WORKSHOP ON MATHEMATICAL BIOLOGY, AIMS GHANA

29–30 August 2024

Thursday 29 August

07:30 Breakfast

09:00 Opening remarks

09:15 Nicholas Opoku (AIMS Ghana)
Tool Development for Detecting Copy Number Variations

09:45 Rosa Kreider (University of Bonn)
Modeling interferon-driven immune cell priming in viral infections

10:15 Anas Musah (Kwame Nkrumah University of Science and Technology)
Dynamics of disease models with self-diffusion: a study of cholera

10:45 Refreshments

11:15 Millicent Afrifa Opoku (AIMS Ghana)
Modelling Early Human Embryo Development Using the Cellular Potts Model

11:45 Madhesh Suresh (University of Bonn)
Computational insights into COVID-19 and beyond: Deciphering kinetic signatures of hyperinflammation in innate immunity

12:15 Michael Asamani Pobbi (University of Cape Coast).
Analysis of Stochastic COVID-19 and Hepatitis B Coinfection Model with Brownian and Lévy noise

13:00 Lunch

14:00 Specioza Nambooze (AIMS Ghana).
Modelling malaria drug resistance

14:30 Lisa Li (University of Bonn)
A homogenization approach to model spatial cytokine distributions

15:00 Ignatus Nunana Dorvi (West African Centre for the Cell Biology of Infectious Pathogens).

Markov Chain Monte Carlo Gibbs Sampling approach for Estimating Multiplicity of Infection in Plasmodium falciparum clinical Isolates

15:30 Refreshments

16:00 Fameno Rakotoniaina (AIMS Ghana)
Biophysical modelling of Malaria parasite invasion in red blood cell

16:30 Lisa Steinheuer (University of Bonn)
Unraveling immune cell dynamics through data analysis

17:00 Abdulzeid Yen Anafo (University of Mines and Technology).
Modelling the Impact of Expanding Seasonal Malaria Chemoprevention to older Age Group and five cycles on malaria incidence in Ghana

18:00 Dinner

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09:00 Stephen Moore (University of Cape Coast).
Trends in Mathematical Modeling
09:45 Monica Crankson (University of Mines and Technology).
Optimal control and cost effectiveness analysis of a two-strain bacterial meningitis epidemic model
10:15 Richard Mantey Larbi (University of Cape Coast)
Global Dynamics of a Harvested Predator-Prey System with Additional Food and Cosner Type Functional Response

10:45 Refreshments

11:15 Patience Aba Sakyi (AIMS Ghana)
Adaptive Robustness: The Dynamic Balance of Robustness and Sensitivity in Living Systems
11:45 Nissrin Alackhar (University of Bonn)
From molecular to cellular behaviour of immune cells: Gene Expression Heterogeneity & T Cell Decision-Making in Cancer
12:15 Reindorf Borkor (Kwame Nkrumah University of Science and Technology).
Investigation of Fractional Compartmental Models in Pharmacokinetics with Application to Amiodarone Drug Diffusion

13:00 Lunch

14:00 Isabel Mensah (Kwame Nkrumah University of Science and Technology).
WAVDeSc: A Wavelet Based Denoising Pipeline for single-cell RNA Sequencing Data Analysis
14:30 Shaibu Osman (University of Health and Allied Sciences).
Modelling the Dynamics of Some Commonly Reported Crimes with Optimal Control: An Evidence-based Modelling Framework for Policy Decision-making in Ghana
15:00 Closing remarks

15:30 Refreshments

16:00 Discussion
17:00 Closing
18:00 Dinner

ABSTRACTS

Nicholas Opoku (AIMS Ghana)

Tool Development for Detecting Copy Number Variations

One key kind of structural Variation that causes human diseases are Copy Number Variations. Advancing in algorithm designs to find these CNVs at base-pair resolution has been driven by mathematical techniques. Herein, we present an algorithm based on wavelet and Hidden Markov concepts to develop a tool for CNV detection.

