Mathematical Modelling of Ecological, Evolutionary and Infectious Disease Dynamics
Modélisation mathématique de la dynamique des maladies écologiques, évolutives et infectieuses
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ELAHEH ABDOLLAHI, York University
Assessing control strategies and timelines for Mycobacterium tuberculosis elimination, Nunavut as a case study

Tuberculosis (TB) continues to have a disproportionate impact on Inuit communities in Canada, with reported rates of active TB that are over 300 times higher than those of Canadian-born, non-Indigenous individuals. The Inuit Tuberculosis Elimination Framework aims to reduce the incidence of active TB by at least 50% by 2025, with the ultimate goal of eliminating it by 2030. However, whether these objectives can be achieved with the resources and interventions currently available is not assessed yet. During this colloquium, I will present an agent-based model (ABM) of TB transmission that we developed to assess the feasibility of these goals in Nunavut, Canada. Our model takes into account factors such as case identification, contact tracing and testing, patient isolation, housing infrastructure, and the potential impact of a therapeutic vaccine. Our findings suggests that the time-to-identification of active TB cases is a crucial factor in achieving the goals, emphasizing the importance of investment in early case detection.

FRANCIS ANOKYE, Memorial University of Newfoundland
Newfoundland and Labrador Two-Peaked BA.1 Wave

Before establishing the Omicron variant, Canada's province, Newfoundland and Labrador (NL), pursued a containment strategy and reported more than 150 weekly SARS-CoV-2 cases only twice out of 98 weeks. Ninety-seven (97) weekly cases were reported in the first full week after establishing the BA.1 (Omicron) variation, and over 150 cases were reported each week for the next 12 weeks. There are three months (December 15, 2021 - March 17, 2022) when both the BA.1 variant is spreading, and most individuals with at least one COVID-19 symptom are eligible for testing at the NL provincial sites. Analysis of epidemiological data reported during this period is critical to understanding SARS-CoV-2 spread in the province. Therefore, we fit an integrated Bayesian-based and machine learning framework, particle Markov-chain Monte Carlo, and a stochastic compartmental model to the epidemiological data. During this period, the trend in reported cases has two peaks: first, in early January, corresponding to the implementation of stricter non-pharmaceutical interventions (NPIs), and second, in mid-March, corresponding to when most symptomatic residents lost eligibility for COVID-19 testing at local sites. We use our parameterized epidemiological model to explore counterfactual scenarios and find that stricter NPIs and high vaccination rates could have prevented 28,897 SARS-CoV-2 cases. Our analysis suggests that implementing stricter NPIs in NL in early 2022 may have led to a switch from an increasing to a decreasing trend in SARS-CoV-2 cases. We know of little other evidence suggesting that stricter NPIs can have this effect on the highly transmissible Omicron variant.

DAN COONEY, University of Pennsylvania
Long-Time Behavior of a PDE Replicator Equation for Multilevel Selection in Group-Structured Populations

In many biological systems, natural selection acts simultaneously on multiple levels of organization. This scenario typically presents an evolutionary conflict between the incentive of individuals to cheat and the collective incentive to establish cooperation within a group. Generalizing previous work on multilevel selection in evolutionary game theory, we consider a hyperbolic PDE model of a group-structured population, in which members within a single group compete with each other for individual-level replication; while the group also competes against other groups for group-level replication. We derive a threshold level of the relative strength of between-group competition such that defectors take over the population below the threshold while cooperation persists in the long-time population above the threshold. Under stronger assumptions on the initial distribution of group compositions, we further prove that the population converges to a steady state density supporting cooperation for between-group selection strength above the threshold. We further establish long-time bounds on the time-average of the collective payoff of the population, showing that the long-run population cannot outperform the payoff of a full-cooperator

group even in the limit of infinitely-strong between-group competition. When the group replication rate is maximized by an intermediate level of within-group cooperation, individual-level selection casts a long shadow on the dynamics of multilevel selection: no level of between-group competition can erase the effects of the individual incentive to defect. We further extend our model to study the case of multiple types of groups, showing how the games that groups play can coevolve with the level of cooperation.

