BIOMATH 2025

International conference on Mathematical Methods and Models in Biosciences

Conference Abstracts

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ИЗСЛЕДВАНИЯ

The conference obtained financial support aid by the Bulgarian National Science Fund through contract KP-06-MNF-49/16.12.2024, as well as by the Society for Mathematical Biology (International grant) and the European Society for Mathematical and Theoretical Biology (grant for the School for Young Scientists).

Table of contents

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

BIOMATH 2025: A conference overview

Roumen Anguelov[1,3], Milen Borisov[1], Nina Pesheva[2], Peter Rashkov[1]

[1]Institute of Mathematics and Informatics - BAS
roumen.anguelov@math.bas.bg, milen_kb@math.bas.bg,
p.rashkov@math.bas.bg

[2]Institute of Mechanics - BAS
nina@imbm.bas.bg

[3]University of Pretoria
roumen.anguelov@up.ac.za

The BIOMATH 2025 conference is the thirteenth in the series of BIOMATH conferences. The series was initiated in 2011, building similar meetings taking place since 1995. BIOMATH 2025 takes place at the Institute of Mechanics and the Institute of Mathematics and Informatics of the Bulgarian Academy of Sciences in Sofia, Bulgaria, 15-20 June 2025. The conference series is coordinated by an International Steering Committee comprising 18 dedicated scientists from 10 different countries. One of the main driving forces behind the BIOMATH series of conferences and one of the founders of the committee was Prof. Svetoslav Markov from the Institute of Mathematics and Informatics at the Bulgarian Academy of Science, who sadly passed away in 2023. The conference acknowledged his contribution to both the conference series and the publications associated with it.

BIOMATH conferences are forums for latest research in the life sciences based on applications of mathematics, as well as mathematics applied to or motivated by biological research. It is a multidisciplinary meeting forum for researchers who develop and apply mathematical and computational tools to study phenomena in the broad fields of biology, ecology, medicine, biophysics, biochemistry, pharmacokinetics, chemoinformatics, biotechnology, bio-engineering, environmental science and etc. In addition, BIOMATH 2025 includes a special topic session *Mathematical models of the immune system in human disease*, where advances in genetics and biochemistry have opened up new opportunities to gain knowledge about the organization, dynamics, and regulation of the human immune system. Further, the following priority directions are emphasized:

- Health and quality of life;
- Environmental protection. Utilization of raw materials and bioresources;

- Information and communication technologies.

Particularly important role is assigned to biomathematics in the first two priority directions, including mathematical modeling and applications in medicine and pharmacy, cellular processes, cancers, infectious diseases, biotechnology. There is traditional wide diversity of participation of BIOMATH both in terms of research topics in the filed and affiliation promoting the development of new ideas and building of international research teams. The 2025 edition of BIOMATH the conference is attended by 86 participants from 23 countries in Europe, North and South America, Africa and Asia. The scientific program includes 6 keynote lectures, 67 contributed oral presentations and 16 posters.

The BIOMATH conferences pay special attention to the participation and support of young researchers. The School for Young Scientists is an integral part of the conference and it offers to doctoral students and early career researchers additional developmental and networking opportunities. In 2025 these include three excellent topical lectures presented by top scientists. The school's full program is available on the conference website.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

In remembrance of the Life and Legacy of Svetoslav Marinov Markov

Roumen Anguelov[1,2]

[1]University of Pretoria, South Africa
[2]Institute of Mathematics and Informatics, Bulgarian Academy of Sciences
roumen.anguelov@up.ac.za

On behalf of the Biomath International Steering Committee

The Biomath International Steering Committee lost in 2023 one of its founding and most valuable members, Svetoslav Markov. In 2025 we host in Bulgaria the first conference without him. Hence, the Committee would like to acknowledge at this forum the exceptional contribution of Svetoslav Markov to the Biomath series of conferences, to the associated School for Young Scientists as well as to publications related to the conference.

1943 - 2023

Prof. Markov's scientific work encompassed a broad spectrum of topics all to varied extend related to biomathematical modeling. He was a great enthusiast and supporter of the field. Having a School for Young Scientists as an integral part of the Biomath conferences promoted the field to young people, many of whom are already established researchers.

When promoting Biomathematics, Svetoslav never put his research first. It was always about us, the researchers from all fields. Nevertheless, through his research, he led by example - introducing new ideas, forging connections between previously unrelated fields, and posing new questions.

The conference Biomath took place every year since 2011, with few exceptions (2020 and 2022) for understandable reasons. The journal Biomath has already published 12 volumes and is indexed by Scopus and all relevant to the

field indexing agencies. Svetoslav Markov's leadership, wisdom, and remarkable efforts are largely responsible for this success They will be remembered, [2].

Head of the Department of Mathematical Modeling in Biology, Institute of Biophysics, BAS

Conference photo of Biomath 2023 - Svetoslav's last Biomath conference, [1].

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Keynote Presentations

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Stackelberg evolutionary games for managing evolving resources, pests and cancer

Joel S. Brown

Moffitt Cancer Center, Tampa, Florida, USA
squirrel@darwiniandynamics.org

Nature plays games, evolutionary games that is. Organisms evolve strategies to better survive in their environment and to more successfully interact with conspecifics, competitors and predators. For example, one can ask the almost Zen-like question: "Why is there wood?" The answer lies as the solution to an evolutionary arms race for height as woody plants strive for light. Human actions also exert selection forces. Humans can wittingly or unwittingly become part of nature's games. When humans alter the ecologies of other species the wrong question to ask is "Will they evolve?"; rather we should ask "How fast and into what will they evolve?". As humans alter the eco-evolutionary dynamics of other species – valuable and pesky ones alike – the game can and should become a Stackelberg evolutionary game where the manager or decision makers take the lead by anticipating and steering both the ecological and evolutionary dynamics of the managed species. Using the G-functions approach to evolutionary game theories (akin to adaptive dynamics), managing fisheries falls with the realm of Stackelberg evolutionary games. Cancer does as well. The evolution of therapy resistance by cancer cells explains most patient deaths. Novel evolutionary therapies have proven effective in several clinical trials of prostate cancer. In these clinical trials and others, mathematical models are leading the way towards "algorithms as drugs" (sensu Christopher Gregg) with the goal of rendering some currently incurable cancers as containable, and others as curable.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical insights into tumour-immune dynamics: Navigating a shifting landscape

Helen Byrne

Mathematical Institute,
University of Oxford, UK
helen.byrne@maths.ox.ac.uk

The presence of immune cells within solid tumours was initially viewed as a positive sign of the body's attempt to eliminate a foreign threat. However, it is now understood that tumours can hijack immune cells, turning them from tumour-fighting agents into tumour-promoting allies. Immunotherapy seeks to counteract this by enhancing or restoring normal immune function. While immunotherapy has shown significant promise, the underlying tumour-immune dynamics are highly complex. This complexity makes it challenging to predict why some patients respond well to immunotherapy while others do not. In this talk, we will investigate how diverse mathematical approaches – including mathematical modelling and topological data analysis – can help unravel these intricate interactions. We will present recent findings that demonstrate the complementary insights these methods offer in understanding and improving immunotherapy outcomes.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

PDE models for the growth of phenotypically heterogeneous cell populations

Tommaso Lorenzi

Politecnico di Torino, Italy
tommaso.lorenzi@polito.it

In this talk, PDE models for the growth of phenotypically heterogeneous cell populations will be considered. Both models with discrete phenotype states, which consist of coupled systems of nonlinear PDEs, and models wherein the phenotype enters as a continuous structuring variable, which are formulated as nonlocal PDEs, will be examined. Connections between such population-level models and underlying individual-based models will be addressed, analytical and numerical results summarising the behaviour of the solutions to the model equations will be presented, and the insights into the mechanisms that underpin collective cell migration generated by these results will be briefly discussed.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Combining image analysis with dynamic models to improve understanding of vascular disease

Mette Olufsen

North Carolina State University, Raleigh, USA
msolufse@ncsu.edu

The incorporation of mathematical models in data analysis is essential for understanding physiological processes and developing better diagnosis and treatment strategies. This presentation will focus on cardiovascular diseases, particularly pulmonary hypertension, which is characterized by high blood pressure in the pulmonary vasculature, and effects of aortic remodeling in Fontan patients. Diagnosing the hemodynamic effects of such vascular changes can be challenging, and successful treatment requires early and accurate diagnosis of the disease subtype. To enhance our understanding, we study the features of the vascular network, methods for generating networks for fluid dynamics models, and strategies for designing optimal treatments tailored to individual patients.

For both applications, we employ a multiscale approach to examine the vasculature at both vessel and network levels, constructing models that include large arteries and veins, arterioles and venules, as well as capillaries. We represent the large arteries and veins using a directed graph derived from computed tomography images.

The network of arterioles and venules is modeled as structured trees, with parameters informed by data. The capillary network is depicted as a sheet connected to arterioles and venules in a ladder-like arrangement. In the large vessels, we solve the one-dimensional Navier-Stokes equations, while in the network of smaller vessels and capillaries, we solve linearized equations. These smaller-scale equations are connected to the larger vessels through outflow boundary conditions. The model is calibrated to patient data through simulations and data emulation.

We emphasize the significance of sensitivity analysis and parameter inference in customizing the model for individual patients and demonstrate how the calibrated models can predict treatment effects effectively.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Numerical challenges for peroperative liver tumor ablations by electroporation

Clair Poignard

Inria Research Center,
University of Rennes, France
clair.poignard@inria.fr

Electropermeabilization (also known as electroporation) refers to a significant increase in the electrical conductivity of the cell membrane when cells are exposed to high-voltage pulses (typically a few hundred volts per centimeter).

If the pulse duration is sufficiently short (ranging from a few microseconds to a few milliseconds, depending on the amplitude), the permeabilised membrane can reseal within tens of minutes. This reversible electroporation preserves cell viability and is used in electrochemotherapy to facilitate drug delivery into the cell.

However, if the pulses are too long, too frequent, or of excessively high amplitude, the membrane is irreversibly damaged, leading to cell death. This irreversible electroporation (IRE) serves as a promising, non-thermal, and minimally invasive tumor ablation technique, particularly for patients who are not candidates for traditional treatments such as surgery, radiofrequency (RF) ablation, or cryoablation.

Despite its advantages, this predominantly non-thermal approach— which preserves the tissue scaffold and reduces bleeding— remains largely restricted to easily accessible tumors. This limitation arises mainly from the technical challenges associated with these therapies, particularly the difficulty in precisely determining the treated zone in advance compared to standard ablative techniques.

In this talk, I will first present recent findings on the mathematical modeling of electroporation across different scales, from individual cell membranes to whole tissues. Next, I will introduce a numerical strategy that integrates medical imaging (C-arm Cone Beam CT) and advanced computational methods to accurately assess clinical procedures by mapping the electric field distribution.

Finally, I will discuss a few case reports on percutaneous liver tumor ablation via IRE, demonstrating the feasibility of real-time numerical evaluation of IRE procedures.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Detecting multiple timescales and computing high-order phase reductions

Bob W. Rink

Department of Mathematics, Faculty of Science,
Vrije Universiteit Amsterdam, The Netherlands
b.w.rink@vu.nl

In this talk, I will present a new mathematical method for computing slow manifolds in geometric singular perturbation problems. Our method, which is reminiscent of the so-called computational singular perturbation method, works by computing expansions of embeddings of slow manifolds, together with the dynamics on them in a local coordinate chart. In this way, one can approximate slow manifolds to arbitrarily high precision, which makes our method particularly suitable for the study of systems with multiple (i.e., three or more) timescales. I will show for example how it helps to uncover surprising hidden timescales in nonstandard slow-fast systems. Applications to reaction network problems will also be presented.

In addition, I will discuss an extension of the method that allows us to compute high-order phase reductions of coupled oscillator networks. This extension is then applied to predict remote synchronization and multi-stability in a network of delay-coupled Stuart-Landau oscillators.

This is joint work with Chris Bick, Sören von der Gracht, Ian Lizarraga, Eddie Nijholt, Martin Wechselberger and Babette de Wolff.

Contributed Talks and Posters

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Management of EBHSV-infected eastern cottontail invasion in Italy using Z-type control method

Francesca Acotto[1], Fabiana Camattari[2], Ezio Venturino[1,3]

[1]Dipartimento di Matematica "Giuseppe Peano",
Università di Torino, Italy
francesca.acotto@unito.it

[2]MIDA, Dipartimento di Matematica, Università di Genova, Italy
Osservatorio Astrofisico di Torino, Istituto Nazionale di Astrofisica, Italy
fabiana.camattari@edu.unige.it

[3]UMR CNRS 6249 Chrono-environnement,
Université Marie et Louis Pasteur, France
ezio.venturino@unito.it

The introduction in Italy of eastern cottontail (*Sylvilagus floridanus*) for hunting has influenced the local predator-prey dynamics of red fox (*Vulpes vulpes*) and native European hare (*Lepus europaeus*). No direct competition seems to occur between the two lagomorphs, but invasive cottontails cause hyperpredation of red foxes on native hares and are also carriers of the European brown hare syndrome virus (EBHSV). This talk focuses on a scenario in which EBHSV-infected eastern cottontails are introduced in a region of virus-free European hares. To avoid the extinction of native lagomorphs and to contain the invasive ones, we consider two possible biological control actions using the Z-type control method on a four-population reference system. In particular, we look at indirect control of invasive prey by removing predators and combination of this indirect control with direct control of native prey.

Keywords: Z-type control, invasion management, biodiversity conservation, eastern cottontail, European hare, hyperpredation effect, EBHSV transmission

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modeling dengue dynamics: unraveling the impact of homologous reinfections

Maíra Aguiar[1,2], Vizda Anam[1], Akhil Kumar Srivastav[1], Vanessa Steindorf[1], Nico Stollewnerk[1]

[1]Basque Center for Applied Mathematics (BCAM), Bilbao, Spain
maguiar@bcamath.org
vanam@bcamath.org
asrivastav@bcamath.org
vsteindorf@bcamath.org
nstollenwerk@bcamath.org

[2]Ikerbasque, Basque Foundation for Science, Bilbao, Spain

Dengue fever, caused by the dengue virus and transmitted by Aedes mosquitoes, remains a major public health concern in tropical and subtropical regions. The co-circulation of multiple serotypes increases the risk of severe disease due to antibody-dependent enhancement (ADE) during heterologous reinfections. Mathematical models have long explored the complex dynamics of dengue transmission, incorporating key factors such as temporary cross-immunity (TCI) and ADE [1, 2].

