**Models for transmission of communicable diseases (CAIMS)**
**Modèles pour la transmission de maladies contagieuses (SCMAI)**
(Org: **Fred Bauer** (UBC) and/et **Pauline van den Driessche** (Victoria))

**CHRIS BOWMAN**, Institute for Biodiagnostics, National Research Council of Canada, 435 Ellice Ave., Winnipeg, Manitoba R3B 1Y6

*Population-Wide Emergence of Antiviral Resistance during an Influenza Pandemic*

The selective pressure induced by anti-viral drugs on their target virus may allow drug-resistant strains to survive and replicate. While these resistant strains may initially emerge with compromised fitness, mutations that compensate for this can arise to produce a resistant strain with only slightly impaired replication and transmission fitness compared to the original wild type strain. I will discuss the modeling of such resistance development in the context of pandemic influenza under several mathematical models.

High treatment levels can encourage a resistant outbreak to occur, by suppressing the spread of the wild type infection, leaving the population susceptible to the resistant strain. Thus, increasing population levels of treatment can, ironically, in some cases lead to increased prevalence of infection. Strategies for controlling the development of resistance, including treatment timing and interruption, and their implications for public health policy, especially given the likelihood of limited drug stockpiles during an influenza pandemic, will be discussed.

**DAN COOMBS**, University of British Columbia

*Within-host evolution of viruses and epidemiological implications*

Within-host adaptation and evolution of viruses during chronic infections is a common phenomenon: consider, for instance, the appearance of drug resistant HIV in a treated patient. In this talk I will describe mathematical techniques for analyzing viral evolution and show, in some simple cases, how insights from these models can be applied to understand changes in viral strain at the population level.

This is joint work with Jennifer Hubbarde, Colleen Ball and Michael Gilchrist.

**DAVID FISMAN**, Hospital for Sick Children, 123 Edward Street, Room 428, Toronto, Ontario, Canada M5G 1E2

*. . . But the Bugs Bounce Back: Simple Transmission Models and 'Failure' of Bacterial STD Control Programs*

Genital tract infections caused by Neisseria gonorrhoeae and Chlamydia trachomatis are a major cause of sexually transmitted disease. Although infections caused by these pathogens differ in important respects, there is overlap in the spectrum of associated illness, the limited duration of immunity conferred by infection (and hence the possibility of re-infection), and in the focus of control efforts on identification and treatment of infectious individuals. For both pathogens surveillance data suggest that incidence has increased after initially falling in the face of intensified control efforts. We evaluate the likely mechanisms behind such rebound using simple compartmental "susceptible-infectious-recovered-susceptible" (SIRS) models (Chlamydia) or SIS models (gonorrhoea), and explore the implications of such rebound for disease control practice. In the case of Chlamydia, we model apparent rebound in prevalence in the Philadelphia High School STD Screening Program. We show that the degree of rebound observed could be explained by truncation of transient immunity through treatment, through "risk compensation" (increased sexual risk-taking), or through reduced participation in screening programs, but that neither the presence of rebound, nor the underlying mechanism leading to rebound, substantially diminishes the economic attractiveness of Chlamydia screening. For gonorrhoea, we explore SIS models that include and exclude the possibility of antibiotic resistance. When antibiotic resistance is not possible, strategies that focus on treatment of highest risk individuals (the so-called "core group") result in collapse of disease transmission; however, when antimicrobial resistance exists, a focus on the core group causes rebound in incidence, with maximal dissemination of antibiotic resistance.

**HONGBIN GUO**, York University, Toronto
*Global Dynamics of an SP Model with Random Amelioration and Deterioration*

We analyze the global dynamics of a mathematical model for infectious diseases that progress through distinct stages within infected hosts with possibility of random amelioration and deterioration. An example of such diseases is HIV/AIDS which progresses through several stages with varying degrees of infectivity; amelioration can results from a host's immune action or more commonly from anti-retroviral therapies such as HARRT, and deterioration results from other diseases such as TB co-infection which could accelerate the progression to AIDS. For a general $n$-stage model with constant recruitment and bilinear incidence that incorporates amelioration and deterioration, 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, a unique endemic equilibrium $P^*$ is globally asymptotically stable, and the disease persists at the endemic equilibrium. The proof for global stability of the endemic equilibrium uses the graph-theoretical approach to the method of Lyapunov functions recently proposed by Guo, Li and Shuai.