SONIA GAZEAU, University of Montreal

Constructing virtual patient populations to understand immune responses in immunosuppressed and cancer patients with COVID-19

The COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has significantly affected the lives of billions of people, causing millions of deaths. It was recognized that particular groups of people, including the elderly, experienced more severe COVID-19. Additionally, patients with existing immunosuppression and those undergoing active cancer treatments are known to respond more poorly to the virus and the disease. However, clinical studies in those populations are difficult to perform, time and money consuming, and there is overall a lack clinical data to relate mechanisms of dysfunction to outcomes. Therefore, mathematical modelling, which enables studying complicated immune response mechanisms, can be a promising solution to the need for extensive longitudinal human data.

To study the immune dynamics after infection with SARS-CoV-2 in immunosuppressed and cancer patients, we adapted our existing mathematical model of the immune response in COVID-19. Using our established virtual patient cohort generation procedure, we used our model to generate virtual patient cohorts of cancer and immunosuppressed patients. Model predicts that both cancer and immunosuppressed virtual patients with severe COVID-19 have decreased CD8+ T cells and delayed IFN peaks. Additionally, our results show that cancer patients experience higher viral loads likely caused by decreased initial neutrophil counts (i.e. neutropenia), a frequent toxic side-effect of anti-cancer therapy. Together, our study suggests that immune dysregulation in COVID-19 is determined by dysfunction in IFN and CD8+ T cells, and that these may be considered as biomarkers of severity. Further, they represent potential treatment targets in susceptible patient groups.

QING HAN, York University

Evaluation of the impact on pertussis transmission dynamics of adult and maternal boosting programs in the province of Ontario

Pertussis, a highly contagious infection of the respiratory tract, was one of the main causes of child morbidity and mortality in developed countries, in the pre-vaccine era. Following the scale-up and roll-out of childhood vaccination programs in the 1940s–1960s, the incidence and severity of pertussis decreased drastically. However, despite high vaccination coverage rates for more than 50 years, pertussis is now still a re-emerging disease and new vaccination strategies are in demand. Here, we developed a novel age-structured mathematical model which allows progressive waning of natural and vaccine-induced immunity, and distinguishes between clinical and sub-clinical infections. Imported cases and seasonal infections from out-of-province traveling were also considered. After fitted to and validated by the age-stratified pertussis incidence data, the model was used to produce simulations to evaluate maternal immunization and repeated adult boostings in the province of Ontario.

JUDE KONG, York University

Dynamics of a cholera transmission model: from Microscopic Cycles to Macroscopic Cycles

Cholera remains epidemic and endemic in the world, causing thousands of deaths annually in locations lacking adequate sanitation and water infrastructure. Yet, its dynamics are still not fully understood. In this talk, I will present a cholera transmission model that includes the dynamics of bacteriophage and bacteria (V. cholerae), and also contains an indirect infection term which accounts for a minimum infectious dose of the bacteria. Using this model, I determine what drives cyclical outbreaks of cholera in endemic regions and suggest ways by which such outbreaks can be prevented. In addition, I will present a region in the parameter space of our model that leads to chaotic behaviour. This could be used to explain the irregularity in the seasonal patterns of outbreaks amongst different countries, especially if the positive relationship between bacterial proliferation and temperature is considered.

MICHAEL LI, University of Alberta
Nonidentifiability in Parameter Estimation of Simple and Complex Epidemic Models

Nonindentifiability in parameter estimation from data refers to the situation when multiple values of a set of parameters can produce the same best fit between the model and data (e.g. positive case reports of COVID-19), but different best-fit parameter values lead to significantly different predictions on un-observed quantities (e.g number hidden infections or total infections). A root cause of nonidentifiability in parameter estimation for diseases of viral infections (e.g. COVID-19, influenza, and HIV) is that the positive case report data only represents a fraction of all infections in a day (or week, year), and that fraction is also unknown and high variable during different phases of the epidemic. I will explain using examples of COVID-19 how nonidentiofiability occurs in a simple and a more complex model, and potentially how we can resolve it.