Traditionally, homologous reinfections, secondary infections with the same serotype, were not considered, as individuals were assumed to acquire lifelong immunity to a single serotype. However, recent studies suggest that homologous reinfections, though rare, can occur [3]. While typically asymptomatic due to a rapid immune response, these reinfections may contribute to viral circulation and influence epidemiological patterns.

We present a modeling framework that captures dengue immune dynamics mediated by antibodies, integrating both homologous and heterologous reinfections. Our model reproduces the viral load and antibody production dynamics observed in primary and secondary infections, aligning with empirical immunology studies [4].

This framework lays the foundation for an extended multi-strain population model incorporating primary and secondary infections, TCI, ADE, and homologous reinfections. We explore the epidemiological impact of homologous reinfections in endemic settings and assess their broader implications for dengue transmission, particularly in temperate regions like Europe, where established vectors and local transmission are primarily driven by viremic imported cases.

Acknowledgments: This research is supported by the Basque Government through the "Mathematical Modeling Applied to Health" Project, BERC 2022-2025 program and by the Spanish Ministry of Sciences, Innovation and Universities: BCAM Severo Ochoa accreditation CEX2021-001142-S / MICIN / AEI / 10.13039/501100011033. Maíra Aguiar acknowledges the financial support by the Ministerio de Ciencia e Innovacion (MICINN) of the Spanish Government through the Ramon y Cajal grant RYC2021-031380-I.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Bioeconomic modeling for the sustainable exploitation of three key marine species in Morocco

Ilham Ait El Harch, Khalid Outaaoui, Youssef El Foutayeni

Laboratoire Mathématiques et Dynamiques de Population,
Faculté des Sciences Semlalia de Marrakech (FSSM),
Université Cadi Ayyad de Marrakech, Morocco
i.aitelharch.ced@uca.ac.ma
Unité de Modélisation Mathématique et Informatique des Systèmes Complexes (UMMISCO), Institut de recherche pour le développement (IRD), France

This study aims to deepen the understanding and optimize fishing activity in Morocco by holistically integrating biological and economic aspects. On the biological front, we examine the rivalry between three marine species: sardine, mackerel, and tuna, and the need to preserve the balance of their biomass. On the economic side, we focus on maximizing fisherman's profits.

We develop a biological equilibrium model for fishermen operating in the Atlantic region, where the three species coexist. These competing species exhibit their natural growth represented by logistic curves. We propose a mathematical model that takes into account the density and competition between species to explain population dynamics. Integrating human intervention adds a realistic dimension to our modeling. Fishermen specifically target all three species, thereby influencing population dynamics based on their fishing activities. This approach allows us to explore the effects of human-nature interaction on the biological equilibrium of sardine equilibrium of sardine, mackerel, and tuna populations.

Keywords: mathematical modeling, biological equilibrium, optimization techniques
MSC2020: 92B05

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modelling CD8 T cell dynamics in adoptive T cell therapy of melanoma

Nissrin Alachkar[1], Michael Hölzel[1], Kevin Thurley[1]

[1]Institute of Experimental Oncology, University Hospital Bonn, Germany
nissrin.alachkar@ukbonn.de

CD8+ T cells play a critical role in anti-tumour immunity by directly targeting and eliminating cancer cells. However, during chronic antigen exposure, as occurs in cancer, these cells progressively lose their effector functions through a process known as exhaustion, ultimately compromising tumour control. The differentiation trajectory of CD8+ T cells—particularly into effector or stem-like progenitor exhausted, progenitor exhausted, and terminally exhausted phenotypes—critically shapes the outcome of the immune response in cancer [1, 2].

To investigate this process, we analyse high-dimensional flow cytometry data from a murine melanoma adoptive T cell therapy experiment. Using unsupervised clustering [3], we identify and quantify distinct CD8+ T cell subsets across multiple organs and time points, enabling us to track their kinetics during tumour progression. We propose a set of candidate mathematical models representing alternative CD8+ T cell differentiation pathways, defined by distinct lineage relationships between subsets. Each model is fitted to the experimental data, and model selection criteria are used to identify the differentiation motif that best explains the observed dynamics.

This integrated data-driven approach allows us to reconstruct CD8+ T cell differentiation trajectories in vivo and offers a framework for testing mechanistic hypotheses about T cell fate in the context of tumour immunity.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modeling radiotherapy response to tumor heterogeneity and its microenvironment

Francesco Albanese[1], Giulia Chiari[2], Marcello Edoardo Delitala[1]

[1]Department of Mathematical Sciences "G. L. Lagrange",
Politecnico di Torino, Italy
francesco_albanese@polito.it
marcello.delitala@polito.it

[2]Basque Center for Applied Mathematics (BCAM), Bilbao, Bizkaia
gchiari@bcamath.org

Research has revealed that the interaction between tumors and abiotic elements is crucial for therapy outcome. Notably, hypoxia serve as an environmental stressor that not only promotes the emergence of more aggressive cell types but also influences therapeutic effectiveness in a twofold way. First, the cells that adapt to these harsh conditions exhibit a high resistance to environmental stresses, enabling them to persist in regions where radiotherapy is less effective due to insufficient oxygen, being the latter an element essential for amplifying the damaging effects of ionizing radiation. Second, these adapted cells tend to have slower proliferation rates, rendering them less susceptible to radiotherapy, which primarily targets dividing cells by damaging their DNA.

This talk introduces a continuous mathematical model designed to investigate the influence of hypoxia on the evolutionary dynamics of cancer cells. The model is based on [1] and is developed within the framework of phenotype-structured population dynamics. It is expressed through a system of coupled nonlinear integro-differential equations and encompasses a four-dimensional domain: one dimension for time, two for spatial representation, and one for the phenotypic state, which describes the metabolic response of cells to environmental stress in terms of resistance. Furthermore, the model integrates radiotherapy by examining how both oxygen spatial distribution and the phenotypic characteristics of the tumor influence treatment outcomes.

The primary objective is to generate a reliable epigenetic map of the tumor within its microenvironment and to exploit it to explore alternative radiotherapy schedules beyond the standard of care. This approach aims to account for the evolving phenotypic heterogeneity and capitalize on the well-known reoxygenation effect. Preliminary numerical simulations indicate that strategically timed treatment schedules can significantly improve therapeutic outcomes and may provide valuable insights for designing future clinical trials.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

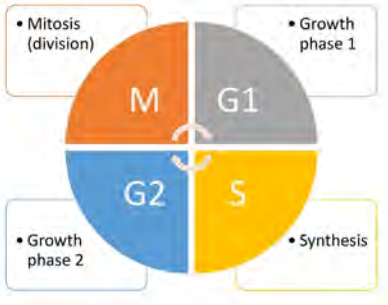
Nonsmooth dynamical systems: Application to a cell cycle model

Roumen Anguelov[1,2]

[1]Department of Mathematics and Applied Mathematics
University of Pretoria, South Africa
roumen.anguelov@up.ac.za

[2]Institute of Mathematics and Informatics - BAS,
Sofia, Bulgaria

The cycle consisting of repeating growth(Intermediate stages G1, S and G2) and division (Mitosis) is an extremely complex process. Among the key regulators of the cell cycle are Cyclin-Dependent Kinase 1 (CDK1) and the Anaphase-Promoting Complex (APC). We consider a mathematical model of the cell cycle, which is derived in [2] and is based on the dynamics CDK1 and APC. This model considers the cell cycle as a cyclin driven process and is convenient to investigate anti-cancer treatments which block this compound. Denoting the level of activation of CDK1 by x and the level of activation of APC by y and the rate of synthesis of cyclin by α_1 the model is



$$\frac{dx}{dt} = \alpha_1 - \beta_1 x h(n_1, K_1, y) + \alpha_3(1-x)h(n_3, K_3, x), \quad (1)$$

$$\frac{dy}{dt} = \alpha_2(1-y)h(n_2, K_2, x) - \beta_2 y, \quad (2)$$

where $h(n, K, z) = \dfrac{z^n}{K^n + z^n}$ is the well known Hill function, a sigmoidal function between 0 and 1. The rest of the constants are easily identified as: β_1 - the natural decay of x when y is at close to its maximum, α_3 - rate of filling existing capacity when x is close to its maximum, etc. Clearly, in this model the Hill function is smoothly switching on and off the terms in which it is involved. One may remark that any switching function can be used and that we can also consider

$$\lim_{n\to\infty} h(n, K, z) = H(z - K),$$

where H is the Heaviside function, that is $H(z) = \begin{cases} 1 \text{ if } z > 0, \\ 0 \text{ if } z < 0. \end{cases}$

We show that by using this discontinuous switch function, it is possible to get a better insight into the possible values of the involved rates and to have a better understanding of the impact of the rate of cyclin synthesis on the cycle period.

The righthand side of (1)-(2) represents a continuous vector field. There is a well developed theory, which among other things includes the Poincare-Bendinxon theorem applied to mathematically prove the existence of a unique limit cycle of (1)-(2). When the Hill function is replaced in (1)-(2) by the Heaviside function, we have a discontinuous righthand side and the model is within the realm of Nonsmooth Dynamical Systems, [3]. The version of the Poincare-Bendixon theorem derived for such systems in [1] is not directly applicable, but we show a direct proof for this case. Overall, the talk promotes the idea that modelling should be guided by biological insight and not be restricted by known or popular mathematical theory.

Keywords: cell cycle, reducing cancer growth rate, nonsmooth dynamical systems

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Predicting cleavage sites of Cathepsin-V using machine learning models

Nida Ansari, Georgi Momekov, Ivan Dimitrov

Faculty of Pharmacy,
Medical University of Sofia, Bulgaria
n.ansari@pharmfac.mu-sofia.bg
gmomekov@pharmfac.mu-sofia.bg
idimitrov@pharmfac.mu-sofia.bg

Cathepsins are an enzyme family involved in the antigen processing pathway, especially in the protein cleavage in the endo/lysosome. Accurate prediction of protein substrate cleavage sites by the cathepsins could help to determine the potential antigens for processing by the antigen-presenting cells. In this study, advanced machine learning techniques were employed to create models for predicting Cathepsin V cleavage sites in the protein sequences. The models were trained on a dataset of peptides derived by mass spectrometry after the Cathepsin V cleavage of proteins. The peptides were encoded by Z-scale numerical descriptors, representing the physicochemical characteristics of the amino acids within peptide sequences. The models were built upon the peptide dataset after 10-fold cross-validation on the training set and validation on an external test set. Their performance was assessed using binary classification metrics, where the XGBoost, Support Vector Machine, Multilayer Perception, and Quadratic Discriminant Analysis showed superior results with high sensitivity. Feature selection was performed to identify the most important features of the amino acid's key positions within the peptides and to improve model performance. Future research will seek to utilize this approach to other cathepsins and combining in silico modelling with the knowledge in the biochemical processes in cells to expand the domain of antigen-processing research.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Comparing different interpretations of the set-based Dempster-Shafer theory for explainable and fair prediction of hereditary *BRCA1/2* mutations

Ekaterina Auer[1], Wolfram Luther[2], Lorenz Gillner[1], Pascal Müller[1]

[1]Department of Electrical Engineering and Computer Science,
University of Applied Sciences Wismar, Germany
ekaterina.auer@hs-wismar.de
lorenz.gillner@hs-wismar.de
pascal.mueller@stud.hs-wismar.de

[2]Department of Computer Science and Applied Cognitive Science,
University of Duisburg-Essen, Germany
luther@inf.uni-due.de

In recent decades, the use of the Dempster-Shafer theory (DST [1]) for software-based decision-making or classification, for example, in the context of machine learning, has gained significant importance. This is largely due to the theory's ability to provide a detailed explanation of the underlying reasoning that generates the results, thereby increasing the software's interpretability and trustworthiness. Another advantage of the DST framework is its capacity to handle conflicting or missing decision criteria and data.

DST captures the uncertainty associated with incomplete or imprecise knowledge, in addition to the uncertainty inherent in random events. Specifically, the traditional (discrete) DST assumes that the probability $P(X = x) = p_i \in \mathbb{R}$ of a random variable X taking on a realization $x \in \mathbb{R}$ holds not for a point (or crisp) value of $x = x_i \in \mathbb{R}$ but rather for a set of values, such as an interval $x \in [\underline{x}_i, \overline{x}_i] \subset \mathbb{R}$. Further, p_i itself may be considered not as a crisp value but as ranging within a certain set (e.g. $[\underline{p}_i, \overline{p}_i] \subset \mathbb{R}$). This latter extension of DST can be achieved in various ways, each with its own strengths and limitations.

This talk centers on the hereditary breast and ovarian cancer syndrome (HBOC) and evaluating the cumulative risk of inheriting a harmful mutation in the *BRCA1/2* genes. In our recent papers (e.g. [2]), we introduced an interval DST method to categorize individuals into risk classes based on their personal and family history, providing explainable results. Here, we explore approaches using further interval-based arithmetics and discuss their merits and limitations

for this specific application, with a special focus on computing fair lower risk bounds for individuals with low risk.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Stabilization of a prey-predator system via targeted control in space and across populations

Teodora Baciu

Faculty of Mathematics,
"Alexandru Ioan Cuza" University, Iaşi, Romania
teodorabaciu11@yahoo.com

This work addresses the challenge of eradicating an invasive predator population in an environment that varies seasonally – a topic of increasing relevance in ecological management and conservation biology. The problem is approached through a general prey-predator framework that incorporates nonlocal reaction terms, local diffusion and time-periodic coefficients, allowing us to capture the complex dynamics of such systems.

Our research emphasizes the effectiveness of selective control strategies – applied either directly to the predator population or indirectly through their prey – in achieving long-term eradication. We establish criteria for successful eradication, formulated in terms of the sign of the principal eigenvalue of a non-self-adjoint parabolic operator. As part of our analysis, we also compare the efficiency and feasibility of different types of controls.

These findings contribute to a deeper understanding of species management in dynamic reaction-diffusion ecosystems and provide a foundation for developing more refined, ecologically informed intervention strategies in future work.

Keywords: zero-stabilization, prey-predator system, reaction-diffusion system, regional control

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical analysis of coupled one-dimensional blood flow in an artery

Mapundi Kondwani Banda

University of Pretoria, Faculty of Natural and Agricultural Sciences,
Department of Mathematics and Applied Mathematics, South Africa
mapundi.banda@up.ac.za

First-order hyperbolic systems are commonly used to model blood flow in arterial networks. These networks are composed of interconnected segments, or edges, which are coupled at junctions referred to as nodes. At these nodes, half-Riemann problems are solved to ensure the well-posedness of the overall system. This presentation will discuss both the theoretical framework and numerical simulations of these systems, emphasizing the role of appropriate boundary conditions at the network nodes. Computational results will be presented to illustrate key dynamical features of the flow.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Application of mathematical biology in agriculture: The case of the Soybean Aphid

Aniket Banerjee

Sorbonne Université, Université Paris Cité, CNRS,
Laboratoire Jacques-Louis Lions, LJLL, F-75005 Paris, France
aniket.banerjee@sorbonne-universite.fr

Soybean Aphids have changed Soybean agriculture by acting as an invasive pest. A genetic modification was developed in the Soybean plant to make it resistant to Aphids. Colonization and feeding by an Aphid can alter the plant's physiology, favouring the subsequent colonization of additional conspecifics. There are two mechanisms by which this susceptibility can be induced: feeding facilitation and the obviation of resistance. The results can be seen in soybean fields and is a seasonal phenomenon.

