CMPD6 abstracts

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Azmy Ackleh (MS talk) - A Multiple-Strain Susceptible-Infected Model with Diffusion Formulated on the Space of Radon Measures

Azmy Ackleh
University of Louisiana at Lafayette
USA

Minisymposium presentation
(Ecological and Epidemiological Models with Dispersal)

We formulate a multiple strain susceptible-infected model with diffusion on the space of Radon measures which has the advantage of unifying discrete and continuous strain spaces under one framework. We first establish the well-posedness of this model. Then we study the long-time behavior for the case of discrete strain spaces. We define the basic reproduction number for each strain. We establish the existence of a disease-free equilibrium and a strain-specific endemic equilibrium including a competitive exclusion equilibrium where the density of individuals at one strain is positive and the density at the remaining n-1 is zero and a coexistence equilibrium where the density of individuals at more than one strain is positive. We study the global asymptotic stability of these equilibria. In particular, for the endemic equilibrium, we establish conditions guaranteeing its global asymptotic stability under the assumption that the diffusion rate of the susceptible individuals is equal to the diffusion rate of the infected individuals. We then extend some of the long-time behavior results from the discrete strain space case to the continuous strain space case.

Folashade Agusto (MS talk) - Exploring the effects of prescribed fire and rising temperature on tick-borne diseases

Folashade Agusto
University of Kansas
USA

Minisymposium presentation
(Vector-Borne Disease Dynamics)

In recent times tick ranges have been expanding due in part to rising temperatures as a consequence of climate change, thereby increasing the risks and prevalence of tick-borne illnesses across the country. Thus, it is vital to find practical ways of managing tick populations. Prescribed fires are a common form of land management practices; it is time and cost-efficient when applied across large amounts of land. In this seminar, I investigate the effects of prescribed fire intensity and the duration between burns on the prevalence of tick-borne illnesses as temperature rises. Using stage-structured tick-host models with impulsive differential equations our results indicate that prescribed fire intensity has a larger impact in reducing disease prevalence than frequency between burns. Exploring the use of prescribed burns in preventing the establishment of ticks in new areas shows that fewer burns are ineffective at preventing their establishment because ticks can recover relatively quickly following a burn but frequent, long-term prescribed burns can slow and possibly prevent their establishment.

Folashade Agusto (P talk) - Modeling the role of human behavior and perception of risks on disease transmission

Folashade Agusto
University of Kansas
USA

Plenary presentation

Ephraim Agyingi (MS talk) - Modeling immune system priming: the miracle that saved Sub-Sahara Africa from COVID-19

Ephraim Agyingi
Rochester Institute of Technology, Rochester, New York
USA

Minisymposium presentation
(Within-host and between-host mathematical models of biological dynamics)

COVID-19 in sub-Saharan Africa has been a topic of interest since the onset of the pandemic, as the region faces unique challenges in responding to the virus. Although the number of reported cases and deaths in sub-Saharan Africa has been relatively low compared to other regions, it is unclear how much of this is due to low testing rates and reporting capacity. Moreover, the region's high prevalence of infectious diseases and malnutrition may weaken the immune system and increase the risk of severe COVID-19 outcomes. Despite these challenges, it appears that individuals in sub-Saharan Africa have mounted robust immune responses to the virus, suggesting that factors such as prior exposure to similar viruses and genetic differences may have played a role in priming their immune response to COVID-19. Immune response priming, the process by which the immune system is prepared to respond to a future infection, can occur through various mechanisms, including natural infection or vaccination. Using mathematical modeling we hope to shed some light in the ongoing research that is needed to fully understand the immune response to COVID-19 in sub-Saharan Africa.

Vitalii Akimenko (C talk) - Numerical Method for the Age-structured SIPCV Epidemic Model of Healthy cells, Dysplasia, Cervical Cancer Cells and HPV Dynamics

Vitalii Akimenko
Department of Mathematics
University of Manitoba
Canada

Contributed presentation

The numerical method for simulation of an age-structured SIPCV epidemic model with age-structured subclasses of susceptible, infectious, precancerous and cancer cells and unstructured population of human papilloma virus (HPV) dynamics with incubation period is developed. The model assumes two time-delays: (i) the time between viral entry into a target susceptible cell and the production of new virus particles and (ii) duration

of the first stage of delayed immune response to HPV population growing. The model of cell population dynamics is described by the initial-boundary value problem for the semilinear hyperbolic equations with age- and time-dependent coefficients and time delay and the dynamics of HPV virus is described by nonlinear delayed ODE. The model considers the immune functional response of organism by the HPV-density dependent death rate. The numerical method is based on the method of characteristics for the semi-linear hyperbolic equations, trapezoidal rules for integrals and has the second order of approximation. Convergence of the numerical approximations is studied both theoretically and numerically. We prove the stability and second rate of convergence of the approximate solutions to the exact solution of the SIPCV epidemic nonlinear system. Numerical experiments with vanished mesh spacing illustrate the convergence of numerical solution to the benchmark solution. Simulations illustrate the second order of accuracy of the obtained numerical method and show the various dynamical regimes of population dynamics. Simulations for model parameters of the system reveal two unstable dynamical regimes of SIPCV population which correspond to the cancer tumor growth and formation of cancer metastases.

Asami Anzai (MS talk) - Estimating importation cases using mobility data

Asami Anzai
Kyoto University
Japan

Minisymposium presentation
(Real time epidemiology in various geographic scales)

Background Mobility restrictions were commonly used to limit interaction with other people and stop the spatial spread of the COVID-19 infection. A statistical model was developed to estimate the number of imported cases in each Japanese prefecture using epidemiological data and inter-prefectural mobility.

Methods The inter-prefectural mobility rate based on mobile phone data and prevalence estimates in the origin prefectures was used to predict the number of imported cases crossing prefectural borders. Using surveillance data of cases with a history of inter-prefectural travel, the simplistic model was quantified. The impact of the mobility rate and prevalence at the origin on imported cases was then explored with simulations.

Results Compared with the observed number of imported cases, the overall pattern was captured over time. Although Hokkaido and Okinawa are northernmost and southernmost prefectures, respectively, they were sensitive to differing prevalence rates in Tokyo and Osaka and the mobility rate. Other prefectures were also sensitive to mobility change, assuming that an increment in the mobility rate was seen in all prefectures.

Conclusions Our findings indicate the need to account for the weight of an inter-prefectural mobility network when implementing human mobility-related countermeasures. If the mobility rate were maintained lower than the observed rate, the number of imported cases could have been maintained at lower levels than the observed, potentially preventing the unnecessary spatial spread of COVID-19 in late 2020.

Julien Arino (MS talk) - Role of case introductions in the community spread of infectious diseases

Julien Arino
Department of Mathematics
University of Manitoba
Canada

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

Joseph Baafi (C talk) - Modelling the Impact of Seasonality on Mosquito Population Dynamics: Insights for Vector Control Strategies.

Joseph Baafi
Memorial University of Newfoundland
Canada

Contributed presentation

Mosquitoes are important vectors for the transmission of some major infectious diseases of humans, i.e., malaria, dengue, west Nile virus and Zika virus. The burden of these diseases is different for different regions, being highest in tropical and subtropical areas, which have high annual rainfall, warm temperatures, and less pronounced seasonality. The life cycle of mosquitoes consists of four distinct stages: eggs, larvae, pupae, and adults. These life stages have different mortality rates and only adults can reproduce. Seasonal weather may affect the population dynamics of mosquitoes, and the relative abundance of different mosquito stages, since the maturation rate to the next stage depends on temperature, and because egg survival depends on rainfall. We developed a stage-structured model that considers laboratory experiments describing how temperature and rainfall affects the reproduction, maturation and survival of different Anopheles mosquito stages, the species that transmits the parasite that causes malaria. We consider seasonal temperature and rainfall patterns and describe the stage-structured population dynamics of the Anopheles mosquito in Ain Mahbel, Algeria, Cape Town, South Africa, Nairobi, Kenya and Kumasi, Ghana. We find that regional differences in seasonal weather patterns affect mosquito population dynamics. Control strategies often target one specific life stage, for example, applying larvicides to kill mosquito larvae, or spraying insecticides to kill adult mosquitoes. Our findings suggest that differences in seasonal weather patterns affect mosquito stage structure, and best approaches to vector control may vary between regions.

Rebecca Bekker (MS talk) - Black Holes in TIME: the Effect of GRID Radiation on the Tumor-Immune Micro-environment

Rebecca Bekker
H. Lee Moffitt Cancer Center and Research Institute
USA

Minisymposium presentation
(Mathematical and computational approaches to modelling immunology)

Tumor-immune interactions shape a developing tumor and its tumor immune microenvironment (TIME) resulting in either well infiltrated, immunologically inflamed 'hot' tumor beds, or 'cold' immune deserts with low levels of infiltration that are suppressive in nature. The pre-treatment immune state of the TIME is associated with treatment outcome; immunologically hot tumors generally exhibit better responses to radio- and immunotherapy than cold tumors. However, radiotherapy is known to induce paradoxical immunological consequences, resulting in both immunostimulatory and inhibitory responses. In fact, it is thought that the radiation-induced

tumoricidal immune response is curtailed by subsequent applications of radiation. It is thus conceivable that spatially fractionated radiotherapy (SFRT), administered through GRID blocks to create areas of low or high dose exposure, may protect regions of the tumor immune microenvironment, thereby preserving anti-tumor immune responses. We use an agent-based model of tumor-immune interaction to investigate the therapeutic utility of SFRT. We evaluate the immunological consequences of various GRID architectures, radiation doses and dose scheduling, to identify which GRID architectures result in superior immune infiltration for each pre-treatment immune state. Additionally, we investigate TIMEs for which SFRT may be better suited, in an immune context, than conventional radiotherapy.

Jacques Bélair (MS talk) - Modeling the use of Fangsang Shelter Hospitals in Wuhan

Jacques Bélair
Université de Montréal
Canada

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

Motivated by China's experience of using Fangcang shelter hospitals (FSHs) to successfully combat the epidemic of COVID-19 in its initial stages, we present a two-stage, functional differential delay model considering the average waiting time of patients' admission to study the impact of hospital beds and centralized quarantine on mitigating and control of the outbreak. We compute the basic reproduction number in terms of the hospital resources, and perform a sensitivity analysis of the average waiting times of patients before admission to the hospitals. We discuss the rôle played by FSHs in mitigating and eventually curbing the epidemic.

Jacques Bélair (MS talk) - Population models with state-dependant delays

Jacques Bélair
Université de Montréal
Canada

Minisymposium presentation
(Delay-differential equations in applications)

Nonlinear delay-differential equations with state-dependant delays occur naturally in a number of regulatory processes, including production and control of physiological populations. Some instances of the physiologically proper formulation of the state dependance in haematological systems will be presented, and a historical example (from MPD2) will be revisited.

Ranjini Bhattacharya (C talk) - Angiogenesis in Cancer: A Tragedy of Commons

Ranjini Bhattacharya
Moffitt Cancer Center
USA

Contributed presentation

Cancer is the result of evolution within the tumor microenvironment. Natural selection selects for cells capable of efficient nutrient uptake. Cancer cells achieve this by overexpressing angiogenic factors (VEGF) that induce the formation of blood vessels that carry nutrients to the tumor. Traditionally, angiogenesis has been viewed as a cooperative phenomenon resulting in the evolution of free-loaders. Using a game theoretic framework, we model VEGF production as an evolutionary strategy and show that the over-production of VEGF is the result of a tragedy of commons.

A cell's investment in VEGF depends on the degree to which it aids its nutrient uptake. If higher production of VEGF leads to higher nutrient uptake, then cells are incentivized to produce VEGF. If nutrients are equally divided within a given neighborhood, an individual cell's incentive to produce VEGF decreases. Our simulations predict that cancer cells produce 100 times more VEGF than typically seen in normal cells, and what would be their collective team optimum. This means that VEGF production by a cancer cell aims to co-opt nutrients from neighboring cells resulting in an evolutionary arms race. Increasing the number of cancer cells in a fixed neighborhood results in lower per-cell VEGF production while exacerbating the tragedy of the commons collectively. Next, we simulate anti-angiogenesis therapy and find that in response to therapy, cells adopt a low VEGF production strategy that continues to sustain growth in the cancer population. This results in evolutionary rescue. These results are in line with clinical observations. Our model challenges the existing paradigm of angiogenesis as a cooperative activity and provides novel insights into therapy in a clinical setting.

Amanda Bleichrodt (MS talk) - Multi-model forecasts in the context of the Mpox outbreak in multiple countries (July 28th, 2022 through January 26th, 2023)

Amanda Bleichrodt
Georgia State University
USA

Minisymposium presentation
(Real time epidemiology in various geographic scales)

In late July, public health officials noted an unprecedented surge in Mpox cases in non-endemic cases around the World. In response, our team began producing weekly forecasts for the most heavily afflicted areas. As the case levels have significantly decreased, evaluating model performance is essential to advance the growing field of epidemic forecasting. We obtained reported Mpox case data from the CDC and OWID teams through the week of 1/26/2023 to produce retrospective weekly forecasts (e.g., 1-week, 2-week, 3-week, and 4-week) for study areas using auto-regressive moving average (ARIMA), general additive model (GAM), simple linear regression (SLR), spatial-wave, and ensemble n-sub-epidemic modeling frameworks. Model performance was then compared via MSE, MAE, WIS, and 95% PI coverage metrics. The spatial-wave modeling framework performed superior across most locations and forecasting horizons in average MSE, MAE, and WIS compared to the other included frameworks. It was followed closely in success by the n-sub-epidemic top-ranked, weighted, and un-weighted ensemble (2) models. Regarding average 95% PI coverage, the n-sub-epidemic unweighted ensemble (2) model

performed best across all forecasting horizons for most locations. However, there was more widespread success noted across all modeling frameworks, with many locations seeing multiple models performing equally well in terms of average 95% PI coverage. Model performance tended to increase as we entered the declining phase of the outbreak. Overall, the spatial-wave and ensemble n-sub-epidemic frameworks outperformed other established models (e.g., ARIMA, SLR, GAM). Similar to past performance under different scenarios (e.g., COVID-19), the success seen with both frameworks highlights the continued utility of the models for short-term forecasting epidemic outbreaks.

