
Mathematical Epidemiology
Épidémiologie mathématique

(Org: **Lin Wang** and/et **James Watmough** (University of New Brunswick))

JESSICA CONWAY, Pennsylvania State University

HIV viral rebound: infection following treatment suspension

Antiretroviral therapy (ART) effectively controls HIV infection, suppressing HIV viral loads. Typically suspension of therapy is rapidly followed by rebound of viral loads to high, pre-therapy levels. However, case reports suggest that initiating ART early after infection may delay viral rebound, for months, years, or maybe permanently, after ART suspension. We will discuss our multi-type, branching process model to gain insight into these post-treatment dynamics. Li et al. (2016) report that the size of the expressed HIV reservoir and a patient's drug regimen correlate with the time between ART suspension and viral rebound to detectable levels. We incorporate this information and viral rebound times to parametrize our model. The results we will discuss represent first early towards a model that can make predictions of a patient's rebound time distribution based on patient characteristics, and help identify patients with expected long viral rebound delays. We will further discuss epidemiological implications of treatment suspension. ART is invaluable in preventing onwards transmission by controlling infection; similarly, individuals with controlled infection post-ART will have low risk of transmission. But that risk will increase at viral rebound, at which time an individual would re-initiate ART. We will also discuss model predictions that can be used to guide management of treatment suspension.

ABDOU FOFANA, Memorial University of Newfoundland

Mechanistic movement models to understand epidemic spread

An overlooked aspect of disease ecology is considering how and why animals come into contact with one and other resulting in disease transmission. Mathematical models of disease spread frequently assume mass-action transmission, justified by stating that susceptible and infectious hosts mix readily, and foregoing any detailed description of host movement. Numerous recent studies have recorded, analysed and modelled animal movement. These movement models describe how animals move with respect to resources, conspecifics and previous movement directions and have been used to understand the conditions for the occurrence and the spread of infectious diseases when hosts perform a type of movement. Here, we summarize the effect of the different types of movement on the threshold conditions for disease spread. We identify gaps in the literature and suggest several promising directions for future research. The mechanistic inclusion of movement in epidemic models may be beneficial for the following two reasons. Firstly, the estimation of the transmission coefficient in an epidemic model is possible because animal movement data can be used to estimate the rate of contacts between conspecifics. Secondly, unsuccessful transmission events, where a susceptible host contacts an infectious host but does not become infected can be quantified. Following an outbreak, this enables disease ecologists to identify 'near misses' and to explore possible alternative epidemic outcomes given shifts in ecological or immunological parameters.

JANE HEFFERNAN, York University

Memory cells and the HIV reservoir

HIV persists in patients undergoing highly effective antiviral therapy. Virus persists in long-lived infected CD4 T-memory cells. Current research on HIV control and eradication in-host points to the reactivation of the infected memory cell pool when the immune system is primed (via immune system stimulants) to neutralize the virus and kill active infected cells. In this talk, I will discuss our modelling studies of this process, and I will highlight biological outcomes that are supported by our analysis.

KIYEON KIM, Hokkaido university

Inferring epidemiological dynamics of infectious diseases using Tajima's D statistic on nucleotide sequences of pathogens .

The estimation of the basic reproduction number is essential to understand epidemic dynamics, and time series data of infected individuals are usually used for the estimation. However, such data are not always available. Methods to estimate the basic reproduction number using genealogy constructed from nucleotide sequences of pathogens have been proposed so far. Here, we propose a new method to estimate epidemiological parameters of outbreaks using the time series change of Tajima's D statistic on the nucleotide sequences of pathogens.

FUXIANG LI, Memorial University of Newfoundland

A Periodic SEIRS Epidemic Model with Time-dependent Latent Period.