We develop a non-local population model that holds the dynamics of the mechanisms seen biologically. We consider the effect of non-smooth Allee-type mechanisms on the two species Lotka-Volterra competition model. This mechanism can alter classical competitive dynamics in the ODE setting.

In particular, an Allee effect present in the weaker competitor could lead to bi-stability dynamics and competitive exclusion reversal. We discuss applications of our results to pest management strategies for soybean aphids in the context of a changing climate. We validate the model dynamics with on-field dynamics and analyse them using numerical simulations.

Keywords: soybean, biotype, insecticide-resistant management, nonlocal ODE model, Allee effect, bi-stability, bifurcations, finite time extinction, differential fitness, soybean aphid control, climate change

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modeling the dynamics of leptospirosis in India

Antima, Sandip Banerjee

Department of Mathematics,
Indian Institute of Technology Roorkee, Uttarakhand, India
antima@ma.iitr.ac.in
sandip.banerjee@ma.iitr.ac.in

Leptospirosis, a formidable zoonotic threat spawned by Leptospira, plagues tropical and subtropical realms. This study delves deep into tropical Indian states, namely, Kerala, Gujarat, Karnataka, Maharashtra, and Tamil Nadu, unraveling the dynamics of leptospirosis through a comprehensive mathematical model that embraces temperature-driven growth rates of Leptospira.

Sensitivity analysis and parameter estimation techniques fortified the model's accuracy, unraveling the factors shaping leptospirosis transmission. Notably, the numerical results highlight the significant impact of rainfall, fishing, climate, mining, agriculture, and cattle farming on leptospirosis prevalence in the endemic states of India.

Finally, our study urges resolute preventive action to control and combat leptospirosis in India. Strengthening surveillance, impactful awareness campaigns, targeted interventions, and improved hygiene practices among high-risk individuals are vital. Embracing these proactive strategies will alleviate the burden of leptospirosis and enhance public health in India and beyond.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Numerical analysis of a Keller–Segel model describing immune cell dynamics

Georgi Bazlyankov[1], Tihomir Ivanov[1]

[1]Faculty of Mathematics and Informatics,
Sofia University St. Kliment Ohridski, Bulgaria
gbazljanko@fmi.uni-sofia.bg
tbivanov@uni-sofia.bg

We study a Keller–Segel type partial differential equation model with logistic term and a flux-limiting chemotactic sensitivity function. The model aims to recreate the dynamics of immune cells after entering the central nervous system in the presence of a chemoattractant, as is the case in diseases such as multiple sclerosis.

We study traveling wave-type solutions as an intermediate asymptotic of the system as well as the different modes of pattern formation. Numerical experiments for the system are conducted, and the obtained solutions are compared to theoretical results derived for similar models such as special cases of Keller–Segel systems and the Fisher–KPP equation.

We derive a necessary condition for instability of the non-trivial steady state using Turing instability analysis. The numerically obtained solutions are used to illustrate the different modes of pattern formation—static, periodic, and irregular.

Keywords: immunology, partial differential equations, numerical analysis, traveling wave solutions, pattern formation

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Feasibility and optimisation of fly elimination by adult mass trapping and larval treatment : a stage-structured metapopulation approach

Pierre-Alexandre Bliman[1], Manon de la Tousche[1,3], Yves Dumont[2,3,4]

[1]Sorbonne Université, Université Paris Cité, CNRS, Inria, Laboratoire Jacques-Louis Lions, LJLL, EPC MUSCLEES, F-75005 Paris, France
pierre-alexandre.bliman@inria.fr, manon.de-la-tousche@inria.fr

[2]CIRAD, UMR AMAP, Pôle de Protection des Plantes, F-97410 Saint Pierre, France,
yves.dumont@cirad.fr

[3]AMAP, Univ Montpellier, CIRAD, CNRS, INRA, IRD, Montpellier, France

[4]University of Pretoria, Department of Mathematics and Applied Mathematics, Pretoria, South Africa

This work explores optimal strategies for the elimination of a fly population through adult mass trapping and larval treatment. Building on the results of [1] for (single-stage) metapopulation models with logistic growth, we extend here the analysis to a structured model that distinguishes between larvae, females and males. Linear migration of adults between patches is included, and the dynamic in each patch is inspired by the model in [2, 3].

Under appropriate conditions, we derive a condition that guarantees either elimination in all patches or convergence to a unique positive equilibrium.

Then, additional larval and adult mortality terms are introduced in a subset of 'controllable' patches, where intervention is allowed. We show that the feasibility of population elimination is determined by an algebraic property on the Jacobian at the origin of a so-called residual system. When elimination is feasible, the successful strategies that minimise a suitable treatment effort are analysed and compared with those established for the simpler logistic model considered in [1].

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Reinfection induced multistability in an epidemic model

Pierre-Alexandre Bliman, Marcel Fang

Sorbonne Université, Université Paris Cité, CNRS, Inria, Laboratoire Jacques-Louis Lions, LJLL, EPC MUSCLEES, France
pierre-alexandre.bliman@inria.fr
marcel.fang@inria.fr

We consider in this presentation the effects induced on the transmission of a disease with imperfect immunity, by differences between primary and subsequent infections (i.e. reinfections), due e.g. to differential susceptibility or differential infectiousness. To this end, an 8-dimensional *two-stage* SEIRS reinfection model that extends the classical SEIRS model [1] is proposed, in which the parameters characteristic of the disease dynamics are different between primary infections and secondary infections.

The number of steady states of this model is assessed, depending upon the parameter values. It is shown that the reinfection induced heterogeneity may cause up to two endemic equilibria when the basic reproduction number of the model is less than one, and up to three endemic equilibria when it is greater than one. This suggests that, according to the parameter values, the model may present backward bifurcation, a feature quite important from the point of view of disease control. Simulations confirm this situation. The persistence of the disease is also examined.

Finally, we turn our attention to the study of several models with partial immunity, which can be considered as particular cases of the previous one. Based on a geometric approach developed by Li and Muldowney [2], it is shown that every trajectory of these simpler models converges asymptotically to an equilibrium, which depends upon the initial condition in case of multistability. More details may be found in [3].

Keywords: compartmental models in epidemiology, reinfection models, multistability, backward bifurcation, persistence, Li and Muldowney theory

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Dynamics of prey-predator network model with application to virus and immune response evolution

Cameron Browne

Department of Mathematics,
University of Louisiana at Lafayette, USA
cambrowne@louisiana.edu

Recent work has sought to understand assembly and coexistence of interacting species in ecosystem models. However, the overwhelming number of species combinations and connecting the models to evolution have challenged researchers, especially in higher dimensional systems. Here, we aim to address this gap by looking through an evolutionary genetics lens in a prey-predator model of virus-immune dynamics, where viral variants can be represented by binary sequences which encode their resistance to immune responses. First, persistence and stability of equilibria are studied using Lyapunov functions and invasion analysis. Then, bifurcations between distinct ecological network structures are linked to epistasis (non-additivity) in the viral fitness landscape. Results are discussed in the context of HIV escape of host immune responses and, more generally, finding simplifying rules for prey-predator network evolution.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

A model for biological transport gTASEP with OBC: some recent rigorous results

Nadezhda Zh. Bunzarova[1], Alexander M. Povolotsky[2], Nina C. Pesheva[1]

[1]Institute of Mechanics,
Bulgarian Academy of Sciences, Bulgaria
nadezhda@imbm.bas.bg
nina@imbm.bas.bg

[2]Bogoliubov Laboratory of Theoretical Physics,
Joint Institute for Nuclear Research, Dubna, Russia
alexander.povolotsky@gmail.com

Here we provide a brief overview of the applications of the Totally Asymmetric Simple Exclusion Process (TASEP) to various biological transport processes [1] and some recent developments in the study of the generalized TASEP (gTASEP) [2]. The TASEP is essentially a one-dimensional model where particles move unidirectionally along one-dimensional tracks, jumping probabilistically to the nearest empty neighboring site, subject to a hard-core exclusion interaction. In the generalized version, additional interaction is introduced between particles, modeling attractive or repulsive interaction between particles.

The process was first introduced in 1968 to model kinetics of protein synthesis [3], but later found a number of applications to other biological transport processes, e.g., the motion of molecular motor proteins, kinesin and dynein along microtubules, a process that accounts for nearly all intracellular transport in eukaryotic cells etc. Many other applications were suggested as well describing diverse phenomena, ranging from one-lane vehicular traffic flow, transport in chemical systems, forced motion of colloids in narrow channels, interface growth etc. Even though the TASEP is very simple model, it captures key characteristics of these systems while remaining an analytically solvable model.

The one-dimensional (T)ASEP (and its different versions) is a useful toolmodel for understanding a variety of nonequilibrium phenomena [4]. It represents one of the simplest examples of self-driven many-particle systems with particle-conserving stochastic dynamics, exhibiting nontrivial behavior in one dimension through phase transitions between stationary nonequilibrium phases. The gTASEP enables the investigation of aggregation-fragmentation phenomena, fluctuations, and finite-size effects in nonequilibrium stationary states influenced by boundary conditions.

Over the past few years, research on nonequilibrium models has advanced rapidly; however, the aim remains to study model systems that provide more realistic approximations of real systems. Here, our focus is on one such model – the generalized TASEP (gTASEP) [2, 5].

Keywords: nonequilibrium model systems, nonequilibrium phase transitions, nonequilibrium stationary states, traffic flow, biological transport

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical modeling of innate immune response dynamics in early-stage inflammation

Mehtap Lafcı Büyükkahraman

Department of Mathematics,
Uşak University, Uşak, 64200, Türkiye
mehtap.lafci@usak.edu.tr

Innate immune cells respond to infections by triggering an acute inflammatory reaction that restores tissue homeostasis and promotes subsequent repair. Their activation must be tightly regulated to prevent tissue damage, organ dysfunction, or even death. This study presents a new set of mathematical models to analyze the dynamics of the innate immune response to tissue damage and to improve our understanding of its role in early-stage inflammation. Various damaged cell production functions are introduced to account for secondary tissue damage caused by the immune system. Stability and bifurcation analysis reveal a critical threshold parameter that can be regulated to prevent chronic inflammation and ensure successful healing. Numerical simulations further support the theoretical findings and highlight the medical relevance of the proposed model.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

A double free boundary model for biofilm growth and microbially induced corrosion in wastewater concrete pipes

Antonella Capuozzo, Alberto Tenore, Fabiana Russo, Luigi Frunzo

Department of Mathematics and Applications,
University of Naples, Italy
antonella.capuozzo2@unina.it
alberto.tenore@unina.it
fabiana.russo@unina.it
luigi.frunzo@unina.it

Microbially induced corrosion (MIC) is a significant global issue impacting infrastructure, economies, and environment. In wastewater systems, MIC is primarily associated with biofilm formation on concrete sewer pipes, leading to severe degradation due to microbial metabolic activity. The proliferation of sewer biofilms occurs in both submerged and unsubmerged conditions, leading to distinct microbial communities. Commonly, these biofilms host microorganisms such as fermentation bacteria, hydrogen-producing acetogens, denitrifying bacteria, sulfate-reducing bacteria, sulfur-oxidizing bacteria, and methanogens. In particular, sulfur-oxidizing bacteria play a crucial role in corrosion, as they oxidize hydrogen sulfide from wastewater effluents, generating sulfuric acid that accelerates concrete deterioration.

A one-dimensional model with double free boundaries has been developed to investigate the proliferation of biofilms and the related corrosion process in wastewater concrete pipes. The domain is composed of two free boundary regions: a biofilm that grows towards the interior cavity of the pipe, sitting on a gypsum layer formed by corrosion, which penetrates the concrete pipe. Diffusion-reaction equations govern the transport and the metabolic production or consumption of dissolved substances, such as hydrogen sulfide, oxygen, and sulfuric acid within the biofilm layer. The biofilm free boundary tracks the growth of the microbial community, regulated by microbial metabolic activity and detachment phenomena. The corrosion process is incorporated into the model through a Stefan-type condition, which drives the advancement of the gypsum free boundary into the concrete pipe, governed by microbial production of sulfuric acid.

Numerical simulations have been carried out to investigate the model behavior, encompassing the development and progression of the biofilm as well as the corrosion advancement, with the aim of elucidating the key factors governing both phenomena.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Beyond impaired DNA repair: Exploring the radiosensitizing mechanisms of hyperthermia through mathematical modeling and Monte Carlo simulations

Adriana M. De Mendoza[1], Edwin Munévar[2], Cesar Herreño[2], Jose L. Rodríguez[2], Diego A. Rodríguez[3]

[1]Faculty of Sciences – Physics Department,
Pontificia Universidad Javeriana, Colombia
a.demendoza@javeriana.edu.co

[2]Faculty of Science and Education,
Universidad Distrital – Francisco José de Caldas, Colombia
emunevare@udistrital.edu.co
caherrenof@udistrital.edu.co
jolrodrigueza@correo.udistrital.edu.co

[3]Faculty of Sciences,
Universidad Nacional de Colombia, Colombia
dirodriguezco@unal.edu.co

Hyperthermia therapy (HT) presents significant advantages when compared to other alternatives in the fight against cancer. HT is relatively inexpensive and is among the most effective and least toxic treatments for patients. Heat is a form of energy that does not produce secondary (or higher orders) radiation and does not lead to secondary tumors as part of its side effects [1]. Localized heat, among other effects on the body, has the potential to improve blood perfusion and tumor oxygenation, in addition to stimulating the immune system. Due to these features, HT also works as a powerful sensitizer of other therapeutic modalities such as radiotherapy, reducing the doses, therefore improving the treatment's effectiveness and reducing side effects [2]. The synergy between radiotherapy and hyperthermia is widely documented across *in vitro*, *in vivo*, and clinical studies, offering rich hypotheses for therapeutic benefits.