JUNLING MA, University of Victoria
Estimating the Effect of Contact Tracing During the Early State of an Epidemic

Contact tracing is an important intervention measure to control infectious diseases. We present a new approach that tracks contacts in a randomly mixed population, which allow us to precisely model the contact tracing process. The model resulting from this new approach allows us to study the effect of contact tracing and isolation of diagnosed patients on the control reproduction number and number of infected individuals. However, we found that case counts alone during an early stage of an outbreak before susceptible population have been depleted is not sufficient to identify key contact tracing parameters such as coverage probability (the fraction of contacts successfully tracked) and testing rate. We need the reason that a patient is tested for diagnosis, i.e., whether they are quarantined and showing symptom, or voluntarily tested due to symptom, or contact tracing while showing symptom. We then apply our model to estimate the effect of contact tracing on the basic reproduction number and epidemic size in Ontario, Canada.

CHINWENDU MADUBUEZE, York University, Toronto
Modelling transmission dynamics of Lassa fever transmission with environmental pathway transmission

Lassa Fever, caused by the Lassa virus, is an animal-borne disease endemic in some regions of Africa with a rodent called a natal multimammate rat as a natural reservior. It occurs more during the dry season when the bushes are dry and burned in preparation for the farming season, making the rodents move into human habitats for food to survive. The rodents excrete their faeces and contaminate the environment making environmental transmission vital in Lassa fever transmission dynamics. Therefore, studying the contaminated environment's impact on Lassa fever is essential. This study used a deterministic model to examine the situation of Lassa fever transmission incorporating two environmental pathway transmissions. First, the model's stability is established regarding the model's basic reproduction number, R_0. Further, the model implements the sensitivity analysis to identify the parameters that fuel the Lassa fever spread using the Partial Rank Correlation Coefficient technique based on the Latin hypercube sampling.

TYLER MEADOWS, Queen's University
Microbial Competition in a Serial Transfer Culture

Serial transfer culture is a common method used in microbiology to cultivate microorganisms. In this technique, a growth medium is inoculated with a small amount of microbes. After a fixed amount of time, a sample is taken from this medium and used to inoculate fresh growth medium. We expand on an existing impulsive differential equation model for microbial competition in this scenario. We establish conditions for when multiple species will coexist and conditions for when competitive exclusion holds.

ZAHRA MOVAHEDI NIA, York University
Predicting Hotspots of Marburg Virus in Africa using Ecological Niche Modeling

Straw-coloured or Eidolon helvum bats are known as the reservoir of many re-emerging zoonotic diseases such as filoviruses, i.e. Ebola and Marburg virus. On March 22, 2023, a Marburg virus outbreak was reported in Equatorial Guinea. Marburg virus is a dangerous disease with up to 90% fatality rate. In this work, Ecological Niche Modeling (ENM) is used to identify the hotspots in Africa where the Marburg virus may re-emerge, in the future. MaxEnt is a powerful machine learning technique based on the maximum entropy theory that uses presence-only data and returns the probability of suitability of the environment for the species to survive. Presence data of Eidolon helvum fruit bats were collected from online sources. Raster images provided by Africlim were used to characterize the background data by 21 different factors. The model was able to accurately predict the hotspots of the Eidolon helvum fruit bats in Africa (Area Under the Curve (AUC) > 0.8). Despite the limitations in the prediction due to not having adequate presence samples, a risk map was provided through the trained model. The results of this work could help policy-makers and health officials control and contain the Marburg virus disease in the future.

BLESSING OGBUOKIRI, York University
Vaccine Hesitancy Hotspots in Africa: An Insight From Geotagged Twitter Posts

Many social media users express concerns about vaccines and their side effects on Twitter, leading to a compromise in confidence that results in vaccine hesitancy. In Africa, vaccine hesitancy poses a significant challenge for health policymakers in the battle against COVID-19. By leveraging the geotagging feature available in most tweets, it is possible to cluster them based on their sentiments, thereby facilitating the identification of locations that are more likely to experience vaccine hesitancy. This information can be valuable for health policy and planning purposes. In this study, we collected 70,000 geotagged vaccine-related tweets from nine African countries, spanning from December 2020 to February 2022. These tweets were categorized into three sentiment classes: positive, negative, and neutral. We employed various machine learning classifiers, namely Naïve Bayes, logistic regression, support vector machines, decision tree, and K-nearest neighbor, to achieve high-quality classification outputs. Among these classifiers, logistic regression demonstrated the highest accuracy, reaching 71%, with an average area under the curve of 85%. To determine the hotspots, we employed a point-based location technique that utilized the geographic information associated with the classified tweets. On the resulting map, locations with green, red, and gray backgrounds indicate hotspots for positive, negative, and neutral sentiments, respectively. The outcomes of this research highlight the potential of analyzing social media discussions to identify hotspots during disease outbreaks. This valuable information can inform health policy, aiding in the planning and management of vaccine hesitancy in Africa.