Anuraag Bukkuri (C talk) - Models of Resistance in State-Structured Cancer Populations

Anuraag Bukkuri
Moffitt Cancer Center and Lund University
USA

Contributed presentation

Neuroblastoma is a pediatric brain cancer of variable clinical presentation. The causes behind the initiation, progression, and ultimate resistance of this cancer is unknown, though it is recognized that two cellular phenotypes underpin its deadliness: adrenergic (ADRN) and mesenchymal (MES). How these phenotypes influence the eco-evolutionary dynamics of neuroblastoma cell populations (especially under therapy) remains a mystery. This is due to the confusion surrounding whether the ADRN and MES phenotypes represent different cell types (species) or cell states (stages in the life cycle of a single species). This distinction is critical in understanding and ultimately treating neuroblastoma. In this talk, we will introduce theoretical methods to model the eco-evolutionary dynamics in state-structured neuroblastoma populations and use these models to tease apart cell type vs. cell state hypotheses. We will then expand and generalize this framework to continuous-structured models and discuss implications for cancer and bacterial resistance more generally.

Robert Stephen Cantrell (MS talk) - Resource Matching in Spatial Ecology and Evolutionary Advantage

Robert Stephen Cantrell
University of Miami
USA

Minisymposium presentation
(Ecological and Epidemiological Models with Dispersal)

A convergence of concepts from game theory (evolutionary stable strategy), ecological theory (the ideal free distribution), and mathematics (line sum-symmetry and its functional analytic generalizations) combine to explain how resource matching in spatially heterogeneous but temporally constant habitats can convey evolutionary advantage robustly across a range of modeling formats. The ideal free distribution (IFD) is an ecological construct that posits that when organisms have full knowledge of the landscape they inhabit (ideal) and are able to locate themselves as they wish (free), they will locate themselves to maximize reproductive fitness. The IFD can readily be translated into mathematical terms for models wherein the environment is spatially varying but temporally constant. In this talk we will discuss how this is done across a range of modeling formats and how it consequently leads to predictions of evolutionary advantage in such modeling formats. We then report

on ongoing efforts to define the ideal free distribution mathematically in cases when the environment varies in both space and time, focusing on the case wherein habitats vary periodically in time.

Fabian Cardozo-Ojeda (MS talk) - Mathematical modeling of gene and cell therapy for HIV cure

Fabian Cardozo-Ojeda
Fred Hutchinson Cancer Center
USA

Minisymposium presentation
(Multiscale models of infectious diseases)

Antiretroviral therapy (ART) suppresses levels of plasma Human Immunodeficiency Virus (HIV) below detection limits in standard assays. However, due to a latent reservoir of long-lived, HIV-infected cells, ART does not cure HIV and must be taken daily. Only five known cases of HIV cure have resulted in individuals receiving allogeneic hematopoietic stem cell transplantation (HSCT) for their hematological malignancies. Ongoing gene and cell therapy strategies appear promising to attain an HIV remission like the ones achieved during allogeneic HSCT by either protecting susceptible cells from HIV or boosting the immune system with infusions of T cells or antibody-like peptides targeting HIV-infected cells. We have developed ordinary differential equation models that parsimoniously recapitulate viral load and T-cell measurements from SHIV-infected, non-human primates (NHP) receiving several gene/cell therapies. We have simulated each data-validated model to find optimal conditions in which those strategies provide ART-free HIV remission. Although gene and cell therapy strategies for HIV cure are in the early stages, mathematical modeling might contribute to accelerating the success of these approaches.

Bernard Cazelles (C talk) - Modeling infectious disease dynamics: the challenge of non-stationarity

Bernard Cazelles
Sorbonne Université
France

Contributed presentation

The spread of disease through human populations is complex. The characteristics of disease propagation evolve with time, as a result of a multitude of environmental and anthropic factors, including social distancing. This non-stationarity is a key factor in the complexity of disease propagation. In the absence of appropriate external data sources, to correctly describe disease propagation, I propose a flexible methodology, based on stochastic models for disease dynamics, and on Brownian processes for parameter evolution. Using such a diffusion process has the advantage of not requiring a specific mathematical function for the parameter dynamics. Coupled with Bayesian inference using Particle MCMC, this approach allows us to reconstruct both the time evolution of some key parameters of an epidemiological dynamic and its incidence. I will demonstrate the efficiency of this methodology on toy epidemiological models where the parameters and the observation process are known, and also on more complex epidemics, such as flu, dengue and Covid-19.

Stanca Ciupe (MS talk) - Multiscale models of SARS-CoV-2 infection

Stanca Ciupe
Department of Mathematics
Virginia Tech
USA

Minisymposium presentation
(Multiscale models of infectious diseases)

Designing control strategies for managing SARS-CoV-2 infections requires multiscale investigation of heterogeneity in virus transmission, population susceptibility, and disease outcomes. In this talk, I will investigate the role of individual infections in transmission as well as the role of immune responses in disease outcomes. The models will be used to suggest testing-vaccination combinations needed for limiting an outbreak and provide explanations for immune mechanisms resulting in severe disease.

Jessica Conway (MS talk) - Heterogeneity in HIV viral rebound

Jessica Conway
Penn State
USA

Minisymposium presentation
(Mathematical and computational approaches to modelling immunology)

Antiretroviral therapy (ART) effectively controls HIV infection, suppressing HIV viral loads. While typically suspension of therapy is rapidly followed by rebound of viral loads to high, pre-therapy levels, recent observations give nuance to that statement: in a small fraction of cases, rebound may be delayed by months, years, or even possibly, permanently. We will discuss modeling to investigate that heterogeneity in outcome of treatment suspension. Specifically we will focus on time to rebound. We will first discuss our data-validated, mechanistically-motivated survival function for time-to-rebound using time-inhomogeneous branching processes. We show good agreement with data for both rapid and significantly delayed viral rebound. We will then use this model to characterize the impact of covariates such as treatment initiation time on time to rebound.

Jessica Conway (MS talk) - Modeling PrEP-on-demand strategies to prevent HIV transmission

Jessica Conway
Penn State
USA

Minisymposium presentation
(Multiscale models of infectious diseases)

In 2010, analysis of the iPrEx study results demonstrated that daily dosing with antiretroviral therapy (ART) in advance of exposure to HIV, termed pre-exposure prophylaxis (PrEP), can significantly reduce the risk of HIV

transmission and population spread. However, daily adherence to a drug regimen can be difficult to maintain and may come with side-effects. In contrast, the IPERGAY study published in 2015 suggested that short-term use around the time of exposure may be just as effective at reducing HIV risk as daily use. Here we investigate short-term use, termed "on-demand" or "event-based" PrEP. We aim to make model-based predictions of effective on-demand drug regimen. Focusing on transmission through sexual exposure, we incorporate a deterministic model of tissue-level pharmacokinetics and pharmacodynamics (PK/PD) of Truvada into a branching-process model of early HIV infection. Thus, we predict the risk of HIV transmission and risk reduction associated with dose size and timing relative to exposure. To evaluate effectiveness of dosing strategies, we simulate strategies by sampling a virtual population and performing extensive sensitivity analyses. Hence, we aim to identify practical dosing strategies that most effectively reduce risk of HIV transmission through sexual exposure.

Morgan Craig (MS talk) - Delays in the cell cycle: implications in immune responses

Morgan Craig
Sainte-Justine University Hospital Research Centre / Université de Montréal
Canada

Minisymposium presentation
(Delay-differential equations in applications)

The cell cycle is critical to ensuring a cell functions and proliferates correctly, and is regulated by intrinsic and extrinsic factors. In the blood system, cytokines help stimulate and inhibit blood cell production, ultimately determining cell fate. In this talk, I will discuss our recent studies incorporating delay differential equations to model the cell cycle with immunology-related applications, including immuno-oncology and immune responses to viral infections.

Morgan Craig (MS talk) - The TME determines the efficacy of immunotherapies to treat glioblastoma

Morgan Craig
Sainte-Justine University Hospital Research Centre / Université de Montréal
Canada

Minisymposium presentation
(Modelling the Cancer Microenvironment)

Glioblastoma is a deadly brain and central nervous system cancer for which standard-of-care only moderately extends survival. New treatment options, including immunotherapies, are under intense study but have so far failed to achieve efficacy in clinical trials. In this talk, I will show how agent-based modelling of glioblastoma and its tumour microenvironment combined with state-of-the-art experimental approaches provide important biological insight into the regulation of the immune response to oncolytic viruses and immune checkpoint blockade, pinpointing mechanisms of treatment success.

Jim Cushing (P talk) - Discrete-time models of infectious diseases: a project in memory of Aziz-Abdul Yakubu

Jim Cushing
University of Arizona
USA

Plenary presentation

This talk is dedicated to the late Aziz-Abdul Yakubu who passed away suddenly and unexpectedly last August, 2022. To honor Aziz's memory, I will briefly discuss a project on which he and I were working at the time of his death, naming a chapter on infectious disease models to appear in a book on discrete-time models in population dynamics co-authored with Saber Elaydi. In this chapter we provide a general framework for the formulation of such models and give some general theorems concerning disease-free equilibria and the fundamental bifurcation of endemic equilibria that occurs upon the destabilization of a disease-free equilibrium. This basic bifurcation theorem will be related to the reproduction number R , for which we provide a general definition. We also give an extension of this fundamental bifurcation phenomenon for periodic disease-free and endemic cycles. I will illustrate the application of the theorems using a few specific disease models.

Tanuja Das (C talk) - Effect of a novel generalized incidence rate function in SIR model: stability switches and bifurcations

Tanuja Das
University of New Brunswick, NB, Canada
Canada

Contributed presentation

In the event of a disease outbreak in a population, the incidence rate function initially increases with an increase in the number of infectives, but then decreases due to inhibitory effects before reaching saturation. To address this, a new generalized incidence rate function is proposed, and an SIR compartmental model is studied with a Holling type II saturated treatment rate function. The non-monotonic nature of this incidence rate function has an impact on the stability of endemic equilibria. Backward bifurcation, forward (transcritical) bifurcation, saddle-node bifurcation, and Hopf bifurcation are observed, leading to the possibility of multiple endemic equilibria and multi-stability. When the model system accounts for the delay in incubation, multiple Hopf bifurcations with the same frequency and two frequency Hopf-Hopf bifurcations exist, resulting in two different oscillatory solutions. The exhibition of these two-frequency oscillations are novel and have not been explored much in epidemiological models.

Xiaoyan Deng (MS talk) - Predicting heterogeneous CD8+ immune memory responses in COVID-19 using a virtual patient cohort

Xiaoyan Deng
Université de Montréal
Canada

Minisymposium presentation
(- Within-host and between-host mathematical models of biological dynamics)

Throughout the COVID-19 pandemic, considerable efforts have been made to understand the mechanisms of the immune response to SARS-CoV-2 infections and discover the key factors causing heterogeneous COVID-19 responses. Moreover, durable viral immunity to SARS-CoV-2 generated after infection in naïve hosts or after vaccination is of high importance, given its implication for protection from severe disease. To better understand the formation and function of cellular immunological memory after SARS-CoV-2 infection, we developed a mechanistic, computational model of COVID-19 immunopathology that explicitly describes the interactions between epithelial cells, innate and adaptive immune cells, and cytokines, as well as the differentiation process of naïve CD8+ T cells into effector and memory cell subsets. Through calibration and validation against a broad range of experimental and clinical immunological data, we studied heterogeneity in CD8+ T cell-mediated immunity to SARS-CoV-2. Using our model, we identified key mechanisms distinguishing COVID-19 severity and reducing inflammation in reinfections using a virtual patient cohort. These include the monocyte-to-macrophage differentiation rate, the IFN production rate by infected cells, and the monocyte recruitment rate. Our results show that memory CD8+ T cell generation is critical to offering durable protection against severe COVID-19 and reduces heterogeneous outcomes upon re-exposure to the same virus. We can also apply our model to predict the humoral immune response post-vaccination to study breakthrough infections. Thus, this work provides a platform for investigating key questions about heterogeneity in the response to SARS-CoV-2.

Preeti Deolia (C talk) - Epidemiology of Age in COVID-19: A model with m-heterogeneous contact rates and saturated treatment function

Preeti Deolia
Atal Bihari Vajpayee-Indian Institute of Information Technology and Management, Gwalior
India

Contributed presentation

The heterogeneity of the host population plays a vital role in the transmission and outbreak of infectious diseases. The contact pattern among various individuals can be different based on their age. This work investigates an m-age heterogeneous epidemic model incorporating limited treatment facilities. The expression for the basic reproduction number and conditions for the global stability of the system is derived. It is observed that the disease-free equilibrium is globally stable if $R_0 \leq 1$ while an endemic equilibrium exists uniquely if $R_0 > 1$. The numerical simulation is demonstrated to illustrate the results.