While HT exhibits promise in enhancing cancer treatment efficacy, it has not yet achieved standard care status due to: (1) Technical Challenges: Achieving precise and uniform heating in the targeted area poses technical difficulties, (2) Ongoing Device Development: HT devices with the required precision are

still in development, and (3) Integration Complexity: Achieving seamless integration with standard cancer treatments poses a challenge, requiring further research for optimal timing, sequencing, and combination of therapies [3]. The development of accurate mathematical models is pivotal for predicting treatment outcomes and facilitating the integration of HT into the clinical workflow [4, 5, 6]. Overcoming these challenges through ongoing research and technological advancements is crucial for establishing hyperthermia as a standard care protocol.

In this study, we develop mathematical models to better understand and predict the effects of heat, especially when combined with ionizing radiation simultaneously or sequentially. To this end, we investigate the causes of thermal enhancement by examining DNA rupture probability. Theoretical calculations reveal that temperature-dependent variations in DNA-ion interactions may affect therapeutic outcomes, and Monte Carlo simulations using the Geant4 toolkit support this hypothesis. Our theoretical calculations and simulations indicate that the radiosensitizing effect of HT depends on the temperature effects on 4 factors: the cellular capacity for DNA repair, the vulnerability of the bonds in the DNA, DNA cross-section, and DNA density. This research thus provides unique insights into multifaceted processes shaping radiosensitization.

Keywords: hyperthermia therapy (HT), radiosensitization, DNA damage, mathematical modeling

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

From guesswork to groundwork: A tool to quantify disease upscaling decisions

Afonso Dimas Martins[1], Frits Vlaanderen[1], Lapo Mughini Gras[1,2]

[1]Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment), The Netherlands
afonso.moreira.dimas.martins@rivm.nl

[2]Faculty of Veterinary Medicine, Utrecht University, The Netherlands

When a disease outbreak is first detected, experts must decide whether that disease should be *upscaled* – that is, if it should be promoted to a higher priority ranking. This means more resources should be invested into containing this outbreak and in many cases it could also mean alerting the general public. All of this is resource-intensive so making sure that we correctly capture the true positives is vital. Experts have regular meetings and collectively assess factors such as how many people have tested positive, whether transmission between animals has been detected, and other variables. The issue is that, at the moment, this is done relying heavily on guesswork: the final decisions come down to qualitative judgment, and may be subject to unconscious biases. We adapt classifier models such as random forests and XGBoost models to turn this decision-making more quantitative, by taking into account several intrinsic factors of each disease and historical information of previous upscalings. With this ongoing project, we aim to develop a systematic data-driven groundwork to estimate the probability of scaling up a disease, and create a user-friendly tool to guide evidence-based decisions in public health.

Keywords: machine learning, public health, outbreak prioritization, data-driven decision-making

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Application of the information entropy and machine learning algorithms for the prediction of peptide binders to the HLA-DRB1*03:01 allele

Ivan Dimitrov, Mariyana Atanasova, Irini Doytchinova

Faculty of Pharmacy,
Medical University of Sofia, Bulgaria
idimitrov@pharmfac.mu-sofia.bg
matanasova@pharmfac.mu-sofia.bg
idoytchinova@pharmfac.mu-sofia.bg

The HLA-DRB1*03:01 allele is a known genetic risk factor for several autoimmune diseases, including systemic lupus erythematosus, type 1 diabetes, early-onset myasthenia gravis, Sjögren's syndrome, and autoimmune hepatitis type 1. As a key component of the antigen presentation pathway, HLA-DRB1*03:01 has also been associated with allergy and asthma. Predicting peptide binders to this allele could aid in identifying potential antigens linked to these critical autoimmune disorders.

In this study, we applied machine learning algorithms to a dataset of peptides with known binding affinity to the HLA-DRB1*03:01 allele. The information entropy for each peptide was calculated using numerical descriptors representing various physicochemical properties of the amino acids in the peptide sequence. This transformation converted peptide sequences into a numerical matrix, where each vector contained the calculated information entropy for different descriptors.

The dataset was split into training and test sets (80/20 ratio), and an iterative self-consistent algorithm was employed to determine the binding core of each peptide in the training set. Regression models were then used to predict binding affinity to the HLA-DRB1*03:01 allele. The derived models were validated on the test set, and an appropriate classification cutoff was determined.

The performance of the machine learning models was evaluated using classification metrics, revealing that the XGBoost and Support Vector Machine (SVM) models demonstrated superior results, achieving high sensitivity and accuracy.

*Keywords: information entropy, machine learning, HLA-DRB1*03:01 binding prediction*

Mathematical Methods and Models in Biosciences
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New results on the combination of Sterile Insect Technique and enthomopathogenic fungi

Yves Dumont

CIRAD, UMR AMAP, Pôle de Protection des Plantes, Saint Pierre, France
AMAP, Univ Montpellier, CIRAD, CNRS, INRA, IRD, Montpellier, France
Department of Mathematics and Applied Mathematics,
University of Pretoria, South Africa
yves.dumont@cirad.fr

Since 2017, *Bactrocera dorsalis*, the oriental fruit fly, has invaded Réunion island, causing significant damage to many crops, particularly mango orchards. It is necessary to combat this pest, using biological control methods [1].

The Sterile Insect Technique (SIT) is an old autocidal method used against pest and vectors of diseases. It is based on the releases of sterile males supposed to mate with wild females, such that the sterile-mated females will have no offspring, leading to a progressive decay of the wild population. Many SIT models have been developed taking into account that only one mating occurs. In fact, for many fruit flies species, like *Bactrocera dorsalis*, this is not the case: re-mating can occur after a certain time after the first mating. In addition, sterile males are not necessarily 100% sterile: residual fertility can occur such that sterile-mated females may deposit a certain proportion of viable eggs, ε.

In [2], we have developed a complex model to take into account these issues. In particular, we show that SIT is efficient, i.e. elimination is possible, only if $\mathcal{R}_S\varepsilon < 1$, where $\mathcal{R}_S$ is the basic offspring number related to the single and double-mated sterile females. We improve the result obtained in [3].

Then, we consider SIT in combination with an enthomopathogen soil's fungi that is used to control the fruit fly at the pupae stage. We show that this combination relax the constraint on the residual fertility and also decay the critical release rate. This works is part of the AttracTIS project, funded by Ecophyto 2021-2022.

Keywords: sterile insect technique, enthomopathgen fungi, dynamical systems, monotone systems, residual fertility, re-mating, oriental fruit fly

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Long term human-environment dynamics in a peri-forest context

Yves Dumont[1,2,3], Marc Hétier[2], Valaire Yatat-Djeumen[2,4]

[1]CIRAD, UMR AMAP, 3P, F-97410 Saint Pierre, France,
[2]AMAP, Univ Montpellier, CIRAD, CNRS, INRA, IRD, Montpellier, France
yves.dumont@cirad.fr, marc.hetier@cirad.fr

[3]University of Pretoria, Department of Mathematics and Applied Mathematics, Pretoria, South Africa

[4]ENSPY, University of Yaoundé 1, Cameroon
valaire.yatat@univ-yaounde1.cm

In Central Africa, population growth is increasing the demand for resources, leading to significant changes in forest ecosystems. Human activities like infrastructure development, road construction, and over-hunting threaten both vegetation and wildlife [1]. This anthropization of the natural landscape raises concerns about the ecosystem's sustainability and impacts food and health security for forest-dependent communities [2]. We present and study a dynamical system to model human-environment interactions. Based on the fact that the human population relies on food availability, provided either from domestic sources (agriculture, breeding) or from hunt, we assume that the interactions between human population and the environment are limited to hunting activities, which reflect what happens in South Cameroon [3]. The theoretical analysis of the model shows that different kind of dynamics are possible. We identify the conditions on the hunting rate under which humans and wild fauna can coexist, as well as how anthropization may affect those conditions.

This work takes place within the I-CARE project, funded by ExposUM Institute of the University of Montpellier, Occitanie Region, and the investment programme France 2030, ANR-21-EXES-0005.

Keywords: Human-environment Modelling; Dynamical System; Monotone systems; Anthropization; Forest-dependent Wildlife

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical modelling in preclinical drug development in oncology: A perspective from the industry side

Ján Eliaš

Boehringer Ingelheim RCV, Vienna, Austria
jan.elias@boehringer-ingelheim.com

The integration of mathematical modelling in preclinical drug development has profoundly impacted the pharmaceutical industry, enabling more precise and predictive insights into drug behavior. This approach is particularly transformative in the development of Proteolysis-Targeting Chimeras (PROTACs), a novel therapeutic modality that leverages the ubiquitin-proteasome system for targeted protein degradation. By employing mathematical models, we can simulate the pharmacokinetics and pharmacodynamics of PROTACs, optimizing their design and efficacy in cancer research and immunology, and other therapeutic areas. These models facilitate the prediction of PROTAC behaviour in complex biological systems, enhancing our understanding of their therapeutic potential and accelerating their transition to clinical use. In this presentation, we will cover various aspects of these mathematical models, including their application in optimizing PROTAC design and predicting therapeutic in-vivo outcomes, such as target engagement and tumour growth inhibition.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Sensitive detection of copy number alterations in low-quality liquid biopsy sequencing data

Lotta Eriksson, Eszter Lakatos

Department of Mathematical Sciences,
Chalmers University of Technology, Sweden
lottaer@chalmers.se
eszter.lakatos@chalmers.se

Liquid biopsies, coupled with analysis of copy number alterations (CNAs), have emerged as a promising tool for non-invasive monitoring of cancer progression and tumor composition. CNAs, which involve large genomic gains or losses, are prevalent in cancer and can be detected using low-pass liquid biopsy sequencing. This approach offers a cost-effective and minimally invasive alternative to traditional tissue biopsies. However, methods utilizing CNA data from liquid biopsies are limited by the low signal in the samples, caused by a low percentage of cancer DNA in the blood, and the inherent noise introduced during sequencing, which limits the strength of the detectable signal. To address this challenge, we employ a Bayesian changepoint detection algorithm [1, 2] to improve signal detection from low-pass liquid biopsy sequencing. We identify positions in the genome with high posterior changepoint probability to identify the locations of CNAs. We show the effectiveness of the method on synthetically generated datasets, and compare the method to state-of-the-art bioinformatics tools under noisy conditions. Our results show that this novel approach increases sensitivity in detecting CNAs, particularly in low-quality cases.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modelling vectorial capacity and optimising vector control across reservoir and dead-end hosts

Emma L. Fairbanks[1], Matthew Baylis[2], Janet M. Daly[3], Mike J. Tildesley[1]

[1]The Zeeman Institute for Systems Biology & Infectious Disease Epidemiology Research, Mathematics Institute and School of Life Sciences, University of Warwick, UK
emma-louise.fairbanks@warwick.ac.uk

[2]Institute of Infection, Veterinary and Ecological Sciences, Faculty of Health and Life Sciences, University of Liverpool, UK

[3]One Virology – Wolfson Centre for Global Virus Research, School of Veterinary Medicine and Science, University of Nottingham, UK

Vector-borne disease transmission involves complex interactions between vectors, reservoir hosts and dead-end hosts. Our research extends existing mathematical models of vectorial capacity [1] by incorporating multiple host types and their interactions, focusing specifically on West Nile Virus transmission by *Culex pipiens* mosquitoes. We demonstrate how vector control interventions targeting one host type can significantly impact transmission dynamics across all host populations. Our model integrates climate-dependent parameters affecting vector biology with vector control interventions to predict transmission potential under various scenarios. By examining the effects of different vector control tool modes of action (repellency, preprandial killing, disarming and postprandial killing), we develop target product profiles that minimise unintended consequences of vector control. Notably, we identify the optimal intervention characteristics needed to prevent repellency on dead-end hosts from inadvertently increasing transmission among reservoir hosts. This research provides valuable insights for public health officials designing targeted vector control strategies and offers a flexible modelling framework that can be adapted to other vector-borne diseases with complex host dynamics.

Keywords: arbovirus, medical entomology, epidemiology, target product profiles

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Comparing methods for novel insecticide-treated net evaluation for malaria control

Emma L Fairbanks[1], Olukayode Odufuwa[2,3,4,5], Alphonce Assenga[2], Raphael N'Guessa[5,6], Sarah Moore[2,3,4,7]

[1]The Zeeman Institute for Systems Biology & Infectious Disease Epidemiology Research, Mathematics Institute and School of Life Sciences, University of Warwick, UK
emma-louise.fairbanks@warwick.ac.uk

[2]Vector Control Product Testing Unit, Ifakara Health Institute, Tanzania
[3]Vector Biology Unit, Swiss TPH, Switzerland
[4]University of Basel, Switzerland
[5]London School of Hygiene and Tropical Medicine, UK
[6]London Institut Pierre Richet, Côte d'Ivoire
[7]The Nelson Mandela African Institution of Science and Technology, Tanzania

Our research compares two important evaluation methods for insecticide-treated nets (ITNs): semi-field Ifakara Ambient Chamber tests (I-ACT) and experimental hut trials. Using mathematical modelling and Bayesian inference, we analysed how these different bioassays affect assessment outcomes of ITN efficacy against *Anopheles gambiae* and predictions of reduced malaria transmission. While I-ACT and experimental huts show different patterns in estimating specific mosquito behavioral responses, both methods ultimately yield similar predictions for overall reduction in vectorial capacity–a key metric for disease control transmission potential. This finding has significant implications for ITN evaluation strategies, suggesting that semi-field tests can provide reliable initial assessments of vector control efficacy with advantages of faster data collection and flexibility in testing different mosquito strains. Our modelling framework allows for location-specific predictions by incorporating regional vector behaviour patterns, offering a valuable tool for comparing ITN performance across diverse settings. As the malaria control landscape evolves with new dual-active ingredient nets, this approach can help assist country programs in selecting the most appropriate interventions for their specific contexts. This research advances our understanding of how bioassay evaluations translate to real-world effectiveness, supporting more efficient development and deployment of vector control tools.

Keywords: Medical entomology, Epidemiology, Semi-field, Bayesian inference

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Inverse modelling of honeybee hives weight dynamics

Atanas Atanasov[1], Slavi Georgiev[2,3], Lubin Vulkov[3]

[1]Department of Agricultural Machinery, Agrarian and Industrial Faculty, University of Ruse, Bulgaria
aatanasov@uni-ruse.bg

[2]Department of Informational Modelling, Institute of Mathematics and Informatics, Bulgarian Academy of Sciences, Bulgaria
sggeorgiev@math.bas.bg

[3]Department of Applied Mathematics and Statistics, University of Ruse, Bulgaria
lvalkov@uni-ruse.bg

A detailed quantitative analysis of bee colony dynamics is essential for supporting global initiatives aimed at enhancing bee health and bolstering pollination activities. Critical metrics, such as foraging efficiency and the number of actively foraging bees, play a vital role in developing predictive early-warning systems for identifying potential colony collapse or decline.