CARLY ROZINS, York University
Why Are Bat-Borne Viruses So Deadly?

The management of future pandemic risk requires a better understanding of the mechanisms that determine the virulence of emerging zoonotic viruses. Bats host viruses that cause higher case fatality rates upon spillover to humans than those derived from any other mammal. In order to disentangle the fundamental drivers of virulence upon spillover, we develop a nested modelling framework that highlights mechanisms which underpin the evolution of viral traits in reservoir hosts that cause virulence following cross-species emergence. Our work offers a mechanistic explanation for the extreme virulence of bat-borne zoonoses and, more generally, demonstrates how key differences in reservoir host longevity, viral tolerance, and constitutive immunity impact the evolution of viral traits that cause virulence following spillover to humans.

YOGITA SHARMA, University of Victoria
Effect of stochasticity and spatial structure on homing-based gene drive spread

Since the discovery and application of CRISPR as a gene editing tool, interest has grown in gene drive systems and their ability to spread desirable genes into populations. A variety of modeling approaches have been applied to study the spatial spread of gene drive systems, including partial differential equations, metapopulation models, and deterministic, stochastic and individual-based formulations. Here, we focus on reaction-diffusion approaches in which gene drive spread is described as a "pushed" or "pulled" wave. We compare a deterministic reaction-diffusion model of gene drive to one incorporating stochasticity, and explore the impact that stochasticity has on model outcomes. We find that, first, incorporating stochasticity into the model expands the range of fitness costs and initial conditions that lead to spatial spread. Second, increasing the

level of stochasticity causes traveling wave solutions in the model to display decreased wave speed. And third, while a barrier representing a selective disadvantage to gene drive organisms may halt a traveling wave in a deterministic model formulation, in the stochastic model formulation, a small number of gene drive organisms may permeate the barrier and reestablish a traveling wave on the other side. These results highlight the limitations of deterministic reaction-diffusion models and the importance of considering stochasticity and spatial structure in models of gene drive spread as projects move towards field implementation.

ALISON SIMMONS, University of Toronto

Pneumococcal Transmission Dynamics in Canada: 2010–2019

Streptococcus pneumoniae is a bacterium that causes a wide range of diseases, notably invasive pneumococcal disease, community acquired pneumonia, and acute otitis media. It primarily spreads through oral contact and respiratory secretions. Between 20% and 60% of healthy children and 10% of healthy adults in Canada are transiently colonized with *S. pneumoniae*. Currently, most children in Canada receive three or four doses of the 13-valent pneumococcal conjugate vaccine, which aims to protect vaccine recipients from severe disease caused by 13 serotypes of *S. pneumoniae*. Higher valency pneumococcal conjugate vaccines, which cover 15 and 20 serotypes of *S. pneumoniae*, are being considered for use in pediatric populations by advisory groups globally. In addition to preventing severe disease, the 13-valent pneumococcal conjugate vaccine prevents *S. pneumoniae* colonization. The herd effects necessitate the development of a dynamic transmission model to capture the transmission dynamics of *S. pneumoniae* to inform future vaccine recommendations. We developed an age-structured compartmental model that describes pneumococcal transmission dynamics in the Canadian population using a modified 'Susceptible-Infectious-Susceptible' framework. Our model contains additional compartments that incorporate *S. pneumoniae* serotype groupings and vaccination status. We fit our model to the annual incidence of invasive pneumococcal disease by serotype group between 2010 and 2019 in Canada using Latin hypercube sampling.