Clotilde Djuikem (C talk) - Impulsive modelling of rust dynamics and predator releases

Clotilde Djuikem
Université Côte d'Azur, Inria, INRAE, CNRS, Université Paris Sorbonne, BIOCORE
France

Contributed presentation

Authors: Clotilde Djuikem 1 , Frédéric Grognard 1 , Suzanne Touzeau 2,1 1-Université Côte d'Azur, Inria, INRAE, CNRS, Université Paris Sorbonne, BIOCORE, France 2-Université Côte d'Azur, Inria, INRAE, ISA, France

Fungal diseases cause serious damages in crop worldwide. In particular, coffee leaf rust (CLR), caused by fungus Hemileia vastatrix attacks coffee leaves and reduces coffee yield. Its control mainly relies on cultural practices, fungicides, resistant cultivars and biocontrol using hyperparasites. Fungicides are widely used, but have harmful ecological impact an important costs; the other methods need careful analysis for their deployment to be successful on the long term. This work presents a multi-seasonal model of the CLR development in the coffee plantation with continuous dynamics during the rainy season and a discrete event to represent the simpler dynamics during the dry season. Biological control using predators through one or more discrete introduction events over the year is then added. Analytical and semi-numerical studies are performed to identify how much and how frequently predators need to be introduced through the definition of a threshold value, as a function of various parameters. We show that the best strategy to efficiently control the disease depends on the predator mortality: low mortality predators need to be released only once a year, while high mortality predators should be released more frequently to ensure their persistence in the plantation. This work hence provides qualitative and quantitative bases for the deployment of predator-based biocontrol, a promising alternative to fungicides for rust control.

Keywords: crop protection, coffee leaf rust, hybrid model, seasonality, Floquet theory, stability

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Marisa Eisenberg (P talk) - Identifiability and infectious disease interventions: exploring when uncertainty matters

Marisa Eisenberg
University of Michigan, Ann Arbor
USA

Plenary presentation

Identifiability, estimability, and parameter reduction methods provide tools to understand the interactions between parameters, model structure, and outputs—and how these interactions determine what inferences and predictions are possible for a given system. In particular, issues of identifiability and uncertainty can affect whether it is possible to select an optimal intervention—an important question for applied infectious disease and biological modeling. In this talk, we will explore how identifiability can be used in practice to help inform epidemiological decision-making, and when intervention strategies are or are not robust to uncertainty in the model parameters and structure.

Marisa Eisenberg (MS talk) - Models to inform wastewater-based epidemiology: identifiability, uncertainty, and opportunities

Marisa Eisenberg
University of Michigan, Ann Arbor
USA

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

Wastewater monitoring has seen a broad expansion over the pandemic as a useful tool for understanding disease patterns, without relying on clinical testing or care-seeking. Wastewater data has great potential to help us understand the epidemiological patterns of a wide range of diseases—from detecting new outbreaks to understanding seasonal patterns. But challenges remain in understanding how to translate wastewater concentration data into population information on transmission patterns. In this talk, we will explore how mathematical models have the potential to help us bridge that gap and make wastewater data more actionable and interpretable, and examine the uncertainty and identifiability challenges involved in linking models with wastewater data.

Blessing Emerenini (MS talk) - Data Assimilation of Quorum Sensing Regulation of Bacteria-Phage Interaction in Biofilm

Blessing Emerenini
Rochester Institute of Technology
USA

Minisymposium presentation
(Within-host and between-host mathematical models of biological dynamics)

Quorum Sensing is a cell-cell communication induced when an individual bacterium produces small diffusible molecules that can be detected by surrounding organisms. Pseudomonas species are gram-negative bacteria capable of forming a community called biofilm. Biofilms are difficult to eradicate, more especially when formed on living tissues. To facilitate the establishment of infection on its host, pseudomonas aeruginosa produces an impressive array of virulence factors, several of which have been found to be regulated by quorum sensing. The use of phages in bacterial treatment has become a welcoming development over the years. In this study, we explore several modeling approaches, investigating possible contributing factors and parameters in understanding the role of quorum sensing in regulating bacteria-phage interactions in biofilm.

Guihong Fan (MS talk) - Delayed model for the transmission and control of COVID-19 with Fangcang Shelter Hospitals

Guihong Fan
Columbus State University
USA

Minisymposium presentation
(Delay-differential equations in applications)

The ongoing coronavirus disease 2019 (COVID-19) pandemic poses a huge threat to global public health. Motivated by China's experience of using Fangcang shelter hospitals (FSHs) to successfully combat the epidemic in its initial stages, we present a two-stage delay model considering the average waiting time of patients' admission to study the impact of hospital beds and centralized quarantine on mitigating and controlling of the outbreak. We compute the basic reproduction number in terms of the hospital resources and perform a sensitivity analysis of the average waiting times of patients before admission to the hospitals. We conclude that, while designated hospitals save the lives of severely infected individuals, the FSHs played a key role in mitigating and eventually curbing the epidemic. We also quantified some key epidemiological indicators, such as the final size of infections

and deaths, the peak height and its timing, and the maximum occupation of beds in FSHs. Our study suggests that, for a jurisdiction (region or country) still struggling with COVID-19, when possible, it is essential to increase testing capacity and use a centralized quarantine to massively reduce the severity and magnitude of the epidemic that follows.

Marcel Fang (C talk) - A two-stage SEIRS reinfection model with multiple endemic equilibria

Marcel Fang
Sorbonne Université & INRIA, France
France

Contributed presentation

Since the introduction of SIR model by Kermack and McKendrick in 1927, compartmental models have been massively studied and successfully applied to various epidemic processes including characteristics such as quarantine, vaccination, variants, cross-immunity. Recently, a particular attention has been paid to reinfection models in epidemiology. To cite a few, threshold conditions for infection, reinfection and endemicity of various SIRS models are studied in [Gomes and al. 2004], global stability of SEIRS model in [Li and Muldowney 1999], bifurcation analysis for a SIRI model presenting different contact rates for infection and reinfection in [Pagliara and al., 2018], and models counting reinfections in [Katriel, 2011], [Fang and Bliman, 2022]. Nevertheless, in most studies on reinfection, the infection and reinfection processes are assumed to behave essentially in the same way, which is quite limitative.

With the aim of understanding the effects induced by differences between the stage of primo-infection and further reinfections, we introduce here an 8-dimensional two-stage SEIRS reinfection model in which the parameters characteristic of the disease dynamics are different for the primo-infection and for the following reinfections. The value of the basic reproduction number R0 of the model around the (unique) disease-free equilibrium is first derived, and the existence of up to two and three endemic equilibria, respectively in the cases $R0 \leq 1$ and $R0 > 1$, is theoretically established under appropriate conditions on the system parameters. Finally, numerical testing and simulations are achieved, which in particular exhibit bistability in the cases when multiple endemic equilibria arise.

Suzan Farhang-Sardroodi (MS talk) - Mathematical Modelling of the Impact of Human Immune Diversity on COVID-19 transmission

Suzan Farhang-Sardroodi
Department of Mathematics
University of Manitoba
Canada

Minisymposium presentation
(Multiscale models of infectious diseases)

While within-host and between-host models of COVID-19 dynamics have been widely studied in isolation, connecting the immunological and epidemiological scales through multi-scale models is necessary to incorporate individual and population-oriented approaches. Multi-scale models provide a deeper understanding of individual heterogeneity's role in developing epidemics. Intra-individual and inter-individual dynamics of COVID-19 are

intrinsically linked. Thus, finding the appropriate functional links between these two scales are important to accurately model the interactions between epidemiological (between-host) and immunological (within-host) processes. Here, I present a new mathematical model that explicitly combines the individual and population-level dynamics to give new insights and perspectives into how the SARS-CoV-2-immune dynamics at the within-host scale influence the epidemiological transmission dynamics at the between-host scale. Our work casts light on the potential effects of various host immunizations on COVID-19 disease transmission.

Jonathan Forde (MS talk) - Modeling the challenges of optimal resource deployment for epidemic prevention

Jonathan Forde
Department of Mathematics and Computer Science
Hobart and William Smith Colleges
USA

Minisymposium presentation
(Multiscale models of infectious diseases)

During emergent outbreaks of viral infections, public health policy decisions are made on the basis of incomplete information in a changing landscape of scientific knowledge and budgetary and infrastructure constraints. Accounting for the trade-offs necessitated by the resource limitation is essential when formulating an optimal policy response. In this work, we pose optimal control problems to explore the implications of several such trade-off, focusing on testing vs. vaccination and long-term vs. short-term public health objectives. We also explore the how these optimal controls are influenced by the efficacy of the interventions and the frequency with which policy changes can be made.

Hayriye Gulbudak (MS talk) - Extrapolating vaccine effect to epidemiological impacts in an immuno-epidemiological Dengue vaccination model structured by host antibody level

Hayriye Gulbudak
University of Louisiana at Lafayette
USA

Minisymposium presentation
(Bridging the scale from within-host to epidemic models)

Vaccination policy for Dengue (DENV) has been a hotly debated topic. Recently developed vaccines have been linked to increased risk of severe infection in naive individuals, leading some scientists to advise only vaccination of previously infected individuals or to not deploy any vaccine, whereas other experts have downplayed the risk or suggested the benefits of population-wide vaccination outweigh the risks. Furthermore, researchers have called for more refined antibody screening of the target population since pre-existent antibody level modulates infection severity risk. In this study, we formulate an antibody size-structured multi-scale epi- demic PDE DENV model that is linked to a coupled immunological ODE virus-immune response system. In the model formulation, we consider: (i) waning immunity and immune boosting processes induced by sequential infections via multiple co-circulating DENV strains, (ii) reinfection and vaccination of susceptible and recovered individuals, and (iii) individual and population scale evolving immunity. Via threshold analysis, we derive the strain specific basic

reproduction number and invasion numbers along with the equilibria and their stability conditions. Later, via numerical simulations, we show how the bidirectional feedback between immunological scale viral immune kinetics and population scale virus transmission with evolving immunity on both scales can affect population level disease severity and abundance. In particular, we address the question: how can vaccination be employed to eradicate the disease, while avoiding possible severe infection in vaccinated individuals, all at a feasible economic cost?

Hayriye Gulbudak (MS talk) - An Immuno-Epidemiological Vector-Host Model with Within-Vector Viral Kinetics

Hayriye Gulbudak
University of Louisiana at Lafayette
USA

Minisymposium presentation
(Vector-Borne Disease Dynamics)

A current challenge for disease modeling and public health is understanding pathogen dynamics across scales since their ecology and evolution ultimately operate on several coupled scales. This is particularly true for vector-borne diseases, where within-vector, within-host, and between vector–host populations all play crucial roles in diversity and distribution of the pathogen. Despite recent modeling efforts to determine the effect of within-host virus-immune response dynamics on between-host transmission, the role of within-vector viral dynamics on disease spread is overlooked. Here, we formulate an age-since-infection-structured epidemic model coupled to nonlinear ordinary differential equations describing within-host immune-virus dynamics and within-vector viral kinetics, with feedbacks across these scales. We first define the within-host viral-immune response and within-vector viral kinetics-dependent basic reproduction number 0. Then we prove that whenever $0<1$, the disease-free equilibrium is locally asymptotically stable, and under certain biologically interpretable conditions, globally asymptotically stable. Otherwise, if $0>1$, it is unstable and the system has a unique positive endemic equilibrium. In the special case of constant vector to host inoculum size, we show the positive equilibrium is locally asymptotically stable and the disease is weakly uniformly persistent. Furthermore, numerical results suggest that within-vector-viral kinetics and dynamic inoculum size may play a substantial role in epidemics. Finally, we address how the model can be utilized to better predict the success of control strategies such as vaccination and drug treatment.

Abba Gumel (MS talk) - Mathematics of malaria transmission dynamics: the renewed quest for eradication

Abba Gumel
University of Maryland
USA

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

Malaria, a deadly disease caused by protozoan Plasmodium parasites, is spread between humans via the bite of infected adult female Anopheles mosquitoes. Over 2.5 billion people live in geographies whose local epidemiology permits transmission of P. falciparum, responsible for most of the life-threatening forms of malaria. The

widescale and heavy use of insecticide-based interventions, notably long-lasting insecticidal nets and indoor residual spraying), during the period 2000-2015, resulted in a dramatic reduction in malaria incidence and burden in endemic areas, prompting a renewed quest for malaria eradication. Numerous factors, such as Anopheles resistance to all currently-available insecticides and anthropogenic climate change, potentially pose important challenges to the eradication efforts. In this talk, I will discuss a genetic-epidemiology framework for assessing the impact of insecticide resistance on malaria. Specifically, questions on whether eradication can be achieved using existing insecticide-based control resources will be addressed. There may be a brief discussion on the utility of some of the gene drive-based biological interventions being proposed as a plausible alternative pathway for achieving the laudable malaria eradication goal.

Abba Gumel (MS talk) - Mathematics of Wolbachia-based biocontrol of mosquito-borne diseases

Abba Gumel
University of Maryland
USA

Minisymposium presentation
(Vector-Borne Disease Dynamics)

The release of Wolbachia-infected mosquitoes into the population of wild mosquitoes is one of the promising biological control methods for combating the population abundance of mosquitoes that cause deadly diseases, such as dengue. In this lecture, I will present a two-sex mathematical model for the population ecology of dengue mosquitoes and disease, and use the model to assess the potential impact of the periodic release of Wolbachia-infected mosquitoes (into the wild mosquito population in the community) on the population ecology of the dengue mosquitoes and disease.