Mathematical and informational modeling emerges as an indispensable tool in this context, providing structured insights into complex colony behaviors and interactions. Particularly, precise calibration of these mathematical models is of paramount importance. In this paper, we solve ODE inverse problem to fit the complex dynamics of the bees within a hive, and to study their complicated behaviour during the day, which includes foraging and producing honey [1]. By accurately calibrating models to collected data, one can refine predictions, better understand underlying mechanisms of colony dynamics, and formulate effective interventions to safeguard bee populations and their critical ecosystem services. Computational results with synthetic and realistic data are discussed.

Keywords: honeybee population dynamics, daily weight variation, least-squares fitting

MSC2020: 34A55, 65L09, 92D25

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

On the robustness of oscillations in a mixed mechanism phosphorylation system against perturbations in the total amount of the processive enzyme

Kim-Joao Grasse, Carsten Conradi

HTW Berlin – University of Applied Sciences, Germany
kim-joao.grasse@htw-berlin.de
carsten.conradi@htw-berlin.de

Many biochemical oscillators exist, and this work aims to analyse substrate cycles able to oscillate, shown by a periodical in- and decrease in the concentrations of the individual components. Such biochemical oscillators are one of the mechanisms involved in the timekeeping of organisms and the maintenance of the circadian rhythm. Mechanisms sustaining the circadian rhythm ought to be robust against perturbations, because if changes in concentrations of one or more components were to significantly change the properties of the oscillation, the circadian rhythm and hence the timekeeping of the organism would be impaired. Mixed systems consist of a processive and a distributive enzyme. Suwanmajo and Krishnan described a system that consists of a processive phosphorylation and a distributive dephosphorylation [1].

Conradi et al. have already proven that this system can exhibit oscillations, and that these oscillations are robust against variations in the total amount of kinase, the processive enzyme [2]. A similar system consists of a distributive phosphorylation and processive dephosphorylation. We study oscillations and their robustness against perturbations in the total amount of phosphatase, the processive enzyme.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Multi-scale models of infectious disease dynamics and validating with data

Hayriye Gulbudak

Department of Mathematics,
University of Louisiana at Lafayette, USA
hayriye.gulbudak@louisiana.edu

The bidirectional feedback induced through population and individual-level infectious disease and host immune dynamics requires development of innovative multi-scale models. In this talk, I will introduce structured nonlinear partial differential equation models linking immunology and epidemiology, along with novel stability analysis and computational tools for simulating ODE-PDE hybrid systems to understand the nonlinear dynamics and apply them to biological data. Applying the modeling framework to dengue virus, we first demonstrate how intermediate levels of antibodies enhance infection severity within a host, and scale up to population wide antibody level distributions evolving through multiple infections by distinct strains and waning immunity. Then, to test the theoretical results, we fit primary and secondary dengue infection data to provide evidence of antibody dependent enhancement. These results have critical implications for optimal vaccination policy, and the modeling framework is currently being applied to examine the emergence of COVID-19 variants.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Matched asymptotic analysis of the Luria-Delbrück distribution in a reversible fluctuation assay

Anna Hlubinová[1], Pavol Bokes[1], Abhyudai Singh[2]

[1]Department of Applied Mathematics and Statistics,
Comenius University, Slovakia
anna.hlubinova@fmph.uniba.sk
pavol.bokes@fmph.uniba.sk

[2]Department of Electrical and Computer Engineering,
Biomedical Engineering, University of Delaware, USA
absingh@udel.edu

We study a fluctuation test where cell colonies grow from a single cell to a specified population size before undergoing treatment. During growth, cells may acquire resistance to treatment and pass it to their offspring with a small probability. Unlike the classical Luria–Delbrück test, which assumes irreversible resistance, our model allows resistant cells to revert to a drug-sensitive state. This modification, motivated by recent research on drug resistance in cancer and microbial cells, does not alter the central part of the Luria–Delbrück distribution, where the Landau probability density function approximation remains applicable. However, the right tail of the distribution deviates from the power law of the Landau distribution, with the correction factor given by the Landau cumulative distribution function. Using singular perturbation theory and asymptotic matching, we derive uniformly valid approximations and describe tail corrections for populations with different initial cell states.

Keywords: Luria-Delbrück fluctuation test, reversible state switching, mutation rate, Landau distribution, mathematical modeling

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical modelling of the neuromuscular activity of a motor unit

Zdravka D. Ivanova[1], Tihomir B. Ivanov[1], Rositsa T. Raikova[2]

[1]Faculty of Mathematics and Informatics,
Sofia University "St. Kliment Ohridski", Bulgaria
zivanova@fmi.uni-sofia.bg
tbivanov@fmi.uni-sofia.bg

[2]Institute of Biophysics and Biomedical Engineering,
Bulgarian Academy of Sciences, Bulgaria
rosi.raikova@biomed.bas.bg

The excitability of α-motoneurons and muscle cells and their corresponding behaviour is essential for the understanding of muscle contraction and neuromuscular diseases. Mathematical models, capable of accurately simulating muscle contraction, are very useful not only for the better understanding of the underlying processes, but also for numerous bio- and biomedical engineering applications. However, the precise mathematical description even of a single motor unit (MU) twitch, i.e., a single contraction of the MU—the basic functional unit in the skeletal muscle, has shown to be a very challenging task. To the best of the authors' knowledge there are no models describing the underlying mechanisms of the process, which have been fitted with a high level of accuracy to experimental data for a MU twitch.

In the present work, we present an integrated mathematical model of the neuromuscular activity of a motor unit. It is described in terms of ordinary differential equations and couples the models of Izhikevich of neural activity, the Williams model of calcium activity in the muscle fiber, and a Hill-type model of the resultant muscle force. We have introduced an important novelty in the coupling of the latter two, by introducing a sigmoid activation function, which significantly improves the descriptive capabilities of the model from a quantitative point of view. We have validated the model by fitting with a high degree of accuracy experimental data for twitches of nine different motor units (slow, fast fatigable, fast fatigue-resistant)—a result, which is not known in the scientific literature with a descriptive model. We also study numerically and show how the model parameters affect the model solution.

As a result, the present work provides a computational framework, under which one can perform computer simulations, or process and analyze real experimental data of neuromuscular activity and in the same time relate the findings

to main characteristics of the underlying processes. We believe that at present such a framework is missing, but very much needed, in order to computationally study and/or obtain valuable hypotheses for many aspects of the motor unit activity, such as, e.g., neuromuscular disorders.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modeling malaria transmission with age structure: Insights from case studies in Senegal

Rama Seck[1], Diene Ngom[2], Benjamin Ivorra[3], Angel M. Ramos[3]

[1]Laboratory of Numerical Analysis and Computer Science,
Applied Mathematics Section, Gaston Berger University, Senegal
seck.rama@ugb.edu.sn

[2]Mathematics and Applications Laboratory, Mathematics Department,
Assane Seck University, Senegal
dngom@univ-zig.sn

[3]Interdisciplinary Mathematics Institute (IMI) and
Department of Applied Mathematics and Mathematical Analysis,
Complutense University of Madrid, Spain
ivorra@ucm.es
angel@mat.ucm.es

Malaria remains one of the most significant global health threats, especially in tropical regions. To better understand its transmission dynamics, we propose an age-structured mathematical model incorporating both human and mosquito populations. Our model classifies humans into children and adults, considering distinct infection and immunity dynamics for each group, while also incorporating the life stages of the mosquito population.

First, we perform a mathematical analysis of the model. The stability of the Disease-Free Equilibrium is studied using a matrix-tree theorem, while we analyze the global asymptotic stability of the Endemic Equilibrium via graph-theoretical techniques. Additionally, numerical experiments suggest that our stability results may hold under more general conditions.

To demonstrate the practical relevance of our model, we calibrate it using real-world data from two malaria-endemic areas in Senegal: Dielmo and Ndiop. The results highlight the importance of considering age structure and localized parameters in malaria modeling. This approach provides valuable insights for designing effective control strategies tailored to specific demographic and geographic contexts.

Keywords: epidemiological modeling, malaria, deterministic models
MSC2020: 92D30, 92C60

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Mathematical Methods and Models in Biosciences
June 15-20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Cramér-von Mises statistic for continuous distributions: A Monte-Carlo study for calculating its associated probability

Lorentz Jäntschi

Department of Physics and Chemistry,
Technical University of Cluj-Napoca, Cluj, Romania
lorentz.jantschi@chem.utcluj.ro

Literature is abundant on the uses of the Cramér-von Mises test in biological and earth sciences (see for instance [1]), for comparing observed distributions of phenomena against theoretical models and for testing if certain data, like gene expression levels and physiological measurements follow a theoretical distribution as prerequisite in applying parametric statistical methods.

The Cramér-von Mises criterion [2, 3] is used for judging the goodness of fit of a cumulative distribution function. Well-known alternatives to Cramér-von Mises include Watson U^2, Kolmogorov-Smirnov, Kuiper V, and Anderson–Darling. All listed here have something important in common: belongs to the category of order statistics, fundamental tools in non-parametric statistics and inference. A key element related to order statistics of random samples from a continuous distribution, is the fact that the cumulative distribution function reduces the analysis to the case of order statistics of the uniform distribution. In a nutshell, having a very good generator for uniform distributed samples, significantly increases the chances of success for any Monte-Carlo experiment with the order statistics.

A general procedure, described in [4], applicable for any order statistic was particularized for the Cramér-von Mises criterion and a large amount of data was generated. Furthermore, regression analysis was deployed in order to obtain the dependence of the probability as function of the the value of the statistic and of the sample size. The analysis includes a variational analysis, so for the obtained regression coefficients also confidence limits were provided.

Keywords: Monte-Carlo simulation, Cramér-von Mises criterion, goodness-of-fit tests

MSC2020: 62G30, 62P10, 65C05

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modeling activation of pregnane X receptor and mRNA expression of cytochromes P450 in 3D primary human hepatocytes

Ellen Tanaka Kahiya[1], Tomáš Smutný[2], Jurjen Duintjer Tebbens[1], Petr Pávek[2], Veronika Bernhauerová[1]

[1]Department of Biophysics and Physical Chemistry,
[2]Department of Pharmacology and Toxicology,
Faculty of Pharmacy, Charles University, Czech Republic
kahiyae@faf.cuni.cz
smutt6aa@faf.cuni.cz
jurjend@faf.cuni.cz
pavek@faf.cuni.cz
bernhauve@faf.cuni.cz

Pregnane X receptor (PXR) regulates the expression of cytochrome P450 (CYP) enzymes in the liver [1] and thus plays a crucial role in the metabolism of various drugs. Rifampicin (RIF) is a model PXR ligand [1] and forms its primary metabolite 25-desacetyl rifampicin (25-DRIF) [2]. In our previous study, we showed that quantification of PXR activation and its downstream effects on CYP enzymes in response to treatment with RIF is possible using mathematical modeling and the long-term experimental measurements of PXR-controlled CYP mRNA expression obtained from 3D primary human hepatocytes (3D PHHs) [3]. However, these effects may vary depending on ligand concentration and type. Here, we combine mathematical modeling with experimental data to quantitatively distinguish the effects of RIF and 25-DRIF on PXR activation and PXR-dependent transcription of CYP3A4, CYP2C9, and CYP2B6 in 3D PHHs. Our model estimated that 20 µM of 25-DRIF was required to achieve 78% PXR activation, a level comparable to the activation induced by 1 µM of RIF in [3]. 200 µM of 25-DRIF resulted in nearly maximal (99%) PXR activation, a level comparable to the activation achieved by 10 µM of RIF in [3]. We evaluated that the PXR-dependent rate constant controlling transcription of CYP3A4 was higher than that of CYP2B6 in 3D PHHs treated with 25-DRIF whereas the opposite was observed in 3D PHHs treated with RIF. In addition, the PXR-dependent rate constant controlling transcription of CYP3A4 was estimated to be higher in 3D PHHs treated with 25-DRIF than in 3D PHHs treated with RIF. The rate constant controlling PXR-dependent transcription

of CYP2C9 was the same in RIF- and 25-DRIF-treated 3D PHHs. Our results provide quantifications of the ligand-specific nature of PXR activation and suggest that transcription of PXR-controlled CYP enzymes in 3D PHHs may also be CYP-specific.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Exploring the polyreactivity of monoclonal antibodies using igome graphs

Elena Keskinova, Anastas Pashov

Institute of Microbiology,
Bulgarian Academy of Sciences, Bulgaria
eli.keskinova@gmail.com
a_pashov@microbio.bas.bg

Antibody repertoires are studied at the system level using two approaches: high throughput B cell receptor sequencing and high throughput binding experiments using phage display random peptide libraries (igome) or antigen arrays. While the latter can provide insights into the sequences recognized by a mixture of antibodies, such as serum antibodies, it does not reveal the contribution of individual antibodies to the overall reactivity. To bridge this gap, we first need to understand the footprints of single antibodies in the space of mimotopes.

Using the igome data from Ashkenazy et al. [1], we analyzed the structure of the repertoire of 4 different monoclonal antibodies: 3 anti-HIV antibodies and Herceptin. We constructed graphs where nodes represent 7-mer peptide mimotopes, and edges indicate shared subsequences of at least five amino acid residues. With the help of spectral embedding and the Leiden algorithm for graph clustering, we identified groups of highly similar peptides. Such clusters, summarized as sequence motifs, are hypothesized to correspond to different specificities of the antibody.

Our analysis reveals that each antibody has biologically relevant affinity to multiple different mimotope groups with distinct sequence motifs. This supports the idea that even highly specific antibodies can exhibit polyreactivity.

The reported approach provides a framework for dissecting individual antibody specificities and could be utilized to uncover their role in shaping the broader human antibody repertoire.

Keywords: antibody repertoire, graphs, bioinformatics

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

A SIMPL model of phage-bacteria interactions accounting for mutation and competition

Carli Peterson[1], Darsh Gandhi[1], Austin Carlson[1], Aaron Lubkemann[1], Emma Richardson[1], John Serralta[2], Michael S. Allen[2], Souvik Roy[1], Christopher M. Kribs[1,3], Hristo V. Kojouharov[1]

[1]Department of Mathematics,
The University of Texas at Arlington, Arlington, USA
hristo@uta.edu

[2]Department of Microbiology, Immunology, and Genetics,
The University of North Texas Health Science Center, Fort Worth, USA

[3]Department of Teacher and Administrator Preparation,
The University of Texas at Arlington, Arlington, USA

Pseudomonas aeruginosa is an opportunistically pathogenic bacteria that causes fatal infections and outbreaks in hospital environments. Due to the increasing prevalence of antibiotic-resistant strains of *P. aeruginosa*, the need for alternative therapies is critical. Bacteriophage therapy is emerging as a promising approach; however, it remains unapproved for clinical use and is hindered by limited understanding of the complex interactions between bacterial cells and phage virions. Mathematical models provide insight into these interactions. Through a system of ordinary differential equations, we determined necessary biological assumptions to effectively capture the dynamics observed between susceptible, infected, and mutated bacterial cells and bacteriophage virions in a microwell setting. Data fitting based on this model produced a set of parameter estimates unique to our experimental observations of a specific phage and *P. aeruginosa* strain. In translating observed optical density readings into bacterial concentrations, we also found that bacterial debris has a significant impact on optical density, with a lysed bacterium contributing roughly 31% as much to optical density readings as a living cell.

