +\infty, \quad 1 < p < \left(\frac{N+2}{N-2}\right)_+,$$

the diffusion constant is chosen such that $\epsilon \ll 1$ and the time relaxation constant such that $\tau \geq 0$.

We rigorously prove the following results on the stability of spiky solutions:

- (i) If $r = 2$ and $1 < p < 1 + 4/N$ or if $r = p + 1$ and $1 < p < \infty$ then for $a_A > 1$ and τ sufficiently small the interior spike is stable.
- (ii) For $N = 1$ if $r = 2$ and $1 < p \leq 3$ or if $r = p + 1$ and $1 < p < \infty$ then for $0 < a_A < 1$ the near-boundary spike is stable.
- (iii) For $N = 1$ if $3 < p < 5$ and $r = 2$ then there exist $a_0 \in (0, 1)$ and $\mu_0 > 1$ such that for $a \in (a_0, 1)$ and $\mu = \frac{2q}{(s+1)(p-1)} \in (1, \mu_0)$ the near-boundary spike solution is unstable. This instability is not present for the Neumann boundary condition but only arises for Robin boundary condition. Further we show that the corresponding eigenvalue is of order $O(1)$ as $\epsilon \rightarrow 0$.

These results imply that some patterns may become more robust at the expense of others which turn unstable. Results of this type are important to understand the role of the boundary conditions in pattern selection. For some biological applications such as the modelling of skeletal limb development Robin (mixed) boundary conditions are more realistic than Neumann (zero-flux) boundary conditions which are used in most models.

This is joint work with Philip K. Maini (Oxford) and Juncheng Wei (Hong Kong).