Many infectious diseases have seasonal trends and exhibit variable periods of peak seasonality. Understanding the population dynamics due to seasonal change becomes very important for predicting and controlling disease transmission risks. In this talk, I will report our recent research on a periodic SEIRS epidemic model with time-dependent latent period. We introduce the basic reproduction ratio R_0 for this model and establish a threshold type result on its global dynamics in terms of R_0 . More precisely, we show that the disease-free periodic solution is globally attractive if $R_0 < 1$; while the system admits a positive periodic solution and the disease is uniformly persistent if $R_0 > 1$. Numerical simulations are also carried out to illustrate the analytic results. This talk is based on a joint work with Dr. Xiaoqiang Zhao.

JUNLING MA, University of Victoria

Estimation of cross-immunity between drifted strains of influenza A/H3N2

To determine the cross-immunity between influenza strains, we design a novel statistical method, which uses a theoretical model and clinical data on attack rates and vaccine efficacy among school children for two seasons after the 1968 A/H3N2 influenza pandemic. This model incorporates the distribution of susceptibility and the dependence of cross-immunity on the antigenic distance of drifted strains. We find that the cross-immunity between an influenza strain and the mutant that causes the next epidemic is 88 percent. Our method also gives estimates of the vaccine protection against the vaccinating strain, and the basic reproduction number of the 1968 pandemic influenza.

CONNELL MCCLUSKEY, Wilfrid Laurier University

Disease models with immigration of infected individuals

We consider the effect that the immigration of infected individuals has on two phase space features for disease models. First, how does immigration affect disease-free equilibria? We find that the effect is connected to the sign of $R_0 - 1$. Second, how does immigration affect the global stability of an endemic equilibrium?

ELLIOTT (JOE) MORAN, Memorial University of Newfoundland

Mitigation of Chronic Wasting Disease (CWD) in White-tailed Deer through strategic harvest management regimes

This study examines the effect of culling different demographic groups on the spread of Chronic Wasting Disease (CWD) in White-tailed deer (*Odocoileus virginianus*). CWD is a transmissible spongiform encephalopathy (TSE) with an unknown derivation and no antidote. Without intervention, population growth and resilience of deer populations will be stifled. Management and disease suppression by United States game agencies has ranged from minimal action and surveillance, to widespread culls and restricted interstate transport. Culling is the primary method used for mitigation within established CWD areas, however, there is limited research and implementation of strategic harvest management regimes. Two mathematical models were formulated to study CWD in free ranging White-tailed deer. Qualitative and numerical techniques were used to investigate how culling different demographic groups can influence disease prevalence, and subsequently, this gives insight towards management prescriptions and long term population dynamics.

TIMOTHY RELUGA, Penn State

New comments on old pathometry

Given the maturity of mathematical epidemiology today, it is sometimes interesting to look back on the history of the field and reflect on its development. While we tend to remember history as punctuation (Kermack and McKendrick's 1932 article, for instance), the actual progress was messy and mysteries still persist. What was William Farr's actual "normal law" of epidemics? Was Alfred Lotka really responsible for the Reed–Frost epidemic model? Did Kermack and McKendrick knowingly mislead their readers regarding their data on plague incidence? Who was Ross's coauthor H. Hudson? In this talk, I'll discuss these and other tidbits from my recent studies of the gestation (prior to 1904) and infancy (up to 1952) of the field.

BIAO TANG, York University

Optimal dengue vaccination to mitigate Zika cases

Zika and dengue viruses belong to the same Flavivirus family and are primarily transmitted by a common mosquito species *Aedes aegypti*. Zika outbreaks have commonly occurred in dengue-endemic areas, and cocirculation and coinfection of both viruses have been reported. As recent studies on immunological cross-reactivity have confirmed that convalescent plasma following dengue infection can enhance Zika infection, it is important to examine whether and how dengue vaccination in a large population may affect Zika infection dynamics due to antibody-dependent enhancement. In this study, we evaluate the impact of dengue vaccination on Zika infection dynamics through a mathematical coinfection dynamics model. We show that an appropriately designed and optimized dengue immunization program can not only help control the dengue spread but also, counter-intuitively, reduce Zika infections. We estimate that the optimal and critical dengue effective vaccine coverage rates in Mexico, Brazil, and French Polynesia to be (73.6% Xi Huo, Yanni Xiao, Shigui Ruan, and Jianhong Wu).