STACEY SMITH?, The University of Ottawa

Modelling mutation in equine infectious anemia virus infection suggests a path to viral clearance with repeated vaccination

Equine infectious anemia virus (EIAV) is a lentivirus similar to HIV that infects horses. Clinical and experimental studies demonstrating immune control of EIAV infection hold promise for efforts to produce an HIV vaccine. Antibody infusions have been shown to block both wild-type and mutant virus infection, but the mutant sometimes escapes. Using these data, we develop a mathematical model that describes the interactions between antibodies and both wild-type and mutant virus populations, in the context of continual virus mutation. The antibody infusions are modelled using impulsive differential equations, a technique that offers insight into repeated vaccination by approximating the time-to-peak by an instantaneous change. We use impulsive theory to determine the maximal vaccination intervals that would be required to reduce the wild-type and mutant virus levels below one particle per horse. We show that seven boosts of the antibody vaccine are sufficient to eradicate both the wild-type and the mutant strains. In the case of a mutant virus infection that is given infusions of antibodies targeting wild-type virus (i.e., simulation of a heterologous infection), seven infusions were likewise sufficient to eradicate infection, based upon the data set. However, if the period between infusions was sufficiently increased, both the wild-type and mutant virus would eventually persist in the form of a periodic orbit. These results suggest a route forward to design antibody-based vaccine strategies to control viruses subject to mutant escape.

XIAOYING WANG, Trent University

Studying the fear effect in a predator-prey system with apparent competition

Recent experimental evidence shows that the mere presence of predators may largely reduce the reproduction success of prey. The loss of prey's reproduction rate is attributed to the cost of anti-predator defense of prey when the prey perceives predation risks. We propose a predator-prey model where the prey shares a common enemy that leads to apparent competition between the prey and also the cost of anti-predator defense. Analytical results give the persistence conditions for the population densities of the prey and the predator. Numerical simulations demonstrate rich dynamics, such as the bi-stability of an equilibrium and a limit cycle. Results also reveal how the prey and the predator may coexist when the anti-predator defense level varies in prey. A relatively strong anti-predator defense in the prey may drive the population density of the prey to extinction and change the

original coexistence of all the prey and the predator where the population densities oscillate periodically. Alternatively, strong anti-predator defense in the prey may facilitate the coexistence of the prey and the predator at a steady state.

WOLDEGEBRIEL ASSEFA WOLDEGERIMA, York University
Fractional differential equation models for disease dynamics: hepatitis B-virus with two-age structures as an example

I will start with a brief introduction to the fractional calculus and the use of fractional differential equations (FDEs) in different areas including in modelling infectious diseases. I will then consider our work on a fractional order model of hepatitis B virus transmission dynamics with two-age structures under vaccination. In this work, some qualitative properties of the model are presented followed by a numerical simulation to investigate the effect of memory on hepatitis B disease dynamics by varying order of derivatives and to simulate the effects of vaccinating newborns immediately after birth, vaccinating children, and adult vaccination. Then, we compared their effects on hepatitis B disease dynamics in the sense of control. It is observed that the number of infective individuals decreases faster and even falls to zero over the long run for the model with memory than the memory-less model. Comparing results between vaccination of different ages show that increasing newborn vaccination immediately after birth has the highest effect on hepatitis B disease control.

PEI YUAN, York University
Will the vaccination strategies for monkeypox prevent outbreaks at gatherings? —a case study in Canada

The outbreaks of monkeypox in non-endemic countries have led the World Health Organization to declare a Public Health Emergency of International Concern. Festivals, parties, and other gatherings may have contributed to the outbreak, particularly in the post-pandemic period. Public health has prepared vaccines in case of larger gatherings. In this talk, I will present a modelling study on how and if vaccination strategies combined with other public health measures can prevent or contribute to mitigating or halting outbreaks from mass gathering events. Working with public health agencies, we establish dynamic models to mimic the spreading of the virus in human populations and distinguish the human population into higher and low-risk groups. I will present the public health measures essential to mitigate the spread and prevent potential future outbreaks at gatherings. This is joint work with the Public Health Agency of Canada and supported by CDM and OMNI-RÉUNIS, one health modelling network of Canada.