Rosa Kreider (University of Bonn, Germany)

Modeling interferon-driven immune cell priming in viral infections

Type I interferons (IFNs) act as alarm signals during viral infections, initiating immune responses early to prevent viral spread. Plasmacytoid dendritic cells (pDCs), although few in number, are key producers of IFN alpha (IFNa), generating high levels early in infection through a priming mechanism that enhances IFNa production when cells are pre-exposed to IFNa. Our mathematical model shows that this priming creates an optimal relationship between viral load and IFNa production, with peak production at intermediate viral loads. This effect is due to a state-locking property that restricts priming to non-activated cells, preventing excessive IFNa output. In vitro data confirm these model predictions, highlighting the role of pDCs in immune regulation and their potential therapeutic implications for viral infections.

Anas Musah (Kwame Nkrumah University of Science and Technology, Ghana)

Dynamics of disease models with self-diffusion: a study of cholera

The attention to cholera epidemiology has increased, as its epidemics have become a worldwide health problem. In this project, a deterministic compartmental model is proposed with stability analysis on the epidemic and endemic equilibrium. A reaction-diffusion SIR-B mathematical model of cholera epidemiology that incorporates an environmental reservoir of V. cholerae is formulated to capture the movement of human hosts and bacteria in a heterogeneous environment. Here our findings are supported by the results of numerical experiments. Based on these results, we present the evolutionary processes that involves organism distribution and their interaction of spatially distributed population with local diffusion, and find that the model dynamics exhibits a diffusion- controlled formation growth to hole-like pattern replication that indicates that diffusion has a great influence on the spread of the cholera epidemic.

Millicent Afrifa Opoku (AIMS Ghana)

Modelling Early Human Embryo Development Using the Cellular Potts Model

Embryogenesis is a fundamental, complex and crucial stage in the development of many organisms. Despite decades of study, the earliest phases of human embryogenesis,

which cover vital developmental landmarks for the embryo, are not well understood. One reason for this is the limitations caused by ethical and technical factors related to studying human embryos. However, recent work promises to revolutionise this field with the creation of blastoid models, stem cell-based embryo models with morphological and cellular composition that resembles the earliest stages of embryogenesis. These models promise to provide the substantial amounts of data needed to make progress in this area. This study uses cellular Potts model to simulate the early stage of embryogenesis. The long-term aim of this research is not only fundamental understanding, but to help with scoring of embryos in assisted conception, particularly in vitro fertilisation (IVF), enabling a better understanding of human development before birth in health and disease and potentially leading to improved treatments for infertility and developmental disorders.

Madhesh Suresh (University of Bonn, Germany)

Computational insights into COVID-19 and beyond: Deciphering kinetic signatures of hyperinflammation in innate immunity

The cross-regulation of type I IFN and TNF have diverse effects on innate and adaptive immune cells, contributing to immune homeostasis, and dysregulation in this cross-talk is associated with promoting inflammation, autoimmunity, and allergic reactions. In particular, type I IFN and TNF have been identified as essential elements influencing the pathophysiology of COVID-19. Understanding the TNF/IFN cross-regulation in the context of viral infections, such as COVID-19, has been a challenge due to practical and ethical concerns associated with the system's high biological complexity. Mathematical modelling coupled with systematic data analysis can be used to tackle this challenge, providing insights into understanding cell-cell communication dynamics in different perturbatory conditions. Our project aims to develop a data-driven mathematical model that combines systematic data analysis and quantitative modelling approaches to investigate the TNF/IFN interplay in contributing to disease severity in COVID-19.

Michael Asamani Pobbi (University of Cape Coast, Ghana)

Analysis of Stochastic COVID-19 and Hepatitis B Coinfection Model with Brownian and Lévy noise

In this article, we formulate and analyze a mathematical model for the coinfection of HBV and COVID-19 that incorporates the effects of Brownian and Lévy noise. We studied the dynamics and effects of these diseases in a given population. First, we establish the basic reproduction number of the disease-free equilibrium point of the stochastic model by means of a suitable Lyapunov function. Additionally, we provided sufficient conditions for the stability of the model around the disease-free equilibrium points. Finally, using a few simulation studies, we demonstrate our theoretical results. In particularly, we derived threshold values for HBV only R^s_{0H}, COVID-19 only, R^s_{0C}, and coinfection R^s_{0HC} for the stochastic model around disease-free equilibrium point. Next, the conditions for stability in the stochastic sense for HBV only, COVID-19 only submodels, and the full model are established. Furthermore, we devote our concentrated attention to sufficient conditions for extinction and persistence using each of these reproductive numbers.

Finally, by using the Euler–Murayama scheme, we demonstrate the dynamics of the coinfection by means of numerical simulations.