Donglin Han (MS talk) - Retrospective estimation of proportion of total infections of COVID-19 during the first wave in Alberta

Donglin Han
University of Alberta
Canada

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

Mathematical modeling has been extensively used during the COVID-19 pandemic to project the spatial and temporal trend of the transmission and spread of the infection. However, earlier model projections were over-estimated due to factors such as limited data and understanding of the virus at the beginning of the pandemic, rapidly evolving situations, and changes in human behavior. After almost three years of the pandemic, with all the medical knowledge we have gained of the SARS-Cov-2 virus and its variants, information on the public health measures that were implemented, and the epidemiological and public health data on the pandemic that are available, can we use mathematical models to retrospectively estimate the proportion of a population that were infected during a COVID-19 wave? Our study aimed to give an affirmative answer to this question, by demonstrating how simple mathematical models of COVID-19 of SIR type can be used to produce estimations

of the proportion of infected population during the first COVID-19 wave in the Province of Alberta, Canada, during March-May of 2020. We analyzed daily new COVID-19 case and testing data during the period from March 5 - June 1, 2020 from Alberta Health and incorporated information on changes in public health measures related to COVID-19, such as social gathering restrictions, school closures, testing policies, quarantine and isolation, and contact tracing, to ensure accurate reflection in our model. Our estimation accuracy was validated by seroprevalence data for the Alberta population in June 2020 from the Alberta Public Health Precision Lab. Our modeling approach was also adapted to provide dependable long-term model projections for subsequent COVID-19 waves.

Katsuma Hayashi (MS talk) - Reconstructing the temporal dynamics of clustering from cluster surveillance of COVID-19

Katsuma Hayashi
Kyoto University
Japan

Minisymposium presentation
(Real time epidemiology in various geographic scales)

Background: Clusters, defined as a group of cases that share common place of transmission, have characterized local dynamics of COVID-19 transmission, and Japan is one of a few countries that continued to survey clustering events classified by social settings. Japanese government referred to cluster data to design and implement public health and social measures(PHSM), but little has been clarified with respect to the transmission mechanisms of epidemic that propagates with certain types of clusters. Here we aimed to analyze the temporal dynamics of clustering using the cluster surveillance data in Japan.

Methods: Clusters were classified into healthcare facility, welfare facility, school, working place, recreation event, and eating and drinking establishment. The number of cases who were unlinked was simultaneously recorded. We employed the vector autoregression linear non-gaussian acyclic model (VAR-LiNGAM) to describe the time-series causal mechanisms among different types of clusters as a function of time. The reliability of VAR-LiNGAM was assessed by bootstrapping method.

Results: Eating and drinking establishment and workplace were identified as constituting “upper stream” of the temporal order of clustering, and healthcare and welfare facilities tended to be dead-end. The upper-stream clusters predicted subsequent clusters for about 5 weeks ahead. We reconstructed the chain of those clustering patterns. The effectiveness of PHSM that focused on eating and drinking establishment at nights was assessed.

Conclusion: The present study has shown that empirical data based on cluster surveillance greatly helped identify forthcoming epidemic by exploring the type of clusters.

Jane Heffernan (P talk) - Modelling Immunity to SARS-CoV-2

Jane Heffernan
York University
Canada

Plenary presentation

Immunity is generated from infection and vaccination. Immunity can also decay over time, because of natural degradation, or because a pathogen evolves, lessening the protective effects of immunity in a host. We have developed mathematical models of SARS-CoV-2 infection and vaccination. Fitting the models to in-host measures of the immune response and/or pathogen or vaccine load, we quantify the production and decay of the humoral and cell-mediated arms of the immune response. Results are translated to the population level to quantify distributions of immunity by age. These models are used to help inform decision-makers in developing non-pharmaceutical and pharmaceutical intervention programs. In this talk, we will review the in-host models of vaccination and infection, and we will quantify the distributions of immunity in a population over time. We will consider Ontario, Canada as a case study.

Jane Heffernan (MS talk) - Seasonality and Influenza pH1N12009 Vaccination Impact

Jane Heffernan
York University
Canada

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

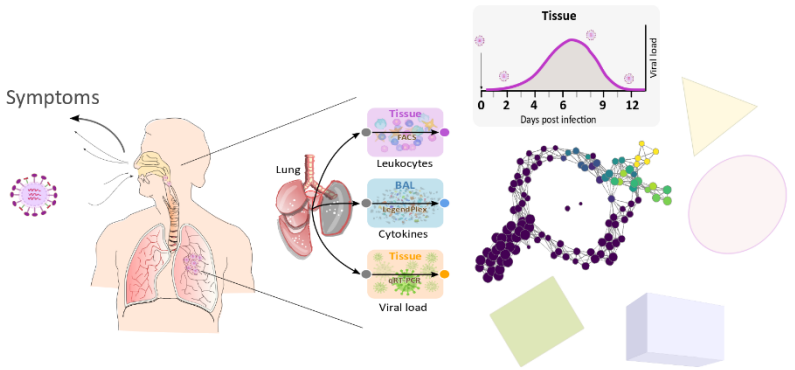
The pH1N12009 pandemic exhibited regional variation in pandemic onset, infection dynamics (one, two or three waves) and attack rates. We have developed a two-strain model of influenza infection that tracks seasonal H3N2 and pH1N12009 dynamics over the pandemic timeframe, including vaccination and heterologous cross protection. The model is calibrated using an Approximate Bayesian Computation (ABC) framework using data for seroprevalence, relative subtype dominance and annual attack rates for Australia and the UK. Results show that the pH1N12009 timing and dynamics, and the impact of the 2009 vaccination campaigns, are influenced by the seasonal influenza cycle in these two regions.

Esteban A. Hernandez-Vargas (P talk) - The Shapes of Immunological Data during Respiratory Infections

Esteban A. Hernandez-Vargas
University of Idaho
USA

Plenary presentation

Pathogens have important implications in many aspects of health, epidemiology, and evolution. Topological Data Analysis (TDA) is used here to identify the behavior of a biological system from a global perspective. Using data sets of the immune response during influenza-pneumococcal co-infection in mice and kinetic data of COVID-19 patients with different disease severity, we employ the mapper algorithm to simplify and visualize high dimensional data sets. Persistent shapes of the simplicial complexes of the data in the infection scenarios are found. In this talk, we will hypothesize that the shape of the infection impacts immunity and subsequent severity.



Sarafa Iyaniwura (MS talk) - Understanding the efficacy of capsid protein allosteric modulators using a multiscale model of hepatitis B virus

Sarafa Iyaniwura
Los Alamos National Laboratory
USA

Minisymposium presentation
(- Within-host and between-host mathematical models of biological dynamics)

As the search for a cure for the Hepatitis B virus (HBV) continues, pharmaceutical companies have continued to develop drugs that target different stages of the intracellular life-cycle of the virus. The earlier developed drugs, the nucleoside reverse transcriptase inhibitors (NRTIs) analogues, have been shown to be effective in suppressing HBV viral load (VL) in patients with chronic infection. However, these drugs need to be taken for a lifetime to maintain VL suppression, creating the risk of adverse effects and the emergence of drug-resistant strains of the virus. The development of a new class of drugs, the capsid protein allosteric modulators (CpAMs), has created renewed hope for finding a functional cure for HBV. These drugs inhibit the encapsidation of polymerase-pregenomic RNA (pgRNA) in infected cells. We developed a multiscale age-structured model of HBV. Our model incorporates the intracellular and extracellular dynamics of HBV RNA and DNA and keeps track of the age of infection of infected hepatocytes. We derived an equivalent ODE system for our multiscale model and fitted the reduced model to the viral loads of chronic HBV patients treated with CpAMs and NTRIs, to understand the efficacies of the drugs.

Harsh Vardhan Jain (MS talk) - A quantitative evaluation of an anti-cancer vaccine for treating advanced prostate cancer

Harsh Vardhan Jain
Department of Mathematics and Statistics
University of Minnesota Duluth
USA

Minisymposium presentation
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In this talk, I will present our mechanistic model of the response of prostate cancer to one of the the first FDA-approved live cell anti-cancer vaccines, sipuleucel-t (Provenge). In clinical trials, Provenge has shown only modest survival benefits. Moreover, an optimal dosing schedule has not been established, even after a decade of use. Our model is calibrated with data from mouse xenograft experiments, and captures the detailed immune response of the body when vaccination is administered. I will then introduce our modeling paradigm — Standing Variations Modeling — which captures the inherent heterogeneity that characterizes individuals in a population, and provides an explanation for the observed clinical outcomes of treatment with Provenge. We also predict an optimal therapeutic regime that maximizes predicted efficacy of the vaccine for a small subset of a heterogeneous population. Our approach readily generalizes to a range of emerging cancer immunotherapies, and more generally, to predicting and understanding how a population responds to any intervention targeting a human disease. An alternative approach to capturing heterogeneity in a population is using agent-based models (ABMs), where each cancer cell is an independent agent. Time permitting, in the second half of the talk, I will present some current research directions wherein we have developed a novel method to parameterize computationally complex ABMs of tumor-immune interactions with coarse-grained and noisy experimental data.

Marek Kimmel (MS talk) - Site frequency spectra and estimation of clonal dynamics of tumors

Marek Kimmel
Departments of Statistics and Bioengineering
Rice University
USA

Minisymposium presentation
(Stochastic population models: Theory and applications in Cancer Research)

We explain how models of population genetics can be used to provide quantitative inference of clonal evolution of cancer. The talk has two parts. Part 1 is devoted to the definition and mathematical properties of the Site Frequency Spectrum (SFS), one of the commonly used characteristics of cell populations undergoing growth and mutation. We explore the basic consistency of the approaches based on Wright-Fisher or Moran coalescents versus those based on birth-death processes. This provides building blocks for Part 2, which introduces the heuristic estimation equations, which employ the observable characteristics of the SFS, and allow an exact solution providing estimates of the growth and mutation rates and origin times of the clones. Examples based on simulations and available tumor data are presented. Accuracy of the estimates and their possible applications are discussed. Contributions of Emmanuel Asante, Khanh Dinh, Roman Jaksik, Andrew Koval, Paweł Kuś, and Simon Tavaré are acknowledged.

Chapin Korosec (MS talk) - Longitudinal immunological outcomes from three doses of COVID-19 vaccines in people living with HIV: antibodies, memory-B cells, cytokines, and a novel within-host immunological model

Chapin Korosec
York University
Canada

Minisymposium presentation
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Chapin S. Korosec [1,2], Vitaliy Matveev [3], Mario Ostrowski [3], Jane M. Heffernan [1,2]

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People living with HIV (PLWH) older than age 55 have an enhanced risk of complications from SARS-CoV-2 infection. It is further unclear whether multiple standard doses of COVID-19 vaccines elicit a durable immunity in this population or whether the vaccines can destabilize HIV reservoirs. In this talk I will discuss our unpublished work where we followed n = 91 PLWH aged 55+ and n = 23 age-matched HIV- individuals over a period of 48 weeks following COVID-19 dose one, capturing longitudinal immunological outcomes from two subsequent booster doses. I will introduce the longitudinal immunological findings for IgG, memory-B cells, and cytokines (IFNg and IL2). I will then motivate our novel within-host immunological model which couples these quantities together, and the findings of our fits to determine dose-dependent decay rates and half life values. Model fit findings, practical identifiability concerns, and biological implications of the within-host modelling approach will be discussed.

Christopher Kribs (MS talk) - Impact of tetravalent dengue vaccination with screening, ADE, and altered infectivity on dengue and Zika transmission

Christopher Kribs
University of Texas at Arlington
USA

Minisymposium presentation
(Vector-Borne Disease Dynamics)

Acquired immunity to a dengue virus serotype (whether by infection or vaccine) can produce antibody-dependent enhancement (ADE) in later infections with another dengue serotype, causing higher viral loads and more severe symptoms such as dengue hemorrhagic fever, unless the person already has immunity to multiple dengue serotypes. Screening to confirm dengue seropositivity is therefore recommended before vaccination. Recent studies suggest that the closely-related Zika virus may also interact with dengue through ADE. The study presented in this talk uses a mathematical model to evaluate the likely impact of imperfect screening and dengue vaccination on the spread of both viruses in a population where only one dengue serotype circulates, although the vaccine may take against any or all of the four recognized serotypes. Analysis focuses on the viruses' reproductive numbers. Results indicate that vaccination increases Zika's spread through induced ADE, while its impact on the spread of dengue depends on screening specificity and serotype-specific vaccine efficacies, as well as the intensity of ADE. Numerical analysis identifies the roles played by age-in and catch-up vaccination as well as screening characteristics and prior dengue exposure.

Brandon Legried (MS talk) - Inferring phylogenetic birth-death models from extant lineages through time

Brandon Legried
School of Mathematics
Georgia Institute of Technology
USA

Minisymposium presentation
(Stochastic population models: Theory and applications in Cancer Research)

Birth-death processes have been used to study population growth, with broad-ranging biological applications such as identifying speciation and extinction rates, calibrating divergence times, and studying the dynamics of pathogens in infection trees. Recent theoretical work on phylogenetic birth-death models offer differing viewpoints on whether they can be estimated from lineages through time. Recently, Louca and Pennell (2020) demonstrated that time-varying birth and death rates are not identifiable from lineage-through-time data. This was a grave result, in view of thousands of published biological and computational studies that use this data. In this talk, I explain how identifiability can be restored, while re-focusing the discussion to what actually makes inference computationally challenging. This is based on joint work with Jonathan Terhorst (University of Michigan, Ann Arbor).