**JANE HEFFERNAN**, York University, 4700 Keele St., Toronto, ON M3J 1P3
*Vaccination and waning immunity: An immuno-epidemiological model for measles*

For infectious diseases where immunization can offer life-long protection, a variety of simple models can be used to analyze vaccination as a control method. However, for many diseases life-long immunity cannot be obtained from vaccination. Instead, immunity wanes over time and is subsequently boosted by asymptomatic encounters with infectious individuals. To study this type of epidemiological process a comprehensive model that captures both the within-host dynamics of the pathogen and immune system and the associated population-level transmission dynamics is needed. We have developed an immuno-epidemiological model (immunology and epidemiology—both carefully parameterized to match the available data) describing measles dynamics in terms of waning immunity and boosting in measles infection; although such ideas have been hypothesized before, it is only through the use of such immuno-epidemiological models that the impact can be quantitatively studied. The model predicts that moderate waning times and high levels of vaccination can induce large-scale oscillations with substantial numbers of symptomatic cases being generated at the epidemic/outbreak peaks. It also predicts that far larger epidemics than previously predicted by standard models will occur when infection is introduced after a long disease free periods. These results have clear implications for public health protocols. They also highlight that a sound understanding of the underlying immunological mechanisms of immunity and vaccination is needed to fully understand epidemiological dynamics.

**RONGSONG LIU**, Purdue University
*Optimal control of vaccination and treatment in a two strain influenza model*

Optimal control theory is applied to a system of ordinary differential equations modeling a two-strain influenza model with vaccination and treatment. For several different objectives, such as to minimize the infectious compartment with the resistant-strain and and the cost, we use controls representing vaccination and treatment. The optimal controls are characterized in terms of the optimality system, which is solved numerically for several scenarios.

**ROBERT SMITH**, The University of Ottawa
*Explicitly accounting for antiretroviral drug uptake in theoretical HIV models predicts long-term failure of protease-only therapy*

Mathematical models of HIV therapy have traditionally amalgamated the action of antiretroviral drugs, trading the complexity of the situation in favour of simpler—and hence mathematically tractable—models. However, the effects of ignoring such dynamics remain underexamined. In this paper, the traditional method of dosing (where the dose is modelled implicitly as a proportional inhibition of viral infection and production) is compared to a model that accounts for drug dynamics via explicit compartments. Four limiting cases are examined: frequent dosing of both major classes of drugs, absence of either drug,

frequent dosing of one drug alone, or frequent dosing of the other drug alone. When drugs are absent, both models predict that the virus will dominate and the uninfected T cell counts will be low. When reverse transcriptase inhibitors are given frequently, both models predict that the virus will be theoretically eliminated and the uninfected T cell counts will be high; this is true regardless of whether the reverse transcriptase inhibitors act alone or in conjunction with protease inhibitors. However, if protease inhibitors alone are given frequently, then the implicit model predicts that the virus will be eliminated and the uninfected T cell counts will be high, whereas the (more realistic) explicit model predicts that the reverse situation may occur. In the latter case, critically, protease-only regimens may ultimately result in the death of the patient. It follows that the impact of drug regimens consisting only of protease inhibitors must be urgently re-examined, if such outcomes have been based on overly simplistic modelling.

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**LIN WANG**, University of New Brunswick
*Oscillations in a Patchy Environment Disease Model*

For a single patch SIRS model with a period of immunity of fixed length, recruitment-death demographics, disease related deaths and mass action incidence, the basic reproduction number $\mathcal{R}_0$ is identified. It is shown that the disease free equilibrium is globally asymptotically stable if $\mathcal{R}_0 < 1$. For $\mathcal{R}_0 > 1$, local stability of the endemic equilibrium and Hopf bifurcation analysis about this equilibrium are carried out. Moreover, a practical numerical approach to locate the bifurcation values for a characteristic equation with delay-dependent coefficients is provided.

For a two-patch SIRS model with travel, it is shown that there are several threshold quantities determining its dynamic behavior and that

1) travel can reduce oscillations in both patches;

2) travel may enhance oscillations in both patches;

3) travel can also switch oscillations from one patch to another.