Specioza Nambooze (AIMS Ghana)

Modelling malaria drug resistance

Malaria is a significant global health issue, particularly in Africa, primarily controlled using antimalarial drugs like artemisinin-based combination therapies (ACTs). However, the emergence of drug-resistant parasites threatens their effectiveness. This study uses mathematical modelling to explore how drug resistance spreads in human and mosquito populations. The model shows that drug-resistant parasites, with their longer infectious periods, gradually become dominant, with the speed of spread influenced by population sizes. Early stages of resistance are critical, and the model offers a framework to study the roles of host immunity and parasite competition in different endemic settings. The model also suggests that including asymptomatic cases is essential for accurately modelling high-incidence malaria, as they extend the effective infectious period.

Lisa Li (University of Bonn, Germany)

A homogenization approach to model spatial cytokine distributions

In secondary lymphoid organs, T helper cells, once activated via an antigen stimulus, secrete cytokines that trigger the activation of nearby cells. Previous studies have revealed considerable inhomogeneities in the spatial distribution of cytokines in tissues, accounting for significant effects in paracrine signaling efficacy. In recent work, we employed a spatial reaction-diffusion model to systematically investigate the formation of spatial cytokine gradients. In our current work, we developed a more efficient analytical cytokine model using a homogenization approach, in order to integrate cell motility and study its effect on cytokine signaling and differentiation patterns.

Ignatus Nunana Dorvi (West African Centre for the Cell Biology of Infectious Pathogens, Ghana)

Markov Chain Monte Carlo Gibbs Sampling approach for Estimating Multiplicity of Infection in Plasmodium falciparum clinical Isolates

Multiplicity of infection (MOI) remains a critical factor influencing transmission dynamics, drug resistance and disease severity. MOI in malaria refers to situations when multiple genetically distinct strains of Plasmodium falciparum infects a single host. While estimating MOI directly using heterozygosity may lead to underestimation, a statistically rigorous process could allow for more accurate modelling of within sample variation. Therefore, we introduced the Gibbs Sampler Markov Chain Monte Carlo (MCMC) approach to accurately capture multiplicity of clones and population allele frequencies in malaria samples. The models were tested on field isolates obtained from high endemic regions like The Gambia and low endemic regions like Bangladesh. The results show a positive correlation with Fws with high multiplicity of infection observed in samples collected from High transmission areas compared to low transmission areas.

The approach offers a novel probabilistic approach to accurately capture multiplicity of clones in infected individuals.

Fameno Rakotoniaina (AIMS Ghana)

Biophysical modelling of Malaria parasite invasion in red blood cell

The life cycle of malaria is complex with several different stages and two hosts. Sexual reproduction occurs in the mosquito but it is the asexual proliferation of malaria parasites inside human red blood cells (RBCs) which causes human disease. When parasites enter the bloodstream from the liver, they must invade RBCs within a few minutes to survive. Thus understanding the invasion mechanism is critical to fighting the disease. The focus is to model the invasion of RBCs to gain scientific understanding of the mechanism. The aim is to calculate the active propulsion force generated by the parasite motor that is necessary for successful invasion.

Lisa Steinheuer (University of Bonn, Germany)

Unraveling immune cell dynamics through data analysis

Progress in high-throughput technologies such as RNA sequencing and mass cytometry now allows us to characterize cell types and excavate changes in transcriptional profiles at single-cell resolution. Furthermore, such high-dimensional data also enables us to investigate and quantify cell-cell communication networks by analyzing the expression of cytokines and cytokine receptors. In collaboration with several groups at the University Hospital Bonn, University of Bonn, and Charite Berlin, we analyzed datasets capturing cell-cell communication in the immune system. We detected profound cell-cell communication pathway topology differences between healthy donors and lupus patients in a systematic, large-scale, and unbiased manner. Additionally, we uncovered predictive markers for treatment efficacy in IBD patients using a machine-learning framework.

Abdulzeid Yen Anafo (School of Mines and Technology, Ghana)

Modelling the Impact of Expanding Seasonal Malaria Chemoprevention to older Age Group and five cycles on malaria incidence in Ghana

Seasonal Malaria Chemoprevention (SMC), where children periodically receive antimalarial medications, is a vital strategy in the fight against malaria within regions characterised by intense seasonal transmission such as Ghana. The strategy of targeting only children under 5 years for malaria control efforts could potentially lead to a shift in the disease burden towards older age groups, particularly those aged 5 to 10 and 10 to15 years. The EMOD malaria model was used to predict the impact of an expanded SMC by age and cycles on clinical and severe malaria cases in children in the Northern region of Ghana.