Kang-Ling Liao (MS talk) - The opposite functions and treatment outcomes of CD200-CD200R in cancer

Kang-Ling Liao
Department of Mathematics
University of Manitoba
Canada

Minisymposium presentation
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In this talk, I will present our mechanistic model of the response of prostate cancer to one of the the first FDA-approved live cell anti-cancer vaccines, sipuleucel-t (Provenge). In clinical trials, Provenge has shown only modest survival benefits. Moreover, an optimal dosing schedule has not been established, even after a decade of use. Our model is calibrated with data from mouse xenograft experiments, and captures the detailed immune response of the body when vaccination is administered. I will then introduce our modeling paradigm — Standing Variations Modeling — which captures the inherent heterogeneity that characterizes individuals in a population, and provides an explanation for the observed clinical outcomes of treatment with Provenge. We also predict an optimal therapeutic regime that maximizes predicted efficacy of the vaccine for a small subset of a heterogeneous population. Our approach readily generalizes to a range of emerging cancer immunotherapies, and more generally, to predicting and understanding how a population responds to any intervention targeting a human disease. An alternative approach to capturing heterogeneity in a population is using agent-based models (ABMs), where each cancer cell is an independent agent. Time permitting, in the second half of the talk, I will present some current research directions wherein we have developed a novel method to parameterize computationally complex ABMs of tumor-immune interactions with coarse-grained and noisy experimental data.

Ernesto Lima (MS talk) - Development and calibration of a stochastic, multiscale agent-based model for predicting tumor and vasculature growth

Ernesto Lima
The University of Texas at Austin
USA

Minisymposium presentation
(Modelling the Cancer Microenvironment)

Agent-based models (ABMs) are a powerful tool for simulating tumor growth. However, they suffer from high computational costs—especially if the stochastic nature of phenotypic transitions is included in the formulation of the model. To address these limitations, we have developed two multiscale ABMs, one avascular and one vascular, and calibrated them to experimental data.

The avascular model is a coarse-grained two-scale ABM (cgABM) calibrated with time-resolved microscopy measurements of BT474 human breast carcinoma cells grown with different initial conditions. The model consists of a reaction-diffusion type model capturing the spatiotemporal evolution of glucose and growth factors in the tumor microenvironment, coupled with a lattice-free ABM to simulate individual cell dynamics. We perform a global sensitivity analysis to identify the relative importance of model parameters, followed by a Bayesian calibration that accounts for the stochasticity of the cgABM. The results show that the cgABM can reliably predict the spatiotemporal evolution of breast cancer cells observed by microscopy data.

The vascularized multiscale model of tumor angiogenesis combines an ABM of tumor and endothelial cell dynamics with a continuum model that captures the spatiotemporal variations in the concentration of vascular endothelial growth factor. We first calibrate ordinary differential equation models to time-resolved protein concentration data to estimate the rates of secretion and consumption of vascular endothelial growth factor by endothelial and tumor cells, respectively. These parameters are then input into the multiscale model while the remaining model parameters are calibrated to time-resolved confocal microscopy images obtained within a 3D vascularized microfluidic platform. The model is able to globally recapitulate angiogenic vasculature density. Additionally, the model's ability to predict local vessel morphology is assessed and shows promising results.

Our multiscale ABMs demonstrate the ability to predict tumor growth and angiogenesis with experimental data, providing a platform for systematic testing of mathematical predictions of tumor dynamics.

Ernesto Lima (MS talk) - Development and calibration of a stochastic, multiscale agent-based model for predicting tumor and vasculature growth

Ernesto Lima
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USA

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Xiaochen Long (MS talk) - A Branching Process Model of Clonal Hematopoiesis

Xiaochen Long
Rice University
USA

Minisymposium presentation
(Stochastic population models: Theory and applications in Cancer Research)

We propose a hierarchical branching process model for clonal hematopoiesis. The model consists of a basic model that simulates clonal expansions and an observation process that represents the detection procedures. We consider two variants for the basic model, both based on Kendall's birth-death branching process: the first with Poisson migration, which models recurrent mutations from a fixed number of hematopoietic stem cells in spatially constrained niches, and the second with a single clone's expansion with a random starting time point. The latter variant assumes that a single mutation event gives rise to the observed mutant clones, which is appropriate when mutations only occur once. The observation process is a binomial sampling with the sequencing coverage as the total number of samples and the ratio of mutants from the basic model as the probability of detection. We also introduce multiple-timepoint observations and formulate the model as a Hidden Markov Model, which can be estimated using Sequential Monte Carlo methods. Particularly, we derive the pmf of the two-timepoint model for estimation and the transition probability within the hidden layer.

Our basic model, particularly Kendall's birth-death branching process with Poisson migration, produces comparable results to Watson et al. (2020), which can be seen as an approximation of our model under a low mutation rate. Our model's predictions are consistent with the sequencing data from nearly 50,000 healthy individuals in various studies. Furthermore, by incorporating multiple-timepoint settings, our model enables the estimation and prediction of samples collected from a single individual at different times, as well as the depiction of the entire clonal expansion history of the mutant clones from their emergence to dominance.

Loïc Louison (C talk) - A Population Harvesting Model with Time and size Competition Dependence Function

Loïc Louison
Université de Guyane
France

Contributed presentation

In this work, we are interested in the problem of forest management. We consider a nonlinear model describing the forest harvesting of a size-structured tree population with intra-specific competition, where the population competes with trees of larger size. Our objectives are to maximize the revenues from timber production while maintaining the regeneration of the forest and meeting the demand for wood from the current and future populations. A fixed-point argument is used to prove the existence and uniqueness of a solution to the nonlinear problem. Then, the optimal control problem is studied, where the existence of an optimal control is proved and its characterization is given by an optimality necessary condition.

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[2] N. Kato, Optimal harvesting for nonlinear size-structured population dynamics. J. Math. Anal. Appl., 342(2), 1388-1398 (2008).

Nadia Loy (MS talk) - A non-local kinetic model for cell migration : a study of the interplay between contact guidance and steric hindrance

Nadia Loy
Politecnico di Torino
Italy

Minisymposium presentation
(Modelling the Cancer Microenvironment)

In this talk, I will illustrate a class of non-local kinetic models for cell migration in response to the external environment. In particular, we shall consider cell migration on the extracellular matrix (ECM) and two phenomena named contact guidance and steric hindrance depending on a single external cue (the ECM) that affects in a twofold way the polarization and speed of motion of the cells. We start from a microscopic description of the stochastic processes underlying the cell re-orientation mechanism related to the change of cell speed and direction. Then, we formally derive the corresponding kinetic model that implements exactly the prescribed microscopic dynamics and, from it, it is possible to deduce the macroscopic limit in the appropriate regime. Moreover, we test our model in several scenarios. In particular, we numerically investigate the minimal microscopic mechanisms that are necessary to reproduce cell dynamics by comparing the outcomes of our model with some experimental results related to breast cancer cell migration. This allows us to validate the proposed modeling approach and, also, to highlight its capability of predicting the qualitative cell behaviors in diverse heterogeneous microenvironments. This is a joint work with M. Conte (PoliTo) .

Chinwendu Emilian Madubueze (C talk) - Modelling transmission dynamics of Lassa fever transmission with two environmental pathway transmissions

Chinwendu Emilian Madubueze
York University, Toronto, Ontario
Canada

Contributed presentation

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 (PRCC) technique based on the Latin hypercube sampling (LHS).

Connell McCluskey (MS talk) - Stability Analysis for Integral Equation Disease Models

Connell McCluskey
Wilfrid Laurier University
Canada

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

In the last 20 years, there has been great progress in global stability calculations for many compartmental disease models that are written in terms of ordinary differential equations (ODE) or delay differential equations (DDE). For a model with many compartments, the calculation becomes tricky, because there are many terms that have to cancel out or be bounded by other terms. Nevertheless, numerical evidence often suggests that the given system is stable.

Many of these ODEs and DDEs can be reformulated as an integral equation. For a complicated system, the integral equation representation would seem to omit a lot of important structure and detail. However, it appears to be precisely this detail that makes Lyapunov's method fail when applied directly to the original equations. Conversion to a comparatively simple integral equation can allow the stability calculation to reach a successful conclusion.

Some early progress on these ideas will be presented.

Jemal Mohammed-Awel (MS talk) - Mathematics model for assessing the impacts of pyrethroid resistance and temperature on population abundance of malaria mosquitoes

Jemal Mohammed-Awel
Morgan State University
USA

Minisymposium presentation
(Vector-Borne Disease Dynamics)

In this study, we developed a novel genetic population deterministic model of nonlinear ordinary differential equations for the temporal dynamics of the immature and adult anopheles mosquito population with sex structure. The deployment of larvicides, pupacides, and adulticides are incorporated into the model. Furthermore, the fitness costs associated with resistance are accounted for, including heterogeneities in fecundity, development rates, and natural mortality rates. The model is used to investigate the spread and management of insecticide resistance in mosquitoes. A threshold for the stability of the insecticide-sensitive-only and insecticide-resistant?only boundary equilibria is derived. Moreover, a conjecture has been established for the stability of the co-existence equilibrium where mosquitoes of all genotypes exist. Furthermore, we show that stratifying the mosquito population by genotype induces a bistability phenomenon. The impact of varying temperatures and insecticide coverage on the mosquito population by genotype in the context of the moderate and high fitness cost scenarios have been explored numerically.

Nicola Mulberry (MS talk) - A nested model for pneumococcal population dynamics

Nicola Mulberry
Simon Fraser University
Canada

Minisymposium presentation
(Bridging the scale from within-host to epidemic models)

Streptococcus pneumoniae is a pathogen of major public health concern globally. Pneumococcal strains exhibit diversity in their capsular serotype, metabolic profiles, and properties of antibiotic resistance (among other traits). Pneumococcal conjugate vaccines have been successful at targeting a subset of the circulating serotypes. Following such perturbation, pneumococcal populations have been shown to undergo significant shifts, indicative of competition both between and within serotypes. Using a nested model with explicit within-host dynamics, we show how competition between these types, along with heterogeneity in duration of carriage, may help explain patterns of vaccine-induced population dynamics.

Toshiyuki Namba (C talk) - Unexpected coexistence and extinction in an intraguild predation system

Toshiyuki Namba
Osaka Metropolitan University
Japan

Contributed presentation

Intraguild predation (IGP) is predation on consumers (IGprey) by predators (IGpredator) that exploit common resources with the consumers.Since the consumer is preyed upon by the predator, a necessary condition for the coexistence of the consumer and predator is supposed that the consumer is superior in resource competition to the predator. Classical mathematical models have predicted that the consumer and predator exclude the others in environments with low and high productivity, respectively, and that they can coexist only in environments with intermediate productivity. However, empirical results show that consumers persist in highly productive environments. Thus, the prevalence of intraguild predation in fertile environments has long been puzzling to the ecologist.

At the CMPD5, We showed that the quality of the resource and consumer as diets to the predator is the essential parameter to determine the dynamics of the IGP system and verified that the consumer never becomes extinct when it is not beneficial to the predator. Furthermore, not the consumer but the predator may become extinct when the consumer is not profitable for the predator. In this presentation, we challenge the supposed necessary condition for coexistence, that consumers must be superior in resource competition. We will show that large amplitude oscillations in the resource-predator system allow the consumer to increase and coexist with predators even if the former is inferior in resource competition Furthermore, if the resource-consumer system is oscillatory, the predator is forced to become extinct when environmental productivity is high. Therefore, the fates of the consumer and predator in the oscillatory systems are very different from those in the stationary systems. To fully understand the intraguild predation system, it is necessary to examine nonlinear dynamics in detail.

Jay Newby (P talk) - Dynamic self organization and microscale fluid properties of nucleoplasm

Jay Newby
University of Alberta
Canada

Plenary presentation

The principal function of the nucleus is to facilitate storage, retrieval, and maintenance of the genetic information. A unique feature of nucleoplasm—the fluid of the nucleus—is that it contains chromatin (DNA) and RNA. In contrast to other important biological polymer hydrogels, such as mucus and extracellular matrix, the nucleic acid polymers have a sequence that encodes both genetic information and strongly influences spatial organization. How does crowding in a sequence specific hydrogel influence spatial organization of the dynamic molecular components responsible for nuclear function? We are becoming increasingly aware of the role of liquid-liquid phase separation (LLPS) in cellular processes in the nucleus and the cytoplasm. Complex molecular interactions over a wide range of timescales can cause large biopolymers (RNA, protein, etc) to phase separate from the surrounding nucleoplasm or cytoplasm into distinct biocondensates (spherical droplets in the simplest cases). I will discuss recent work modelling the role of nuclear biocondensates in neurodegenerative disease and several ongoing projects related to modelling and microscopy image analysis.

Hiroshi Nishiura (MS talk) - Night-time population consistently explains the transmission dynamics of coronavirus disease 2019 in three megacities in Japan

Hiroshi Nishiura
Kyoto University
Japan

Minisymposium presentation
(Real time epidemiology in various geographic scales)

Background: Mobility data are crucial for understanding the dynamics of coronavirus disease 2019 (COVID-19), but the consistency of the usefulness of these data over time has been questioned. The present study aimed to reveal the relationship between the transmissibility of COVID-19 in Tokyo, Osaka, and Aichi prefectures and the daily night-time population in metropolitan areas belonging to each prefecture.