Keywords: pseudomonas aeruginosa, optical density, bacterial dynamics, bacterial debris, non-isolated equilibria, parameter fitting, optimization

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Understanding the impact of social contact patterns in epidemiological models

Evans Kiptoo Korir, Zsolt Vizi

Bolyai Institute,
National Laboratory for Health Security,
University of Szeged, Hungary
evanskorir6@gmail.com
zsvizi@math.u-szeged.hu

Respiratory infections such as influenza and COVID-19 primarily spread through social contacts that vary by age, making it critical to understand how interaction patterns influence disease transmission. Age-structured contact matrices play a central role in epidemic modeling; however, obtaining accurate and representative data remains a challenge, especially in low-resource settings.

This talk presents two complementary sensitivity analysis frameworks applied to an age-structured COVID-19 model. The first approach combines Latin Hypercube Sampling with Partial Rank Correlation Coefficients (LHS-PRCC) to assess how variations in contact matrix elements influence transmission outcomes. The second approach is based on eigenvector perturbation analysis of the Next Generation Matrix, providing insights into how specific age-group interactions contribute to changes in the basic reproduction number ($\mathcal{R}_0$). Together, these methods offer a robust understanding of the role of age-structured contact patterns in shaping epidemic dynamics.

Using contact data from Hungary, we identify the most influential age-group interactions driving epidemic spread. Our findings offer actionable insights for optimizing public health interventions, particularly in tailoring age-targeted strategies for effective disease control.

Keywords: social contact patterns, age-structured models, sensitivity analysis

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Identifiability and observability of some epidemiological systems: SIR vs. SIRS

Alicja B. Kubik[1], Benjamin Ivorra[1], Alain Rapaport[2], Ángel M. Ramos[1]

[1]Instituto de Matemática Interdisciplinar,
Universidad Complutense de Madrid, Spain
akubik@ucm.es, ivorra@mat.ucm.es, angel@mat.ucm.es

[2]Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement, Institut Agro de Montpellier,
Université de Montpellier, France
alain.rapaport@inrae.fr

Compartmental models based on ODEs are widely used for the study of infectious diseases. A typical methodology when applying these models to a real epidemic is (1) setting a model based on the known features of the disease, (2) looking for parameters available in the literature and collecting real data series, and (3) calibrating the remaining unknown parameters and initial conditions using these data. However, before performing (3), one can wonder if these unknowns are uniquely determined by the known data. This is addressed by studying the observability and identifiability properties of the system.

In the first part of the talk, we present some theoretical results about these properties in general nonlinear ODE systems [1]. Then, we illustrate these results by applying them to the case of an SIRS model along with the observation of a portion of infectious individuals [2].

Furthermore, when performing (1), it may not be clear which model suits better when there is little information available; for example, if the population will lose their acquired immunity after some time. Regarding this problem, we also study an SIR model with the same observation and compare both cases. This comparison yields a novel methodology for model discrimination, allowing us to determine whether these observed data come from an SIR or an SIRS model when the observations are available for a short period of time.

Keywords: identifiability, observability, SIRS model, SIR model, model discrimination.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical aspects of organization and disorganization in biology

Mirosław Lachowicz

Faculty of Mathematics, Informatics and Mechanics,
University of Warsaw, Poland
m.lachowicz@mimuw.edu.pl

In the talk I am going to discuss whether and how it is possible to mathematically model *order*, that is *self-organization*, and *disorder*, that is *disorganization*, in life systems. I refer to the theory of integro-differential equations, the so-called *kinetic equations* [1]. I am going to show that the blow-ups of solutions, which usually are treated as "bad", can actually describe some *self-organization*, that can, in some cases, be "positive", like healing processes. The results can be applied to processes in biology; like DNA denaturation; medicine; tendon healing process or invasion of cancer and social sciences; e.g. opinion formation. Moreover, I am going to discuss the importance of nonlocal modeling of some biological phenomena including the invasion of cancer on the surrounding tissue, see [2]. I am going to present various nonlocal models [3, 4], and show their applications.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Catalyst: Fast and flexible modeling of reaction networks

Torkel E. Loman[1,2,3], Vincent Du[4], Yingbo Ma[5], Vasily Ilin[6], Shashi Gowda[7], Niklas Korsbo[8], Nikhil Yewale[9], Chris Rackauckas[2,4,8], Samuel A. Isaacson[10]

[1]Sainsbury Laboratory, University of Cambridge, UK

[2]Computer Science and AI Laboratory (CSAIL), MIT, USA

[3]Mathematical Institute, University of Oxford, UK
loman@maths.oc.ac.uk

[4]Departmen of Chemistry, The University of North Carolina at Chapel Hill, USA

[5]JuliaHub, USA

[6]Department of Mathematics, University of Washington, USA

[7]Department of Mathematics, MIT, USA

[8] Pumas-AI, USA

[9]Department of Applied Mechanics, Indian Institute of Technology Madras, India

[10]Department of Mathematics and Statistics, Boston University, USA

We introduce Catalyst.jl, a flexible and feature-filled Julia library for modeling and high-performance simulation of chemical reaction networks (CRNs). Catalyst supports simulating stochastic chemical kinetics (jump process), chemical Langevin equation (stochastic differential equation), and reaction rate equation (ordinary differential equation) representations for CRNs. Through comprehensive benchmarks, we demonstrate that Catalyst simulation runtimes are often one to two orders of magnitude faster than other popular tools. More broadly, Catalyst acts as both a domain-specific language and an intermediate representation for symbolically encoding CRN models as Julia-native objects. This enables a pipeline of symbolically specifying, analyzing, and modifying CRNs; converting Catalyst models to symbolic representations of concrete mathematical models; and generating compiled code for numerical solvers.

Leveraging ModelingToolkit.jl and Symbolics.jl, Catalyst models can be analyzed, simplified, and compiled into optimized representations for use in numerical solvers. Finally, we demonstrate Catalyst's broad extensibility and com-

posability by highlighting how it can compose with a variety of Julia libraries, and how existing open-source biological modeling projects have extended its intermediate representation.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mixed positive and negative feedback loops drive diverse single-cell gene expression dynamics

Torkel E. Loman[1,2,3], Christian P. Schwall[1], Teresa Saez[1], Yujia Liu[1], James C. W. Locke[1]

[1]Sainsbury Laboratory, University of Cambridge, UK
[2]Computer Science and AI Laboratory (CSAIL), MIT, USA
[3]Mathematical Institute, University of Oxford, UK
torkel.loman@maths.ox.ac.uk

Genetic circuits with only a few components can generate complex gene regulatory dynamics. Here, we combine stochastic modelling and single-cell time-lapse microscopy to reveal the possible behaviours generated by a key gene circuit motif: the mixed positive/negative feedback loop. Our minimal stochastic model of this motif reveals ten distinct classes of output, including stochastic pulsing, oscillations, and bistability. Using an automatic classifier we map these behaviours across parameter space, showing how the behaviours are influenced by a few important biological parameters, such as the strength of the positive and negative feedbacks. Experimental validation in two different mixed feedback circuits in the bacterium *Bacillus subtilis*, σ^B and σ^V, confirms our model's predictive power. Guided by our simulations, we are able to transition between dynamic behaviours by modulating in vivo parameters. Together, these results demonstrate how mixed feedback loops generate diverse single-cell behaviours, improving our understanding of this common biological network motif and informing our efforts to engineer them for synthetic biology applications.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical modeling of biofouling formation on a membrane filtration system

Vincenzo Luongo

Department of Mathematics and Applications,
University of Naples, Italy
vincenzo.luongo@unina.it

Microfiltration is a promising approach for water production and wastewater treatment. However, a primary challenge associated with this technology is the formation of fouling layers, predominantly composed of organic substances such as bacteria and extracellular polymeric substances (EPS). These layers contribute to increased hydraulic resistance and a decline in flux during membrane operation. In wastewater treatment, the development of such biological layers, named biofouling, represents a significant operational cost due to the energy and chemical requirements for cleaning procedures.

Since biofouling is fundamentally a biofilm-related problem, the ability to predict biofilm growth and evolution on membrane surfaces is crucial for optimizing membrane reactor performance and backwashing strategies under different filtration regimes. To address this problem, a one-dimensional mathematical model has been developed, formulated as a free boundary value problem that describes biofilm dynamics and EPS production during microfiltration. This study integrates classical in-series filtration theory (e.g., based on Darcy's Law) with multispecies biofilm growth modeling.

The proposed model, and it's future modifications, serves as a mathematical tool for describing backwashing effects and biofouling kinetics during microfiltration, thereby supporting wastewater treatment facilities in system design and operational management.

Keywords: biofouling, boundary value problem, microfiltration

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical and numerical methods for understanding immune cell motion during wound healing

Giulia Lupi[1], Karol Mikula[1], Seol Ah Park[1], Martin Ambroz[1], Resul Ozbilgic[2], Mai Nguyen Chi[2], Georges Lutfalla[2]

[1]Department of Mathematics and Descriptive Geometry, Slovak University of Technology in Bratislava, Slovakia
giulia.lupi@stuba.sk

[2]Laboratory of Pathogens and Host Immunity (LPHI), CNRS/Université de Montpellier, France

We propose a new workflow to analyze macrophage motion during wound healing. These immune cells play a critical role in tissue repair, as they are attracted to the wound site after an injury. Their motion is a combination of directional movement and random motion. Therefore, we begin by smoothing the original trajectories. The smoothing model is based on curve evolution approach, where the curve evolves under the influence of two key terms: a smoothing term, determined by the local curvature of the trajectory, and an attracting term, which ensures that the curve stays close to the original trajectory.

This model allows us to separate the random parts of motion from the directional parts and study them separately. Once the random sub-trajectories are obtained, their properties are analyzed using the mean squared displacement. This method helps to characterize the type of diffusion exhibited by the cells, providing insights into the stochastic aspects of their motion, namely whether the cells' movement is consistent with normal diffusion, subdiffusion, or superdiffusion.

Finally, we compute the velocities along the smoothed trajectories and use them as sparse samples to reconstruct the wound attractant field. This process involves solving a minimization problem for the vector components and lengths of the velocity field. The solution reduces to solving the Laplace equation with Dirichlet boundary conditions on the sparse samples and zero Neumann boundary conditions on the domain boundary. The result is a vector field where the direction and lengths of the vectors are interpolated/extrapolated from the Dirichlet conditions.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modelling the influence of bacteriophage activity and horizontal gene transfer on the spread of bacterial resistance

Julien Vincent[1], Alberto Tenore[2], Maria Rosaria Mattei[2], Luigi Frunzo[2]

[1]School of Biological and Chemical Sciences and Ryan Institute,
University of Galway, Ireland
julien.vincent@universityofgalway.ie

[2]Department of Mathematics and Applications,
University of Naples, Italy
alberto.tenore@unina.it
mariarosaria.mattei@unina.it
luigi.frunzo@unina.it

The global spread of Antibiotic Resistance Genes (ARGs) or Metal Resistance Genes (MRGs) represents an increasing health concern, and has been mainly attributed to antibiotics abuse and misuse. Dissemination of ARGs and MRGs is largely associated to plasmids, extra-chromosomal genetic elements. Plasmid-carried resistance is transferred to new host cells through Horizontal Gene Transfer (HGT) mechanisms, which play a crucial role in the ecological success of plasmids in bacterial communities. HGT occurs through three main mechanisms, namely conjugation, transformation and transduction, the latter referring to the case where foreign DNA is acquired by the receiver bacterium through infection by bacteriophages.

We develop here a mathematical model for the spread of resistance in biofilm communities by conjugation, natural transformation and generalised transduction. Generalized transduction results from the replication error of a random piece of bacterial DNA by the bacteriophage. This leads to the formation of a transducing phage, which can carry any bacterial gene, including resistance genes. Upon further infection, the transducing phage will release this piece of DNA into the infected bacterium, leading to eventual incision into the chromosome or recircularisation, in case of plasmid DNA.

The model is applied to the dissemination of an MRG plasmid in a growing biofilm. This plasmid carries the *merA gene*, conferring Hg resistance and the ability to reduce cationic Hg into its less toxic elemental form. This detoxification ability allows plasmid carrying bacteria to detoxify their local environment, therefore benefiting sensitive bacteria in their surroundings.

We include in the model the presence of lytic phages, in levels typically associated with water environments, and transducing phages. Their production is considered as a deterministic process resulting from infection by lytic phages of bacterial cells carrying the plasmid. Numerical studies focus on the impact of phage predation on bacterial communities and plasmid spread. We then investigate the relative influence of HGT and VGT (Vertical Gene Transfer) on plasmid dissemination, with a focus on generalised transduction.

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modeling dengue transmission with viral load and antibody levels

Paulo Amorim, M. Soledad Aronna, Débora O. Medeiros

School of Applied Mathematics,
Fundação Getúlio Vargas, Brazil
paulo.amorim@fgv.br
soledad.aronna@fgv.br
debora.medeiros@fgv.br

Dengue fever is a vector-borne disease causing millions of infections every year. This makes dengue a significant public health concern in many regions worldwide. In addition, there is no specific treatment for dengue or severe dengue, which emphasizes the importance of mathematical models for dengue fever [1] combined with control strategies for this disease.

Motivated by works [2, 3], we present a new vector-host model, which considers the micro-dynamics of viral load and antibody (Ab) levels. This consideration is crucial to improving the model, allowing the study of the antibody-dependent enhancement phenomenon (ADE) [4] and the incorporation of control strategies, such as vaccination.

For an initial investigation, we consider the viral load and antibodies of only a single dengue serotype. This leads to a particular case with an associated delayed model. For the obtained delayed differential equation, we present the theoretical and numerical study of the endemic equilibrium and the basic reproduction number. The numerical results also allow us to conclude that the model presents expected behavior for the dynamics examined.