Stephen Moore (University of Cape Coast) *Trends in Mathematical Modeling*

In recent times, several articles have been published on mathematical models, especially epidemiological models. In this talk, I give a general overview of several Differential Equations usually presented in mathematical models. The aim of this talk is towards an attempt to bridge the models with data and mathematical analysis and present some areas of development.

Monica Crankson (School of Mines and Technology, Ghana)

Optimal control and cost effectiveness analysis of a two-strain bacterial meningitis epidemic model

Bacterial Meningitis, which is considered as a major concern by World Health Organization (WHO) is a medical emergency which continues to be one of the most dreaded infections in sub-Saharan Africa and other countries that fall within the meningitis belt due to recurrent nature of the infection and the outcome of debilitating effects among survivors even after treatment. This research presents a two-strain vaccination control model on the transmission dynamics of Bacterial Meningitis, which best describes the scenario in real life. The optimal control model is used to analyse the impact of vaccination and early treatment on the population, especially on the recovered populations. The existence of its solution is established and the characterization of the controls is performed using the Pontryagins Maximum Principle. The Forward Backward Sweep (FBS) method is implemented and used to solve the optimal control problem and its corresponding adjoint equations. In order to determine the impact of combination of the control strategies on the different model compartments, numerical simulations of the model are performed using real life data from Ghana Center for Disease Control. It was established that the most efficient and cost-effective control strategy is the strategy involving all the five control variables. This is followed by the strategy involving only the effective human personal protection (such as face or surgical masks) control. Based on the findings of this research, necessary recommendations are made for the applications of the model to an endemic area.

Richard Mantey Larbi (University of Cape Coast, Ghana)

Global Dynamics of a Harvested Predator-Prey System with Additional Food and Cosner Type Functional Response

The study investigates the global dynamics of a harvested predator-prey model incorporating additional food and a Cosner-type functional response. The model is analysed for positivity, uniform boundedness, persistence, and permanence of solutions. Equilibria are identified, with both local and global stability properties rigorously examined using eigenvalue analysis, suitable Lyapunov functions, and the Bendixson-Dulac criterion. Findings indicate that the system can support continuous harvesting of both predator and prey populations, provided the harvesting rate is less than the biotechnical productivity. This presentation provides foundational

understanding of the model's dynamics, contributing to the broader field of ecological modelling and conservation efforts.

Patience Aba Sakyi (AIMS Ghana)

Adaptive Robustness: The Dynamic Balance of Robustness and Sensitivity in Living Systems

Arabidopsis thaliana serves as a model organism for studying biological pattern formation, particularly in its root and leaf epidermal layers. These patterns, driven by a complex network of transcription factors and signalling pathways, demonstrate a remarkable ability to balance intrinsic robustness with environmental sensitivity. This research focuses on the interaction between these signalling networks and how they adapt to maintain precise pattern formation despite disruptions. In the root epidermis, a mutual support mechanism involving the proteins GL3, WER, and CPC governs the establishment of non-hair and hair cell patterns. This mechanism contrasts with the activator-inhibitor model traditionally used to explain pattern formation in the leaf. Despite these differences, both systems exhibit modularity and the potential for evolutionary redundancy, which may allow for flexible adaptations to environmental conditions and internal perturbations. Our reaction-diffusion model of the root epidermis proposes that pattern formation can arise even with only one diffusible component, regulated by protein complex formation. Preliminary results suggest that GL3 protein movement is not necessary for spontaneous patterning, and regulation of protein stability through complex formation is a critical factor. These findings challenge traditional Turing models of pattern formation and point towards a discrete reaction-diffusion framework that better reflects the spatial organisation of the root epidermis. Our model will also explore the role of local positive feedback in stabilising established patterns, particularly in response to cell division, cell growth, and environmental factors. Comparative studies between root and leaf patterning mechanisms will further elucidate how evolutionary processes like whole genome duplication contribute to the diversification and robustness of biological systems.