Methods: In Japan, the de facto population estimated from GPS-based location data from mobile phone users is regularly monitored by Ministry of Health, Labour and Welfare and other health departments. Combined with this data, we conducted Ta time series linear regression analysis was conducted to explore the relationship between daily reported case counts of COVID-19 in Tokyo, Osaka, and Aichi, and night-time de facto population estimated from mobile phone location data, from February 2020 to May 2022. As an approximation of the effective reproduction number, the weekly ratio of cases was used. Models using night-time population with lags ranging from 7 to 14 days were tested. In time-varying regression analysis, the night-time population level and the daily change in night-time population level were included as explanatory variables. In the fixed-effect regression analysis, the inclusion of either the night-time population level or daily change, or both, as explanatory variables was tested, and autocorrelation was adjusted by introducing first-order autoregressive error of residuals. In both regression analyses, the lag of night-time population used in best fit models was determined using the information criterion.

Results: In the time-varying regression analysis, night-time population level tended to show positive to neutral effects on COVID-19 transmission, whereas the daily change of night-time population showed neutral to negative effects. The fixed-effect regression analysis revealed that for Tokyo and Osaka, regression models with 8-day-lagged night-time population level and daily change were the best fit, whereas in Aichi, the model using only the 9-day-lagged night-time population level was the best fit using the widely applicable information criterion. For all regions, the best-fit model suggested a positive relationship between night-time population and transmissibility, which was maintained over time.

Conclusions: Our results revealed that regardless of the period of interest, a positive relationship between night-time population levels and COVID-19 dynamics was observed. The introduction of vaccinations and major outbreaks of Omicron BA. 2 subvariants in Japan did not dramatically change the relationship between night-time population and COVID-19 dynamics in three megacities in Japan. Monitoring the night-time population continues to be crucial for understanding and forecasting the short-term future of COVID-19 incidence.

Ryo Oizumi (C talk) - Analytical Representation of Eigensystem in Multiregional Leslie Matrix Model: Application to Sensitivity Analysis of Population Declining in Japan

Ryo Oizumi
Senior Researcher, Department of Population Structure Research
National Institute of Population and Social Security Research
Japan

Contributed presentation

The multiregional Leslie matrix is a transition matrix model in which matrices, including interregional migration, represent the fertility and survival entries of the Leslie matrix. By integrating the age structure and interregional migration, this model allows us to evaluate the impact of interregional migration on the population growth rate. We have found a theorem that expresses the eigensystem of the multiregional Leslie matrix using eigenvalues and matrix elements. Using this theorem, we can estimate the contribution of each region to the descendants and the percentage of ancestors in each region in a steady state. For example, in Japan, which has been in a phase of population decline since 2010, there is not only a declining birthrate and an aging population but also a problem of uneven population movement due to the concentration of the population in Tokyo. A sensitivity analysis based on our analysis results and the national census can clarify the mathematical structure of population decline. In this study, we apply our theory to Japanese governmental statistics from 2010 to 2020 to numerically evaluate the impact of age-specific and regional migration and fertility rates on population decline.

Lorenzo Pellis (MS talk) - Multi-scale time-since-infection models in evolutionary epidemiology

Lorenzo Pellis
The University of Manchester
United Kingdom

Minisymposium presentation
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The study of evolutionary epidemiology is vital to understand the complexity of pathogens' dynamics and their impact on public health, but is inherently challenging because pathogen evolution is driven by forces acting at multiple scales: for example, HIV needs to escape the immune system within a host, but also needs to maintain the ability to be transmitted efficiently between hosts. I will argue that time-since-infection models are much more flexible than ODEs if we want to allow for realistic enough aspects of both within- and between-host scales, but that capturing the feedback loops between such scales is a formidable challenge.

Using HIV as an example, I will discuss current models and their limitations, with particular attention to the implications of the fundamental structural assumptions on models' behaviour. Furthermore, I will discuss the main technical challenges I see in developing a general theory for time-since-infection models that allow for superinfection (e.g. multi-strain systems with partial cross-immunity), starting from the problem of characterising the system's steady states.

Tin Phan (MS talk) - Integrating wastewater surveillance data with epidemic models: challenges and opportunities

Tin Phan
Los Alamos National Laboratory
USA

Minisymposium presentation
(Multiscale models of infectious diseases)

Wastewater surveillance has proved to be a valuable tool to track the COVID-19 pandemic. However, most studies using wastewater surveillance data revolve around establishing correlations and lead time relative to reported case data. Yet, wastewater surveillance data is not independent of transmission dynamics and its integration with dynamic within-host and between-host models is necessary to better understand, monitor, and predict viral disease outbreaks. Dynamic models overcome emblematic difficulties of using wastewater surveillance data such as establishing the temporal viral shedding profile. Complementarily, wastewater surveillance data bypasses the issues of time lag and underreporting in clinical case report data, thus enhancing the utility and applicability of dynamic models. The integration of wastewater surveillance data with dynamic models can enhance real-time tracking and prevalence estimation, forecast viral transmission and intervention effectiveness, and most importantly, provide a mechanistic understanding of infectious disease dynamics and the driving factors. Dynamic modeling of wastewater surveillance data will advance the development of a predictive and responsive monitoring system to improve pandemic preparedness and population health.

Tin Phan (MS talk) - Modeling the emergence of viral resistance in SARS-CoV-2 patients treated with an anti-spike monoclonal antibody

Tin Phan
Los Alamos National Laboratory
USA

Minisymposium presentation
(Mathematical and computational approaches to modelling immunology)

The COVID-19 pandemic has led to over 670 million cases and 6.8 million deaths worldwide. To mitigate the loss of lives, emergency use authorization was given to several monoclonal antibody therapies for the treatment of mild-to-moderate SARS-CoV-2 patients with a high risk of progressing to severe disease. Monoclonal antibodies used to treat SARS-CoV-2 target the spike protein of the virus and block its ability to enter and infect target cells. Monoclonal antibody therapy can thus accelerate the decline in viral load, which results in a lower hospitalization rate among high-risk patients. However, viral resistance has been observed, in some cases leading to a transient viral rebound that can be as large as 3-4 logs. Indeed, resistance has compromised the use of all previously authorized monoclonal antibodies. Although resistance can be expected, the large rebounds observed are much more difficult to explain. We hypothesize replenishment of target cells is necessary to generate the high transient viral rebound. Thus, we formulated two models with different mechanisms for target cell replenishment and fit them to data from SARS-CoV-2 infected individuals treated with a monoclonal antibody. We showed that both models can explain the emergence of resistant virus associated with high transient viral rebounds. We found that variations in the target cell supply rate and adaptive immunity parameters have a strong impact on the magnitude or observability of the viral rebound associated with the emergence of resistant virus, which may explain why only some individuals develop observable transient resistant viral rebound. Our study highlights the conditions that can lead to resistance and subsequent viral rebound in monoclonal antibody treatments of acute infection and have broader application in explaining the rebound of virus.

Tanya Philippsen (MS talk) - A retrospective modelling analysis of the effect of control measures on the transmission of SARS-CoV-2 in Canada

Tanya Philippsen
University of Victoria
Canada

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

We consider the COVID-19 pandemic between March 2020 to February 2021 in selected Canadian regions. This period was dominated by the wild-type strain of SARS-CoV-2 and occurred prior to widespread vaccination roll-out. We incorporate age-specific control measures in a Susceptible-Exposed-Infectious-Recovered (SEIR) deterministic model with two age groups: youth aged 0-19 years, and adults aged 20+ years. We fit this model to COVID-19 case data over sequential time frames that capture the various changes in public health control measures during this period in each region. The age-specific control parameters of the fitted model are then adjusted to simulate alternative policy scenarios and assess their relative potential effectiveness in reducing the Fall/Winter epidemic peaks. In this period, we find that a moderate increase in adult-specific control measures has a larger effect on reducing case counts when compared with a drastic strengthening of control measures in youth.

Andrea Pugliese (MS talk) - Combining data from surveillance on mosquitoes and corvids to understand the factors affecting the dynamics of West Nile Virus in Emilia-Romagna, Italy

Andrea Pugliese
Department of Mathematics
University of Trento
Italy

Minisymposium presentation
(Vector-Borne Disease Dynamics)

West Nile Virus (WNV) is now endemic in Northern Italy (as well as in many European countries), with a yearly number of recorded human cases oscillating between few tens up to around 600 in 2018 and 2022. Humans actually are dead-end hosts, while the infection is transmitted between Culex mosquitoes and several species of birds. The region Emilia-Romagna (one of the most affected areas) has in place since 2013 an extended surveillance program of both mosquitoes and corvids. We have analysed these data through an SEI-SEIR model where several parameters depend on temperature, as shown in laboratory experiments, while over-wintering occurs through infected diapausing mosquitoes. We found that an essential factor determining human risk is spring temperature, as confirmed also by a statistical analysis of European data. Another important factor for epidemic dynamics in a given year is pre-existing immunity in birds; as no serological data exist, we reconstructed the trend of seroprevalence over the years, which however has no clear relation with epidemic intensities. Joint work with Alex De Nardi, Giovanni Marini, Francesco Menegale, Marco Tamba

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Erica Rutter (MS talk) - Modeling and Estimating Intratumoral Heterogeneity in Cancer

Erica Rutter
University of California, Merced
USA

Minisymposium presentation
(Modelling the Cancer Microenvironment)

Heterogeneity in biological populations, from cancer to ecological systems, is ubiquitous. Despite this knowledge, current mathematical models in population biology often do not account for inter- or intra-individual heterogeneity. In systems such as cancer, this means assuming cellular homogeneity and deterministic phenotypes, despite the fact that heterogeneity is thought to play a crucial role in therapy resistance. In this talk, I will discuss several approaches I have developed towards incorporating and estimating cellular heterogeneity in partial differential equation (PDE) models of GBM growth. In particular, I will use random differential equations for modeling heterogeneity and the Prohorov metric framework for estimating parameter distributions from aggregate data. Although the phenotypic heterogeneity I examine in this talk is specifically directed towards growth and diffusion rates of cells, the framework is broadly applicable to any model parameters, including those relevant to the tumor microenvironment.

Erica Rutter (MS talk) - Global Sensitivity Analysis of a Structured Model of COVID-19 Transmission on a College Campus

Erica Rutter
Department of Mathematics and Computer Science
University of California, Merced
USA

Minisymposium presentation
(Multiscale models of infectious diseases)

When the COVID-19 pandemic hit, college campuses nationwide switched to online and hybrid courses. At the same time, public health measures were implemented such as social distancing and encouraging mask use in public. We created a data-driven model of COVID-19 spread across a campus with subpopulations representing on-campus undergraduate students, off-campus undergraduate students, graduate students, and faculty/staff. We use this model to investigate the effectiveness of various non-pharmaceutical interventions on controlling COVID-19 spread on campus. Global sensitivity analysis techniques are applied to determine and rank the impact of masks, online courses, and vaccination on total campus spread.

Paul Salceanu (MS talk) - Robust uniform persistence for structured models of delay differential equations

Paul Salceanu
University of Louisiana at Lafayette
USA

Minisymposium presentation
(Ecological and Epidemiological Models with Dispersal)

We consider a general class of delay differential equations systems, typically used to model the dynamics of structured biological populations, and establish necessary conditions for the part of the attractor contained in the boundary of the state space to repel the complementary dynamics contained in the interior of the state space. The conditions are formulated in terms of Lyapunov exponents and invariant probability measures and we use them to prove a robust uniform persistence result.

Leili Shahriyari (MS talk) - Digital twins of cancer patients: a step toward personalized treatments

Leili Shahriyari
Department of Mathematics & Statistics
University of Massachusetts Amherst
USA

Minisymposium presentation
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The creation of digital twins (DTs) of cancer patients can assist us in predicting the evolution of an individual's cancer through modeling each tumor's characteristics and response to treatment. We therefore take advantage of new advances in computational approaches and combine mechanistic, machine learning, and stochastic modeling approaches to create a DT platform, which utilizes biological, biomedical, and EHR data sets. For each patient, the DT receives their information as input and predicts the evolution of their cancer.

We propose to develop a mechanistic model based on the quantitative systems pharmacology (QSP) modeling, which is one of the main computational approaches used to discover, test, and predict dose-exposure response. One of the main challenges of the QSP modeling is parameter estimation. Traditionally, these models assume all patients have similar diseases, and the values of parameters of the QSP model are identical for all patients. Therefore, parameters are commonly calibrated using the data often assembled from disparate sources.

To develop a personalized DT, we use patient-specific data for parameter estimations, sensitivity analysis, and uncertainty quantification. For each patient, we estimate the values of parameters of their QSP model using their data. We perform a multi-dimensional sensitivity analysis and uncertainty quantification on the mechanistic model to find a set of critical interactions and predict the intervals of confidence. Since this QSP model includes the data-driven mechanistic model of cells and molecules' interaction networks, one of the ultimate results of this DT is the prediction of evolution of cancer in response to a given targeted therapy.