Keywords: dengue fever, vector-host models, delay differential equations, numerical simulations

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

A nonconservative kinetic model for the medical treatment of autoimmune response

Marco Menale

Department of Mathematics and Applications,
University of Naples, Italy
marco.menale@unina.it

A nonconservative kinetic framework is developed for modeling immune system dysregulation. The model describes a population of stochastically interacting agents subject to an external action, which has a specific analytical form in view of biomedical applications. Within this setting, some results are obtains concerning local-in-time existence, uniqueness, positivity, and boundedness of the solution to the associated problem. The model is then extended to investigate treatment strategies in the context of autoimmune responses, distinguishing between the autonomous and non-autonomous cases, corresponding respectively to the absence and administration of drugs. The autonomous case allows for an analytical stability analysis, while the non-autonomous case is addressed qualitatively. Numerical simulations are presented for both configurations.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Oscillations and the cycle structure of reaction networks

Maya Mincheva[1], Polly Yu[2]

[1]Northern Illinois University, USA
mmincheva@niu.edu

[2]University of Illinois Urbana-Champaign, USA
pollyyu@illinois.edu

Reaction network models are often represented as systems of parametric ordinary differential equations or directed graphs (digraphs). Oscillations are an ubiquitous phenomenon in reaction networks models, and they usually arise as a result of a Hopf bifurcation. A necessary condition for a Hopf bifurcation is zero determinant of the bialternate product matrix of the Jacobian. We present a corresponding graph-theoretic condition on the cycle structure of the digraph of reaction networks. (This is a preliminary report.)

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Controlling populations of neural oscillators

Jeff Moehlis

Department of Mechanical Engineering,
University of California, Santa Barbara, USA
moehlis@ucsb.edu

Many challenging problems that consider the analysis and control of neural brain rhythms have been motivated by the advent of deep brain stimulation as a therapeutic treatment for a wide variety of neurological disorders. Control of such rhythms comes with a long list of challenges: the underlying dynamics are nonnegligibly nonlinear, high dimensional, and subject to noise; hardware and biological limitations place restrictive constraints on allowable inputs; direct measurement of system observables is generally limited; and the resulting systems are typically highly underactuated.

In this talk, I highlight a collection of recent analysis techniques and control frameworks that have been developed to contend with these difficulties [1]. Particular emphasis is placed on the problem of desynchronization for a population of pathologically synchronized neural oscillators, a problem that is motivated by applications to Parkinson's disease where pathological synchronization is thought to contribute to the associated motor control symptoms.

The first control strategy to be covered will be optimal chaotic desynchronization for finding an energy-optimal stimulus which exponentially desynchronizes a population of neurons, based only on a neuron's phase response curve, and will include recent results on the effect of constraints on stimulus magnitude on the control efficacy. The second control strategy to be covered will be optimal phase resetting which brings the neurons' states near a phaseless set, so that background noise perturbs the neurons onto random isochrons which randomizes their asymptotic phases, and will include recent results on how accounting for stochasticity in the control design can improve performance [2]. These algorithms hold great promise for controlling neural oscillator populations with a variety of control objectives.

Our hope is that these successes will motivate more research on how to implement them in experimental and clinical studies, opening the door to more effective and more efficient treatments for Parkinson's disease and other neurological disorders.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Analysis of the effects of rainfall variability on natural forage resources and the corresponding livestock production: Climate variability and livestock dynamics in Botswana

Thabo S. Nketsang[1], Semu Mitiku Kassa[1], Gizaw Mengistu Tsidu[2], Moatlhodi Kgosimore[3]

[1]Department of Mathematics and Statistical Sciences,
[2]Department of Earth and Environmental Sciences,
Botswana International University of Science and Technology, Botswana
nt13000419@studentmail.biust.ac.bw
kassas@biust.ac.bw
mengistug@biust.ac.bw

[3]Department of Biometry and Mathematics,
Botswana University of Agriculture and Natural Resources, Botswana
mkgosi@buan.ac.bw

Botswana's livestock sector is a cornerstone of the nation's economy and food security, which is primarily based on natural grazing resources. However, climate variability poses significant challenges by altering rainfall patterns, which directly affects forage availability and quality. Traditional farmers, often lacking access to advanced climate data, rely on intuition and historical rainfall trends, making them particularly vulnerable to these changes. Therefore, this study investigates the effects of rainfall variability on livestock production using a mathematical model for plant-herbivore interactions, derived from a prey-predator framework.

The model incorporates plant growth rates and regional rainfall data sourced from the Climate Engine, covering diverse climatic and vegetation conditions in Botswana. In addition, essential threshold values for coexistence were derived, with the average basic reproduction ratio, R_0, correlated to the dynamics of the livestock population. The observed decline in livestock populations from literature and historical data is also confirmed through R_0 analysis. The numerical solution of the model is used to explore the relationships between the timing and intensity of rainfall, plant biomass, and livestock populations.

The results reveal that early onset and higher intensity of rainfall positively influence livestock populations, while delayed or reduced rainfall results in population decline. The findings further suggest that adaptive livestock harvesting

strategies can serve as effective tools for sustainable grazing and livestock management.

Keywords: livestock production, non-autonomous plant-livestock model, climate variability, natural forage, prey-predator model

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical modelling of siderophores-mediated iron acquisition and cross-feeding in bacterial communities

Tosin Samuel Osikoya, Christina Kuttler

Mathematics in Life Sciences Unit, Department of Mathematics,
Technical University of Munich, Germany
tosin.osikoya@tum.de
kuttler@ma.tum.de

The ability to acquire iron is a key determinant of survival, biofilm development and pathogenicity for most microorganisms. Many bacteria produce specialized siderophores that bind iron from the environment, making it available to cells under iron-limiting conditions. Fluorescent pseudomonads, for example, secrete pyoverdines (PVDs) as effective iron-chelating agents. Studies on iron chelation dynamics and cross-feeding models have demonstrated that the ability to produce siderophores and cross-feed provides a fitness advantage to certain species over those that cannot engage in this interaction.

This phenomenon has been empirically investigated in species such as the rhizosphere bacterium *Pseudomonas protegens* Pf-5 and *Pseudomonas aeruginosa* PA-01 which was carried out in a chemostat and batch cultures. However, most studies have not accounted for spatial heterogeneity settings. Unlike well-mixed and homogeneous environments, bacterial populations typically live and grow in spatially structured communities, such as colonies or biofilms on surfaces. We address this question in the present study.

Building on a previously introduced ordinary differential equations model of iron chelation dynamics and cross-feeding, we formulate a reaction-diffusion model for two related species. This approach leads to a highly non-linear system of partial differential equations. To solve it numerically, we use a finite difference method with implicit discretization in both space and time. Our findings indicate that siderophore production and cross-feeding confers a growth advantage even in spatially structured environments. Factors such as diffusion and the length of the spatial domain between the dual species significantly influence cross-feeding. Furthermore, the magnitude of the growth advantage also depends on the initial inoculation of the iron and substrate (carbon). The mathematical model allows for a better understanding of the complex interactions including quantification.

Keywords: siderophores, bacteria, pyoverdines, reaction-diffusion model, partial differential equations, ordinary differential equations, spatial domain, diffusion

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Application of Graphs for System Level Analysis of the Repertoire of Antibody Reactivities

Anastas Pashov[1], Peter Petrov[2]

[1]Institute of Microbiology
Bulgarian Academy of Sciences, Bulgaria
a_pashov@microbio.bas.bg

[2]Institute of Mathematics and Informatics
Bulgarian Academy of Sciences, Bulgaria
pk5rov@gmail.com

The current understanding of antibodies in immunology presents a limited paradigm that overlooks crucial aspects of their diversity. Our studies introduce an innovative analytical framework that integrates phage display, mimotope, igome, and high-throughput binding assays into a unified pipeline for system level analysis of the antibody repertoire.

We employ graph-based formalisms to analyze the data, aligning with the intuitive concept of antigen and antibody reactivity landscapes. This approach reveals novel insights into the relationship between public specificities and idiotypic interactions across various pathologies.

The resulting innovative analytical paradigm yields new information about the relationship between public specificities and idiotypic interactions in the context of different pathologies. Different clustering algorithms and spectral analysis helped in finding large scale structures in the repertoire. This information informed filtering and recursive feature elimination algorithms for dimensionality reduction in the design of proof of principle machine learning models.

Thus, we could show the potential of this approach as a novel diagnostic platform in cancer (brain tumors), autoimmune disease (antiphospholipid syndrome), neurodegenerative disease (Alzheimer's disease and frontotemporal dementia), and probably in all pathologies involving inflammation and immune disturbance.

Keywords: antibody repertoire, graphs, bioinformatics, machine learning

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical model of measles epidemiology with control strategies

Olumuyiwa James Peter[1], Festus Abiodun Oguntolu[2]

[1]Department of Mathematical and Computer Sciences,
University of Medical Sciences, Ondo State, Nigeria
peterjames4real@gmail.com

[2]Department of Mathematics,
Federal University of Technology Minna, Niger State, Nigeria
festus.tolu@futminna.edu.ng

Measles remains a significant public health challenge, particularly in regions with low immunization rates. This paper presents a mathematical model to assess the impact of vaccination on measles control, incorporating additional measures such as quarantine and public health education. The model categorizes the population into five key compartments: susceptible, vaccinated, exposed, infectious, and recovered.

We employ Partial Rank Correlation Coefficient (PRCC) analysis to identify critical parameters influencing measles transmission dynamics, including vaccine efficacy, coverage, and the duration of immunity. Our simulations evaluate the effectiveness of various vaccination strategies, such as booster doses, mass immunization campaigns, and targeted interventions in high-risk populations. The results indicate that high vaccination coverage and efficacy, coupled with timely quarantine measures and robust public health education, can significantly reduce measles incidence and prevalence.

The PRCC analysis reveals that the rate of progression from exposure to infection and the waning of immunity are pivotal in determining the success of these control strategies. We advocate for comprehensive immunization programs, particularly in vulnerable areas, combined with aggressive public health interventions to enhance measles control. The study emphasizes the need for continued research into developing vaccines with higher efficacy and longer-lasting immunity, as well as effective educational campaigns, to further curb the spread of measles.

These findings provide valuable insights for policymakers and public health officials, highlighting the critical role of vaccination and complementary measures in comprehensive measles control programs. By integrating these strategies into public health policies, governments can more effectively combat the measles epidemic and improve health outcomes in affected communities.

Keywords: mathematical model, PRCC analysis, public health epidemiology, vaccine efficacy, health policy

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

A multi-scale PBPK model for predicting mRNA-encoded therapeutic trafficking in mice

Elisa Pettinà[1,2], Chiara Rosati[1], Stefano Giampiccolo[2,3], Luca Marchetti[1,2]

[1]Department of Cellular, Computational and Integrative Biology (CIBIO), University of Trento, Italy
elisa.pettina@unitn.it
chiara.rosati@unitn.it
luca.marchetti@unitn.it

[2]Fondazione The Microsoft Research – University of Trento Centre for Computational and Systems Biology (COSBI), Rovereto, Italy
pettina@cosbi.eu
giampiccolo@cosbi.eu
marchetti@cosbi.eu

[3]Department of Information Engineering and Computer Science, University of Trento, Italy
stefano.giampiccolo@unitn.it

In the field of immunotherapy, mRNA-encoded monoclonal antibodies (mRNA-mAbs) have emerged as a promising treatment for several conditions – in particular, for cancer, infections and inflammatory diseases. Importantly, the successful use of mRNA-mAbs has been made possible by the development of efficient RNA delivery systems, such as Lipid Nanoparticles (LNPs), which protect mRNA from enzymatic degradation and enable targeted intracellular delivery.

Despite great achievements in this field, the mechanistic understanding underlying the metabolism of mRNA-LNP therapeutics remains poorly understood. To address this gap, we developed a ODE-based model that describes the principal events occurring after IV injection of mRNA-LNPs based on the most recent findings in literature, namely their adsorption in the liver, their clearance and subsequently their escape from the endosomes and translation. This mechanist layer is also equipped with a Physiologically Based Pharmacokinetic (PBPK) model, based on the work of Sepp et. al. (2019) [1], which describes the kinetics of mRNA-mAbs throughout 15 different organs and tissues.

To fit the unknown parameters in the model, we leveraged three preclinical studies in mice that report the concentration time-profile of mRNA-mAbs of

different sizes, all delivered with LNPs [2, 3, 4] and targeting cancer cells. Our multi-scale PBPK model accurately predicts the concentration-time profiles of both the mRNA-encoded therapeutics and the relative recombinant proteins. The model was also validated on unseen data presented in the reference literature [2, 3, 4], demonstrating high accuracy also in different dosing schedules and dosages.

Our model can predict mAbs disposition in remote tissues, which experimentally would require the sacrifice of the animal, and their kinetics in different animal models, including humans. Moreover, its inherent modularity enables the exploration of different routes of administration and tropisms of the mRNA-LNPs therapeutic of interest, offering a valid support to the development of these ground-breaking therapies.

Keywords: immunotherapy, mAbs, PBPK, ODE-based models

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical Insights into Alzheimer's Disease: A Multiscale Modeling Approach

Achille Landri Pokam Kakeu[1], Mapundi Kondwani Banda[1]

[1]University of Pretoria, Department of Mathematics and Applied Mathematics, South Africa
al.pokamkakeu@up.ac.za, mapundi.banda@up.ac.za

In this presentation, we study the progression of Alzheimer's disease through a multiscale modeling approach. We begin by formulating a system of partial differential equations that captures the underlying biological mechanisms. The evolution of the system is analyzed within a thin porous heterogeneous medium, reflecting the complex structure of brain tissue. To address the multiscale nature of the problem, we adopt a finite element heterogeneous multiscale method (FE-HMM), which enables us to accurately approximate the macroscopic behavior by systematically incorporating microscale effects. Numerical simulations are carried out to validate the theoretical analysis and to illustrate the impact of tissue heterogeneity on disease progression.