Nissrin Alackhar (University of Bonn, Germany)

From molecular to cellular behaviour of immune cells: Gene Expression Heterogeneity & T Cell Decision-Making in Cancer

Transcription of innate immune mammalian genes occurs in stochastic bursts, leading to single-cell variability. Analysing over 2,000 toll-like receptor (TLR)-response genes, we find that gene expression variability across multiple experimental conditions follows a linear mean-variance relationship, reflecting transcriptional bursting kinetics. Stochastic modelling of temporal scRNA-seq data reveals that increased variability arises from larger and more frequent transcriptional bursts, offering insights into the regulation of innate immune response variability.
Zooming out on cellular behaviour of immune cells; The tumour microenvironment, along with lymph nodes and other compartments, is a complex niche involving tumour, stromal, and immune cells. Understanding the heterogeneity of these environments

across patients is crucial for effective treatment strategies. CD8+ T cell fates significantly impact cancer progression and treatment outcomes. We are developing a quantitative, data-driven model to analyse CD8+ T cell dynamics in these environments. We use response time modelling to simulate accurate transitions between cell-states and annotate the model using longitudinal flow cytometry data of murine melanoma.

Reindorf Nartey Borkor (Kwame Nkrumah University of Science and Technology, Ghana)
Investigation of Fractional Compartmental Models in Pharmacokinetics with Application to Amiodarone Drug Diffusion
This study offers and explores fractional models derived from a classical Pharmacokinetics compartmental system. The fractional models are essentially an enlarged version of the classical model and their distinguishing characteristics are further examined comprehensively. The characteristics of some models are shown to be incompatible with the concept of mass balance. However, they appeared to outlast fractional calculus theory when simulating anomalous kinetics. We proved this behaviour based on the stability analysis of the equilibrium point under the condition of different values of the fractional order and also, fitting the proposed models to an experimental data set (amiodarone) thereby estimating the parameters with the least-square approach. The fractional models predicted an excellent fit to the dataset as compared to the classical model. These models described anomalous diffusion better than classical theories. Additionally, we acquire the numerical solutions by using the Grunwald-Letnikov technique of the Fractional Finite Difference Method, as the analytical results for such models are often difficult to find. The results showed that the proposed numerical method is equally efficient in solving any complex compartmental models, as they performed well in simulations for the classic model.

Isabel Mensah (Kwame Nkrumah University of Science and Technology, Ghana)
WAVDeSc: A Wavelet Based Denoising Pipeline for single-cell RNA Sequencing Data Analysis
Single-cell RNA sequencing (scRNA-seq) has garnered attention in molecular biology for its ability to investigate cell states and functions at the single-cell level. However, it presents inherent challenges, including high noise levels and sparsity, hindering accurate analysis and the identification of differentially expressed genes. We introduce WAVDeSc, a novel denoising pipeline that employs discrete wavelet transforms and Bayesian thresholding to enhance scRNA-seq data quality. This approach effectively reduces noise and improves the identification of differentially expressed genes, outperforming existing methods in both simulated and real datasets. WAVDeSc's computational efficiency and robust performance make it a promising tool for transcriptomic analysis.

Shaibu Osman (University of Health and Allied Sciences, Ghana)

Modelling the Dynamics of Some Commonly Reported Crimes with Optimal Control: An Evidence-based Modelling Framework for Policy Decision-making in Ghana

Crime remains one of the major societal challenges globally, undermining human security and economic development. High crime rates have been a persistent issue in many countries especially in Sub-Saharan Africa. Commonly reported crimes like armed robbery, rape, and theft impose huge economic and psychological costs. This calls for an evidence-based modelling framework for effective policy decision-making to help combat crime. This study proposes and develops a mathematical model using ordinary differential equations (ODEs) to analyse the dynamics of some commonly reported crimes by the Ghana Police Service. The crime model investigates fundamental mathematical concepts like the crime reproduction number, crime-free, and crime- endemic equilibria. The model was extended to an optimal control problem to identify the most effective control strategies with low costs to minimise criminal activities in Ghana. The results provide a quantitative framework to assess interventions against the commonly reported crimes by the Ghana Police Service. The model captures real-world population dynamics and adaptations of epidemiological concepts. It provides novel insights into managing crime. The optimal control analysis gives data-driven policy guidance on implementation of impact-driven control strategies in a resource- constrained environment.

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