Nourridine Siewe (MS talk) - Breast cancer exosomal microRNAs facilitate pre-metastatic niche formation in the bone: A mathematical model

Nourridine Siewe
School of Mathematical Sciences
Rochester Institute of Technology
USA

Minisymposium presentation
(- Within-host and between-host mathematical models of biological dynamics)

Pre-metastatic niche is a location where cancer cells, separating from a primary tumor, find "fertile soil" for growth and proliferation, ensuring successful metastasis. Exosomal miRNAs of breast cancer are known to enter the bone and degrade it, which facilitates cancer cells invasion into the bone interior and ensures its successful colonization. In this paper we use a mathematical model to first describe, in health, the continuous remodeling of the bone by bone forming osteoblasts, bone resorbing osteoclasts, and the RANKL-OPG-RANK signaling system, which keeps the balance between bone formation and bone resorption. We next demonstrate how breast cancer exosomal miRNAs disrupt this balance, either by increasing or by decreasing the ratio of osteoclasts/osteoblasts, which results in abnormal high bone resorption or abnormal high bone forming,

respectively, and in bone weakening in both cases. Finally we consider the case of abnormally high resorption and evaluate the effect of drugs, which may increase bone density to normal level, thus protecting the bone from invasion by cancer cells.

Nourridine Siewe (MS talk) - TGF- inhibition can overcome cancer primary resistance to PD-1 blockade: a mathematical model

Nourridine Siewe
School of Mathematical Sciences
Rochester Institute of Technology
USA

Minisymposium presentation
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Background and methods. Immune checkpoint inhibitors have demonstrated, over the recent years, impressive clinical response in cancer patients, but some patients do not respond at all to checkpoint blockade, exhibiting primary resistance. Primary resistance to PD-1 blockade is reported to occur under conditions of immunosuppressive tumor environment, a condition caused by myeloid derived suppressor cells (MDSCs), and by T cells exclusion, due to increased level of T regulatory cells (Tregs). Since TGF- activates Tregs, TGF- inhibitor may overcome primary resistance to anti-PD1. Indeed, recent mice experiments show that combining anti-PD-1 with anti-TGF- yields significant therapeutic improvements compared to anti-TGF- alone.

Results. The present paper introduces two cancer-specific parameters and, correspondingly, develops a mathematical model which explains how primary resistance to PD-1 blockade occurs, in terms of the two cancer-specific parameters, and how, in combination with anti-TGF- , anti-PD-1 provides significant benefits. The model is represented by a system of partial differential equations and the simulations are in agreement with the recent mice experiments. In some cancer patients, treatment with anti-PD-1 results in rapid progression of the disease, known as hyperprogression disease (HPD). The mathematical model can also explain how this situation arises, and it predicts that HPD may be reversed by combining anti-TGF- to anti-PD-1. Conclusion. The model is used to demonstrate how the two cancer-specific parameters may serve as biomarkers in predicting the efficacy of combination therapy with PD-1 and TGF- inhibitors.

Anuraj Singh (C talk) - Modelling the impact of multiple transmission pathways on disease severity of Coronavirus

Anuraj Singh
ABV-Indian Institute of Information Technology and Management Gwalior
India

Contributed presentation

Coronaviruses are a pervasive group of pathogens for which transmission through the contaminated surface is a concern. The transmission of the virus occurs primarily through person-person contact, with contaminated surfaces providing a secondary transmission route. In this work, a modified SEIR epidemic model incorporating shedding effect is proposed to analyze transmission dynamics of the COVID-19 virus among different individuals' classes. The basic reproduction number (R_0) is calculated using the next-generation matrix method, taking

shedding as a new infection. The bifurcation theory and central manifold theorem are employed to exhibit the conditions for backward bifurcation at $R_0 = 1$. The numerical simulation is demonstrated to illustrate the results, showing that an increase in person-contaminated surface-person transmission parameter leads the system to endemicity.

Anuraj Singh (C talk) - Resonance and bifurcation in a discrete-time predator–prey system

Anuraj Singh
ABV-Indian Institute of Information Technology and Management
India

Contributed presentation

This work studies bifurcation analysis and resonances in a discrete-time model analytically and numerically. The local stability conditions of all the fixed points in the system are determined. Here, codim-1 and codim-2 bifurcation, including multiple and generic bifurcations in the discrete model, are explored. The model undergoes fold bifurcation, flip bifurcation, Neimark-Sacker bifurcation and resonances bi- furcation of codimension two at different fixed points. Using critical normal form theorem and bifurcation theory, this study obtains the normal form coefficients to confirm the nondegeneracy of codim-1 and codim-2 bifurcations in the model. The numerical simulation gives a wide range of periodic cycles and bifurcation in the system. In the system, NSB signifies that both species can fluctuate near critical parameter values and stable fluctuations seem. The resonance bifurcation in the discrete-time map indicates that both species coincide till order 4 in stable periodic cycles near some critical parametric values.

Stacey Smith? (MS talk) - Coupling the within-host process and between-host transmission of COVID-19 suggests vaccination and school closures are critical

Stacey Smith?
The University of Ottawa
Canada

Minisymposium presentation
(Multiscale models of infectious diseases)

We develop a data-driven COVID-19 model linking the within-host viral dynamics to the between-host transmission dynamics on a multi-layer contact network to investigate the potential factors driving transmission dynamics and to inform how school closures and antiviral treatment influence the epidemic. Using multi-source data, we initially determine the viral dynamics and estimate the relationship between viral load and infectiousness. Then, we embed the viral dynamics model into a four-layer contact network and formulate an agent-based model to simulate between-host transmission. The results illustrate that the heterogeneity of immune response between children and adults and between vaccinated and unvaccinated infections can reproduce different transmission patterns. We find that school closures play a significant effect on mitigating the pandemic as more adults get vaccinated and the virus mutates. If enough infected individuals are diagnosed by testing before symptom onset and then treated quickly, the transmssion can also be effectively curbed. Our multiscale model reveals the critical role played by younger individuals and antiviral treatment with testing in controlling the epidemic.

Tracy Stepien (MS talk) - Deciphering Glioma Microenvironment Entry Mechanisms of Myeloid-Derived Suppressor Cells

Tracy Stepien
University of Florida
USA

Minisymposium presentation
(Modelling the Cancer Microenvironment)

While immunotherapy has shown to be effective in treating some cancer types, the highly immunosuppressive tumor microenvironment of glioblastoma (GBM) provides unique challenges. As an example, immune checkpoint inhibitors, such as for the programmed-death-1 (PD-L1/PD-1) pathway, have had promising pre-clinical outcomes but failed to show efficacy in phase III clinical trials. One potential explanation is the infiltration of the tumor microenvironment by immune-suppressive cells such as myeloid-derived suppressor cells (MDSCs). Encouragingly, in experimental studies where MDSCs are targeted by drugs in combination with PD-1 blockade in mice, median survival increased. We develop an ODE model of the interactions between cancer cells, T cells, and MDSCs specific to the glioma microenvironment. We then optimize administration of combination immunotherapy with the overall objective being minimization of the tumor burden and MDSC entry as well as maximization of survival time.

Yasuhiro Takeuchi (C talk) - Stability analysis of a single-species logistic model with time delay and constant inflow

Yasuhiro Takeuchi
Aoyama Gakuin University
Japan

Contributed presentation

We consider a single-species logistic model with Gamma type continuous time delay and constant inflow. By the linear chain trick, the system of integro-differential equations is transformed into the system of the expanded ordinary differential equations. The results show that the average time delay (order of k 2) can destabilize the positive equilibrium through Hopf bifurcation. Furthermore, the precise conditions of Hopf bifurcation of the high dimensional system are obtained by the method of polar form and graphs.

Ryan Thiessen (MS talk) - Travelling waves of a new glioma invasion model

Ryan Thiessen
University of Alberta
Canada

Minisymposium presentation
(Modelling the Cancer Microenvironment)

I will explore travelling waves for a new glioblastoma multiforme model in this talk. In their Nature paper, Osswald and collaborators recently presented a detailed study of in-vivo glioma invasion patterns in the healthy brain tissue of living mice. This paper presents evidence that specialized cancer cells build a network much like a healthy brain neuronal network, which can transmit signals such as calcium waves, forming a glioma-wide communication system. Working jointly with Thomas Hillen, Kevin Painter, and Nadia Loy, our goal is to incorporate the new network formation phenomenon into previous Giloma blastoma models. The model is based on the kinetic model framework, where we can quickly introduce new reaction dynamics for the network formation. We can arrive at a coupled reaction-diffusion equation by making some time scale arguments. From this equation, we will show the existence of Traveling waves with a minimal spreading speed. In addition, we can reduce the system to the classical Fisher-KPP, allowing us to compare the effect of the approximations on the wave speed.

Necibe Tuncer (MS talk) - Immuno-epidemiological co-a ection model of HIV infection and opioid addiction

Necibe Tuncer
Florida Atlantic University
USA

Minisymposium presentation
(Within-host and between-host mathematical models of biological dynamics)

In this study, we present a multi-scale co-affection model of HIV infection and opioid addiction. The population scale epidemiological model is linked to the within-host model which describes the HIV and opioid dynamics in a co-affected individual. CD4 cells and viral load data obtained from morphine addicted SIV-infected monkeys are used to validate the within-host model. AIDS diagnoses, HIV death and opioid mortality data are used to fit the between-host model. When the rates of viral clearance and morphine uptake are fixed, the within-host model is structurally identifiable. If in addition the morphine saturation and clearance rates are also fixed the model becomes practical identifiable. Analytical results of the multi-scale model suggest that in addition to the disease-addiction-free equilibrium, there is a unique HIV-only and opioid-only equilibrium. Each of the boundary equilibria is stable if the invasion number of the other epidemic is below one. Elasticity analysis suggests that the most sensitive number is the invasion number of opioid epidemic with respect to the parameter of enhancement of HIV infection of opioid-affected individual. We conclude that the most effective control strategy is to prevent opioid addicted individuals from getting HIV, and to treat the opioid addiction directly and independently from HIV.

Necibe Tuncer (MS talk) - Determining Reliable Parameter Estimates for Within-host and Within-vector models of Zika Virus

Necibe Tuncer
Florida Atlantic University
USA

Minisymposium presentation
(Vector-Borne Disease Dynamics)

In this presentation, I will introduce three within-host and one within-vector models of Zika virus. The within-host models are the target cell limited model, the target cell limited model with natural killer cells class, and a within-host-within-fetus model of a pregnant individual. The within-vector model includes the Zika virus dynamics in the midgut and the salivary glands. The within-host models are not structurally identifiable with respect to data on viral load and natural killer cell counts. After rescaling, the scaled within-host models are locally structurally identifiable. The within-vector model is structurally identifiable with respect to viremia data in the midgut and salivary glands. Using Monte Carlo Simulations we find that target cell limited model is practically identifiable from data on viremia; the target cell limited model with natural killer cell class is practically identifiable, except for the rescaled half saturation constant. The within-host-within-fetus model has all fetus related parameters not practically identifiable without data on the fetus, as well as the rescaled half saturation constant is also not practically identifiable. The remaining parameters are practically identifiable. Finally we find that none of the parameters of the within-vector model is practically identifiable.

Sonja Türpitz (C talk) - Considering Subpopulations in Modelling Facultative Mutualism Reveals a New Approach to Model Interspecific Interactions

Sonja Türpitz
Friedrich Schiller University Jena
Germany

Contributed presentation

Mathematical modelling of mutualism usually uses generalized Lotka-Volterra equations in which the mutualistic benefit is represented by a positive bilinear interaction term. We propose a minimal ODE model for facultative mutualism between two species that is based on the differentiation of two subpopulations per species.

In facultative mutualism between two species, each species benefits from interacting with the other species but does not rely on this interaction to exist and grow. At the species level there is a subdivision into the mutualistic subpopulation that actively interacts with the other species, and the non-mutualistic subpopulation that does not interact with the other species. The non-mutualistic subpopulation behaves the same way the total species' population would in absence of the other species, but the mutualistic subpopulation additionally receives a benefit due to the mutualistic interaction with the other species' mutualistic subpopulation. Therefore, in our model the interaction term is not dependent on the density of the two species, as it is the case in the generalized Lotka-Volterra equations, but only on the density of the two mutualistic subpopulations. We also took the intraspecific switch of individuals between the two subpopulations into account.

Every mutualistic benefit automatically includes a cost that must be spent in order to provide the benefit for the other species. We investigated to what extent the cost influences the proportion of mutualistic subpopulation in the total species population. If the cost exceeds the benefit for one species, the net-effect of the interaction becomes negative for that species. In that case, the situation no longer refers to mutualism, but to parasitism. We claim that due to this mechanism our model is able to represent several interspecific interactions.

Pauline van den Driessche (MS talk) - Disease-Induced Hydra Effect

Pauline van den Driessche
Department of Mathematics and Statistics
University of Victoria, BC
Canada

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

The seemingly counterintuitive hydra effect of an increase in population size caused by an increase in mortality has been observed and modeled in several ecological systems. Here theoretical and simulation results for an infectious disease-induced hydra effect are presented. This occurs when the total population size (infectious plus susceptible individuals) at an endemic equilibrium is greater than the population size at the disease-free equilibrium. This disease-induced hydra effect occurs in models with continuous or discrete time when the intra-specific competition is strong and disease infection sufficiently inhibits the reproduction of infected individuals.

Marie Betsy Varughese (MS talk) - Incorporating Health Seeking Behaviour in a Deterministic Model for Influenza

Marie Betsy Varughese
University of Alberta
Canada

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

BACKGROUND: Modelling efforts during the COVID-19 pandemic highlighted the significance of health-seeking behaviour on transmission dynamics within a population. Health seeking behaviour such as testing and access of healthcare services are important considerations that impact how cases are identified through surveillance systems. In mathematical modelling, cases reported to surveillance systems are often used for retrospective and prospective analysis. METHODS: An age-stratified SIR model that incorporates case detection for influenza is described. Influenza data and case detections rates for influenza seasons (2016-2019) were estimated from Alberta Health's administrative data. Incorporating constant and time dependent case detection rates in the model will be compared across retrospective (i.e. assess fitting using all data from each season) and prospective (i.e. performance of projections) analysis. RESULTS: Retrospective analysis showed comparable fitting results of influenza cases using both constant and time dependent case detection rates, however the final size differed. Influenza projections performed better using time dependent compared to constant case detection rates. CONCLUSION: It is important to consider implications of incorporating model assumptions that may appear to 'fit well to data'. Based on both retrospective and prospective analysis, using a time dependent case detection rate should be considered when modelling respiratory viruses.