XIUNAN WANG, University of Western Ontario

Threshold Dynamics of a Temperature-Dependent Stage-Structured Mosquito Population Model with Nested Delays

Mosquito-borne diseases remain a significant threat to public health and economics. Since mosquitoes are quite sensitive to temperature, global warming may not only worsen the disease transmission case in current endemic areas but also facilitate mosquito population together with pathogens to establish in new regions. Therefore, understanding mosquito population dynamics under the impact of temperature is considerably important for making disease control policies. In this talk, I will introduce our recent work on the dynamics of a stage structured mosquito population model in the environment of a temperature-controlled experiment. The model turns out to be a system of periodic delay differential equations with periodic delays. We show that the basic reproduction number is a threshold parameter which determines whether the mosquito population goes to extinction or remains persistent. We then estimate the parameter values for *Aedes aegypti*, the mosquito that transmits dengue virus. We verify the analytic result by numerical simulations with the temperature data of Colombo, Sri Lanka where a dengue outbreak occurred in 2017. This talk is based on a joint work with Prof. Xingfu Zou.

JIANHONG WU, Laboratory for Industrial and Applied Mathematics, York University

Modelling Tick-borne pathogen co-feeding transmission

We develop a novel dynamical model for vector-borne disease transmission involving co-feeding and systematic transmission routes. We show that vector-to-host attachment and host grooming behaviors combined may generate nontrivial tick-over-host density distribution and vector population dynamics.

XIAOTIAN WU, Shanghai Maritime University

An epidemic model with multiple delays: impact of co-feeding and diapause

In this talk, a dynamic vector–host–pathogen interaction motivated by tick-borne diseases is considered. The vector population is stratified in terms of the stage before and after the vector's contact with hosts where co-feeding transmission may take place and vector development may involve two time lags due to normal development and diapause. We derive threshold conditions for disease persistence and for nonlinear oscillations in the vector population and in the diseased vector and host populations. Our objective in the current study is to use a simple mechanistic model to show that diapause and co-feeding transmission may generate periodic and irregular oscillations even when seasonal variations of the environmental conditions are ignored.

These oscillations are not necessary in synchrony with the seasonality of vector development, and hence complicated oscillatory patterns of vector borne disease dynamics in the field and surveillance observations should be expected. This is a joint work with Jianhong Wu and Xue Zhang.

XU ZHANG, Southwest University, China

Identifying candidate diagnostic markers for tuberculosis: a critical role of co-expression and pathway analysis

We conducted a systematic bioinformatics analysis to explore an important set of gene expression data with 39 samples infected at different time stages with W- Beijing families of Mycobacterium tuberculosis strains. We took a contrast on the samples at different infection time stages to characterize gene expression features of the THP1 cells to identify sensitive and specific molecular markers for diagnosis. We first confirmed, through the multidimensional scaling unsupervised clustering, that samples were clustered well according to different infection times. Building on this classification result and using the linear modelling and empirical Bayes moderation, we found 287 hits as most significant genes associated with tuberculosis. We generated a gene co-expression network map based on the mutual regulation between the differentially expressed genes. We found that 27 genes are regulatory genes associated with tuberculosis. We constructed 4 gene pathway figures to explain the pathogenicity process that involves 24 key genes. This study implicates that contrast on the gene expression of the classifications in different infection stages provides critical information for the detection of tuberculosis, and our method can be utilized to narrow down the shortlist of disease relevant genes and explore tuberculosis pathogenesis.

XUE ZHANG, York University

Modeling tick diapause dynamics using multiple delays

An essential way of the tick's adaptations to seasonally variable climate is diapause, which ensures the survival of tick. We investigate the effect of diapause phenomena on the amount of tick population for improving understanding of tick-borne disease and propose a tick population model with multiple time delays. We explore the property of parameter tangent function by introducing parametric cosine and sine function. We derive threshold conditions for nonlinear oscillations in the vector population. Our purpose is to show that diapause may generate complex oscillation even though seasonality is not included.