Jorge Velasco-Hernandez (MS talk) - The Ross-Mcdonald model revisited: linking transmission and within-host dynamics

Jorge Velasco-Hernandez
Universidad Nacional Autónoma de México
Mexico

Minisymposium presentation
(Vector-Borne Disease Dynamics)

We present a model that explicitly links the epidemiological Ross-Macdonald model with a simple immunological model through a virus inoculation term that depends on the abundance of infected mosquitoes. We explore the relationship between the reproductive numbers at the population (between-host) and individual level (within-host), in particular the role a certain measure of infectivity (defined in terms of the number of target cells infected) and viral clearance rate play in the coupled dynamics. The conditions for a disease outbreak require, for the average individual in the population, to have an active (within-host) viral infection. This infection depends on the viral load and the proportion of infected cells which are quantities that change in time. Only when these two quantities are sufficiently large, the epidemic outbreak may occur.

Jorge Velasco-Hernandez (MS talk) - Modeling a traffic light warning system for acute respiratory infections

Jorge Velasco-Hernandez
Universidad nacional Autónoma de México
Mexico

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

Balanced enforcement and relaxation of measures guided through a traffic-light system that considers public risk perception and economic costs may improve the public health benefit of the policies while reducing their cost. We derive a model for the epidemiological traffic-light policies based on the best response for trigger measures driven by the risk perception of people, instant reproduction number, and the prevalence of a hypothetical acute respiratory infection. With numerical experiments, we evaluate and identify the role of appreciation from a hypothetical controller that could opt for protocols aligned with the cost due to the burden of the underlying disease and the economic cost of implementing measures.

Amy Veprauskas (MS talk) - The interplay between dispersal and Allee effects in discrete-time population models

Amy Veprauskas
University of Louisiana at Lafayette
USA

Minisymposium presentation
(Ecological and Epidemiological Models with Dispersal)

We develop discrete-time models that describe population dynamics with dispersal between different patch locations. We first present a simple two-patch model for an unstructured population where all individuals are assumed identical, and then extend it to a multi-patch stage-structured model where individuals are distinguished by different developmental stages in their lifecycle. We analyze the dynamics of the two models under a nonlinear fecundity term that exhibits an Allee effect. We show that these systems have rich dynamics including both monostable and bistable dynamics.

Amy Veprauskas (MS talk) - Pathogen dynamic in a tick-host system: A discrete-time modeling approach

Amy Veprauskas
University of Louisiana at Lafayette
USA

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

We study the dynamics of a pathogen within a tick-host system, focusing on metrics that describe pathogen invasion and establishment, namely the basic reproduction number, the disease prevalence, and the time to disease establishment. We model the tick-host-pathogen dynamics using a system of difference equations that are constructed according to the life cycle of a three-host hard-bodied tick population. This model incorporates the developmental stages for a tick, the dependence of the tick lifecycle and disease transmission on host availability, and three sources of pathogen transmission. We first establish the global dynamics of the disease-free system. We then apply the model to two pathogens, Borelliaburgdorferi and Anaplasma phagocytophila, using Ixodes ricinus as the tick species to study properties of the invasion and establishment of these diseases numerically.

Ren-Yi Wang (MS talk) - Analysis of A Countable-Type Branching Process Model for the Tug-of-War Cancer Cell Dynamics

Ren-Yi Wang
Rice University
USA

Minisymposium presentation
(Stochastic population models: Theory and applications in Cancer Research)

We consider a time-continuous Markov branching process of proliferating cells with a denumerable collection of types. Among-type transitions are inspired by the Tug-of-War process introduced in Mcfarland et al. (2014) as a mathematical model for competition of advantageous driver mutations and deleterious passenger mutations in cancer cells. We introduce a version of the model in which a driver mutation pushes the state of the cell L-units up, while a passenger mutation pulls it 1 unit down. The distribution of time to divisions depends on the type of cell, which is an integer. First, we analyze the probability of extinction of the process, using approach in Hautphenne (2013). Then, we consider the properties of the mean process, using theories in Seneta (2006). Finally, we consider the process in an infinitely long cell lineage of cells, using theory of difference equations in Bodine (2015), martingales, and random walk. The analysis leads to the result that under driver dominance, the process escapes to infinity, while under passenger dominance, it leads to a limit distribution. Our analysis reveals an asymmetric relationship between impacts of the two types of mutations. The process is driven to extinction with probability less than 1. Under passenger dominance regime (downward-trend) there exists with a positive probability a "reservoir" of cells with a wide range of types (fitnesses). In the context of cancer cell populations, this may mean that "indolent" cancer cell colonies may allow the biological process to rebound if conditions change, as in the "punctuated equilibria" theory of cancer evolution in Gao et al. (2016) and Davis et al. (2017).

Xuyuan Wang (MS talk) - Detecting and Resolving Nonidentifiability In Infectious Diseases Modeling

Xuyuan Wang
University of Alberta
Canada

Minisymposium presentation
(Recent Advances in Modelling Infectious Diseases)

Nonidentifiability is a common issue exists in various of infectious diseases modeling problems. In general, the parameter estimation process will become complicated when some of the model parameters are nonidentifiable. This phenomenon is caused by the non-uniqueness of the best-fit parameter values base on the current available data set. However, those equally good parameter values do not provide consistent prediction results, which significantly reduce the prediction capability of mathematical models. In this talk, we will present a efficient method to help detect the potential nonidentifiable parameters through Singular Value Decomposition and Variance Decomposition (SVD-VD) techniques under the assumption of normally distributed data noise. Then inspired by the classical ridge regression method, a L_2 regularized parameter estimator (RLSE) is proposed to resolve the nonidenfiability issue. It can be demonstrated that RLSE is locally unique, and hence can produce a much more reasonable prediction result. In the last, a numerical example will be provided to test the effectiveness of the SVD-VD method together with the regularized estimator(RLSE).

Kathleen Wilkie (MS talk) - Modelling the Evolution of the Immune Response to Cancer

Kathleen Wilkie
Toronto Metropolitan University
Canada

Minisymposium presentation
(Mathematical and computational approaches to modelling immunology)

The immune response to cancer causes stimulation and inhibition of the growing malignancy. A part of the tumour microenivronment, the immune response evolves over time as a function of disease progression. Naive immune cells recruited to the tumour microenvironment will sense the local cytokine signals and polarize into either tumour-promoting or tumour-inhibiting immune cell types. These cells then contribute to the signalling milieu evolving the immunological profile. This talk will discuss a mathematical model to capture the evolutionary dynamics of the immune response to cancer. We explore the role of noise and the evolution of the immune response polarization (from a primarily anti-tumour response when the tumour is new, to a primarily pro-tumour response when the tumour is old). We use stochastic DEs to allow us to explore variability in our model results.

Kathleen Wilkie (MS talk) - Modelling Radiation Cancer Treatment with Ordinary and Fractional Differential Equations

Kathleen Wilkie
Toronto Metropolitan University
Canada

Minisymposium presentation
(Modelling the Cancer Microenvironment)

Fractional calculus has recently been applied to mathematical modelling of tumour growth, but it's use introduces complexities that may not be warranted. Mathematical modelling with differential equations is a standard approach to study and predict treatment outcomes for population-level and patient-specific responses. Here we use patient data of radiation-treated tumours to discuss the benefits and limitations of introducing fractional derivatives into three standard models of tumour growth. The fractional derivative introduces a history-dependence into the growth function, which requires a continuous death-rate term for radiation treatment. This newly proposed radiation-induced death-rate term improves computational efficiency in both ordinary and fractional derivative models. This computational speed-up will benefit common simulation tasks such as model parameterization and the construction and running of virtual clinical trials.

Mondal Hasan ZAHID (C talk) - The biting rate of Aedes aegypti and its variability: A systematic review (1970 - 2022)

Mondal Hasan ZAHID
University of Florida
USA

Contributed presentation

Background

Transmission models have a long history in the study of mosquito-borne disease dynamics. The mosquito biting rate (MBR) is an important parameter in these models, however, estimating its value empirically is complex. Modeling studies obtain biting rate values from various types of studies, each of them having its strengths and limitations. Thus, understanding these study designs and the factors that contribute to MBR estimates and their variability is an important step towards standardizing these estimates. We do this for an important arbovirus vector Aedes aegypti.

Methodology/Principal Findings

We perform a systematic review using search terms such as 'biting rate' and 'biting frequency' combined with 'Aedes aegypti' ('Ae. aegypti' or 'A. aegypti'). We screened 3,201 articles from PubMed and ProQuest databases, of which 21 met our inclusion criteria. Two broader types of studies are identified: human landing catch (HLC) studies and multiple feeding studies. We analyze the biting data provided as well as the methodologies used in these studies to characterize the variability of these estimates across temporal, spatial, and environmental factors and to identify the strengths and limitations of existing methodologies. Based on these analyses, we present two approaches to estimate population mean per mosquito biting rate: one that combines studies estimating the number of bites taken per gonotrophic cycle and the gonotrophic cycle duration, and a second

that uses data from histological studies. Based on one histological study dataset, we estimate biting rates of Ae. aegypti (0.60 and 0.56 bite/mosquito-day in Thailand and Puerto Rico, respectively).

Conclusions/Significance

Our review reinforces the importance of engaging with vector biology when using mosquito biting data in transmission modeling studies. For Ae. aegypti, this includes understanding the variation of the gonotrophic cycle duration and the number of bites per gonotrophic cycle, as well as recognizing the potential for spatial and temporal variability. To address these variabilities, we advocate for site-specific data and the development of a standardized approach to estimate the biting rate.

Veronika Zarnitsyna (MS talk) - Competing Heterogeneities in Vaccine Effectiveness Estimation

Veronika Zarnitsyna
Department of Microbiology and Immunology
Emory University School of Medicine
USA

Minisymposium presentation
(Bridging the scale from within-host to epidemic models)

Understanding waning of vaccine-induced protection is important for both immunology and public health. The epidemiological data indicate that protection from the flu and COVID-19 vaccines could wane within a year. Our recent studies showed that the previously proposed extension of the Cox proportional hazards model by utilizing scaled Schoenfeld residuals used to estimate waning of vaccine effectiveness (VE) fails to accurately capture fast intraseasonal waning, especially when vaccination is spread over months. However, a relatively simple method based on including time-vaccine interaction in the model, with further proposed optimization, performs significantly better (Nikas et al., Clinical Infectious Diseases 2022). Population heterogeneities, both in underlying (pre-vaccination) susceptibility and vaccine response, add additional challenge in VE estimation, as they can cause measured VE to change over time even in the absence of pathogen evolution and any actual waning of immune responses. We use a multi-scale agent-based model parameterized using epidemiological and immunological data to investigate the effect of these heterogeneities. Our study suggests heterogeneity is more likely to 'bias' VE estimates downwards towards faster waning of immunity but a subtle bias in the opposite direction is also plausible.

Huaiping Zhu (MS talk) - Predictive modelling and forecasting of the mosquito abundance and risk of West Nile virus in Ontario Canada

Huaiping Zhu
York University
Canada

Minisymposium presentation
(Vector-Borne Disease Dynamics)

The transmission and spread of mosquito-borne disease such as West Nile virus (WNV) in north America are weather-sensitive. Weather conditions, such as daily average temperature and precipitation, not only affect the

abundance but also the biting behavior of the vector mosquitoes, thus determining the outbreak and spread of WNV. In this talk, I will present a hybrid model for weekly forecasting of the abundance and risk of infection of WNV, integrating a weather-driven statistical model and a compartmental model mimicking the transmission of WNV among mosquitoes, birds, and humans. The predictive models are evaluated using the data of human infection, mosquito surveillance and viral test from 2002 to 2020 in Peel Region, Ontario, Canada. With the weekly mosquito surveillance data and the weather forecast, our real time predictive modelling allows us to forecast the weekly vector abundance and risk of WNV infection which has important public health implications. I will conclude with a summary of preliminary dynamics of such hybrid models with weather conditions. This is a joint work with Pei Yuan and Nick Ogden in collaboration with Peel public Health.

Huaiping Zhu (MS talk) - A two-stage model with distributed delay for mosquito population dynamics

Huaiping Zhu
York University
Canada

Minisymposium presentation
(Delay-differential equations in applications)

Studies on the population dynamics of mosquito species are essential for understanding and control the transmission and spread of mosquito-borne diseases. In this talk, I will first introduce a general system of distributed delay differential equations that models the age structure of mosquitoes with lifespan being divided into two aquatic and adult stages. By defining the reproduction number through the model with a general form of delay kernel, we present some analytical results for the general model, including the stability of the boundary equilibrium and the existence of the unique interior equilibrium. The delay kernel serves as a weighting factor which measures the contribution of daily accumulated temperature. For two specific types of popularly used delay kernels, we show the bifurcation and dynamics and present some simulations performed for each system to illustrate how the temperature dependent maturation time impacts the abundance of eggs and adult mosquitoes. This is a joint work with Juan Li and Guihong Fan.