Keywords: Alzheimer's disease; Multiscale modeling; Heterogeneous multiscale method; Two-scale convergence; Numerical simulation

MSC2020: 35B27, 35Q92, 65M60

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Positive feedback from growth burden in stochastic protein expression

Jakub Poljovka[1], Iryna Zabaikina[1], Pavol Bokes[1], Abhyudai Singh[2]

[1]Faculty of Mathematics, Physics and Informatics,
Comenius University, Slovakia
poljovka4@uniba.sk
iryna.zabaikina@fmph.uniba.sk
pavol.bokes@fmph.uniba.sk

[2]Electrical and Computer Engineering,
University of Delaware, USA
absingh@udel.edu

We study a protein that is stochastically expressed and imposes a fitness cost when overproduced by slowing down cell growth. This growth burden creates an inherent positive feedback loop: higher protein levels reduce cellular growth, which slows dilution, thereby sustaining higher protein levels. We develop a discrete-state model to capture this feedback mechanism, integrating stochastic simulations with differential equation approaches. Our analysis explores both single-cell dynamics and population-level behavior, revealing how noise and feedback together shape protein expression distributions.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Exploring the stability of a generalised Lotka-Volterra ecological model

Richard Pretorius, Andriamihaja Ramanantoanina, Jacek Banasiak

Department of Mathematics and Applied Mathematics,
University of Pretoria, South Africa
u20516020@tuks.co.za
a.ramanantoanina@up.ac.za
jacek.banasiak@up.ac.za

Lotka-Volterra models have long been used as a mathematical tool to model relatively simple biotic interactions, especially where interspecific competition occurs. As such, Lotka-Volterra models have been utilised extensively in the study of microbial environments, where the assumptions of the model are more easily shown to be met [1]. However, recent evidence points to the viability of Lotka-Volterra models as qualitative predictors of certain ecosystem patterns in more varied, larger scale ecosystems [2]. Even so, traditional Lotka-Volterra models remain unable to model more complex interactions [3].

In this talk, a generalized Lotka-Volterra model with many species is considered. In contrast with the standard model (as formulated in the 30's) this model does not restrict population growth in the absence of other species to exponential or logistic forms. Various functional responses are also admitted by this model. As such, this model succeeds in capturing the dynamics of systems that would otherwise not be of a Lotka-Volterra type.

This talk develops Lyapunov functions for this generalised Lotka-Volterra model. These Lyapunov functions are used to determine stability criteria in terms of the inter-specific interactions within the community. Finally, explorations of results for various community structures are conducted through numerical simulations.

Keywords: Lotka-Volterra models, Lyapunov functions, stability
MSC2020: 92-10, 92D25, 92D40

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

A mathematical model of methotrexate's effect on adalimumab immunogenicity in axial spondyloarthritis

Peter Rashkov[1], Sara Sottile[2], Denis Mulleman[3,4]

[1]Institute of Mathematics and Informatics,
Bulgarian Academy of Sciences, Bulgaria
p.rashkov@math.bas.bg

[2]Department of Medical and Surgical Sciences,
Alma Mater University of Bologna, Bologna, Italy
sara.sottile4@unibo.it

[3]Université de Tours, Tours, France
[4]Department of Rheumatology, CHRU de Tours, France
denis.mulleman@univ-tours.fr

Spondyloarthritis (SpA) is a chronic inflammatory disease impacting the spine and joints. Tumor necrosis factor inhibitors (TNFi), like adalimumab, are used to treat severe cases, but up to 25% of patients stop due to reduced effectiveness, often from anti-drug antibodies (ADA) forming [1]. Methotrexate (MTX), while ineffective alone in axial SpA, has shown potential in reducing the formation of ADA to TNFi [2, 3].

The objective of the study is to develop a mathematical model that describes the impact of MTX in reducing the immunogenicity of adalimumab in SpA. Based on mathematical models already established in the literature, an Ordinary Differential Equations (ODEs) model was formulated to describe the dynamics of the therapeutic compounds in the study (adalimumab and MTX, if applicable), the immune cells (T cells and B cells), and the relevant cytokines for the disease.

The data used to calibrate the model are sourced from a patient study [4], which involved 110 patients, from whom adalimumab concentration, lymphocyte counts, and antibody titers have been collected along five visits during the course of treatment.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Blue Culture Technology Excellence Hubs in EU Widening Member States

Ivan Georgiev, Miglena Raykovska, Nikolay Petkov, Valentin Petkov, Miryana Raykovska, Martin Tsvetkov, Svetlana Trifonova

Institute of Information and Communication Technologies,
Bulgarian Academy of Sciences, Bulgaria
miglena.raykovska@gmail.com

BCThubs aims to build in the participating Widening countries (i.e. Greece, Bulgaria and Malta), Blue Culture Technology Excellence Hubs, as permanent structures that will serve as beacons of innovation and collaboration. These Hubs are designed to support the development of new innovative solutions and products that will contribute to the sustainable protection, restoration, valorisation, management, accessibility, and promotion of Underwater Cultural Heritage (UWCH). Although the new Hubs will be scoped regionally, they will be interconnected and oriented towards national and international synergies, ensuring a holistic approach that transcends geographical limitations (i.e. beyond regional borders). This framework will actively pursue cross-border collaborations on common strategic goals, fostering partnerships that span across various sectors and communities. Each Excellence Hub will bring together all regional/national actors related to Blue Culture and UWCH, including key stakeholders from research and academia, businesses, the public sector, and societal actors, thereby implementing a comprehensive 4-helix approach. This collaborative dynamic will mutually reinforce their capacities and effectiveness, creating a robust network that enhances knowledge sharing and resource allocation. Ultimately, the mission is to elevate innovation excellence within the sustainable Blue Economy/Culture in respective regions, leading to a significant positive impact on local communities and ecosystems, while also contributing to broader European and global sustainability objectives.

Keywords: Underwater Cultural Heritage, Blue Culture, Cultural Heritage Management

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical modelling of human-domestic animals AMR spread: Exploring the use of colistin in livestock farming in rural areas

Jhoana P. Romero-Leiton[1], Yuliana Rodriguez[2], Carlos Bastidas-Caldes[3]

[1]Department of Mathematical Sciences,
University of Puerto Rico at Mayagüez, Puerto Rico, USA
jhoana.romero@upr.edu

[2]Department of Mathematics,
University of Quindío, Armenia, Colombia
yrodriguez1@uniquindio.edu

[3]One Health Research Group,
University of the Americas, Quito, Ecuador
carlos.bastidas@udla.edu.ec

Colistin, an antibiotic from the polymyxin group, targets gram-negative bacteria by destabilizing their outer membrane [1]. Despite its restricted use in Latin America due to toxicity concerns, colistin has re-emerged, even as a growth promoter for fattening animals, and is also an important option for the treatment of multidrug-resistant bacteria, which are considered a threat to global health [2]. Therefore, this resurgence has coincided with an alarming rise in resistance, particularly due to the mcr-1 and BLEE genes, which enable the horizontal transmission of resistance among bacteria [2, 3]. Intensive livestock farming in Latin America has exacerbated this issue by increasing the risk of resistance gene transmission between animals and humans [4].

Few mathematical models have been developed to analyze the impact of reducing antibiotic use in animals on AMR in humans, highlighting the need for more data on human-animal interactions in the spread of AMR [5]. We propose a mathematical model that incorporates the close contact of humans and domestic animals to study the spread of AMR to colistin. The model is validated using field-collected data, including the presence of BLEE and mcr-1 resistance genes in *Escherichia coli* and *Klebsiella pneumoniae* strains.

The model results suggest that the close contact between humans and domestic animals significantly influences colistin resistance levels, highlighting the need for strict measures to phase out colistin use and implement targeted interventions aimed at reducing its usage while limiting the environmental transmission of resistant strains.

Keywords: BLEE gene, mcr-1 gene, Escherichia coli, Klebsiella pneumoniae, model validation, stability

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Evolution of the maturation period in insect populations

Gergely Röst

National Laboratory for Health Security,
University of Szeged, Hungary
rost@math.u-szeged.hu

Computational Medicine Group,
Hungarian Center of Excellence for Molecular Medicine (HCEMM)

We propose a new mathematical model to address the evolution of maturation period, building on the Nicholson's blowfly equation. First a competition model of two species is formulated as a system of nonlinear delay differential equations with two distinct delays, and we analyze its dynamics. Then we consider the evolutionary dynamics of maturation periods. For some cases, we identify the optimal maturation delay for an insect population, depending on the quality and suitability of the habitat, which is both a globally evolutionary stable and convergence stable strategy. We investigate the potential co-existence of insects with different maturation delays. Mathematically interesting questions raised by the invasibility of oscillatory insect populations. Joint work with Xingfu Zou (Western University, Canada).

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modeling phototrophic biofilm growth: The role of phototaxis in microbial ecology

Fabiana Russo, Alberto Tenore, Luigi Frunzo, Maria Rosaria Mattei

Department of Mathematics and Applications,
University of Naples, Italy
fabiana.russo@unina.it
alberto.tenore@unina.it
luigi.frunzo@unina.it
mariarosaria.mattei@unina.it

Biofilms are complex microbial communities that adhere to surfaces and are encased in a self-produced matrix of extracellular polymeric substances (EPS). These ecosystems constantly evolve in response to environmental fluctuations, and exhibit intricate dynamics governed by interconnected mechanisms. The motility of microorganisms within biofilms is crucial, as it directly affects the biofilm's spatial organization, composition, and overall development. Among the motility mechanisms, phototaxis plays a pivotal role by enabling microorganisms to move in response to light, guiding the positioning of planktonic cells within the biofilm matrix. This movement optimizes light exposure, enhancing beneficial conditions while avoiding harmful intensities. As a result, phototaxis influences microbial spatial distribution, metabolic cooperation, and ecological adaptation within the biofilm.

In this study, a mathematical model that explores the role of phototaxis in biofilm growth and organization is presented. The proposed model is formulated as a hyperbolic-parabolic free boundary value problem, where the biofilm is modeled as a homogeneous, viscous, incompressible fluid with velocity governed by Darcy's law. It considers two state variables representing the planktonic and sessile phenotypes and reproduces the transition from one state to the other. Additionally, two different planktonic cells motion behaviours are considered: random motility governed by the diffusion process, and directional motility driven by phototactic responses to light gradients. A light-dependent sensitivity function captures both positive and negative phototaxis.

Numerical simulations analyze biofilm evolution under biologically relevant conditions and examine the impact of phototaxis on biofilm dynamics and ecology. The distribution of phototrophic biomass emerges from the interaction between random diffusion and phototactic movement. The results indicate that

motile cells accumulate in regions with optimal light, stimulating the growth of sessile phototrophic cells and facilitating biofilm development.

Keywords: biofilm, phototaxis, free boundary value problem, numerical simulations

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Stability and bifurcation analysis in mathematical models for oscillating pregnane X receptor levels

Bechara Saade[1], Jurjen Duintjer Tebbens[1,2], Veronika Bernhauerová[1], Elfriede Friedmann[3]

[1]Faculty of Pharmacy,
Charles University, Czech Republic
saadeb@faf.cuni.cz
bernhauve@faf.cuni.cz

[2]Institute of Computer Science,
Czech Academy of Sciences, Czech Republic
tebbens@cs.cas.cz

[3]Faculty of Mathematics and Natural Sciences,
Kassel University, Germany
friedmann@mathematik.uni-kassel.de

The pregnane X receptor (PXR) is a nuclear receptor that plays a key role in regulating metabolic enzymes and transporters. In various species [1] and under different regulatory mechanisms [2], PXR may exhibit oscillatory behavior in its mRNA concentration. These oscillations can lead to variations in corresponding PXR-controlled drug-handling enzyme expression levels, thereby influencing drug metabolic pathways.

Here, we develop mathematical models to explore two possible drivers of PXR oscillations: circadian rhythm and negative feedback loop. The circadian rhythm model demonstrates how rhythmic inputs from the circadian clock can affect PXR activity. The negative feedback loop model assumes that activated PXR downregulates its gene expression, possibly generating oscillations in PXR mRNA concentrations. A stability analysis in the negative feedback loop model aims to identify the parameter sets that lead to stable or unstable solutions. A bifurcation analysis determines a parameter region where a small change in kinetic or regulatory parameters shifts the system from a stable steady state to limit cycle oscillations.

For instance, the Hill coefficient associated with the feedback loop term serves as the bifurcation parameter, following a Hopf bifurcation. The parameters derived from the mathematical model, related to drug pharmacokinetics,

PXR dynamics, and enzyme kinetics, provide insights into the conditions and periodicity of oscillations in related proteins. These findings enhance our understanding of PXR dynamics and their impact on metabolic regulation and drug response.

Clinically, these information may help in decision-making for determining optimal therapeutic dosages and designing effective multi-drug treatment strategies, especially when the drugs are metabolized by the same cytochrome P450 enzyme.

Keywords: pregnane X receptor, CYP450 enzymes, circadian clock, auto-feedback loops, stability analysis, bifurcation analysis

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

A general kinetic model for the spread of infectious diseases in continuously structured compartments

Emanuele Bernardi[1], Tommaso Lorenzi[1], Mattia Sensi[1,2], Andrea Tosin[1]

[1]Department of Mathematical Sciences "G. L. Lagrange",
Politecnico di Torino, Italy

[2]Department of Mathematics,
Università degli Studi di Trento, Italy
mattia.sensi@unitn.it

We propose a general kinetic compartmental model for the spread of infectious diseases, wherein each compartment is structured by a continuous variable that captures inter-individual phenotypic variability [1, 2, 3].

The model comprises a system of integro-differential equations for the dynamics of the population density functions (i.e. the phenotype distributions) of the different compartments. First, we formally derive this model from an underlying stochastic model, which describes the evolutionary dynamics of single individuals. Then, we explore the connections between this general model and specific compartmental models employed in epidemiology [4, 5, 6].

We derive the classical threshold quantity R_0, the Basic Reproduction Number, after some simplifying assumptions on our general model. Finally, we discuss possible applications of the model in different epidemiological scenarios and compare simulations of the microscopic (Monte Carlo) and macroscopic (ODEs) layers of our construction.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Numerical methods for the controlled degenerate chemotaxis model in a weak formulation

Sarah Serhal[1,3], Georges Chamoun[2], Mazen Saad[1], Toni Sayah[3]

[1]Ecole Centrale de Nantes, Laboratoire de Mathématiques Jean Leray, UMR CNRS, Nantes, France
sarah.serhal@ec-nantes.fr
mazen.saad@ec-nantes.fr

[2]Faculty of engineering (ESIB), Saint Joseph University of Beirut, Lebanon
georges.chamoun1@usj.edu.lb

[3]Laboratoire de Mathématiques et Applications, Unité de recherche Mathématiques et Modélisation, CAR, Faculté des Sciences, Université Saint-Joseph de Beyrouth, Riad El Solh, Beyrouth, Lebanon
sarah.serhal@net.usj.edu.lb
toni.sayah@usj.edu.lb

In this work, we study a controlled chemotaxis model using the finite element method. The model consists of a parabolic-parabolic system with degenerate diffusion and a control term representing the chemoattractant concentration. The goal is to determine an optimal control strategy to regulate the chemoattractant concentration, achieving a desired cell density and concentration, particularly in cancer treatment, where the objective is to limit cancer cells while minimizing effects on healthy tissues.

This is achieved by minimizing a quadratic problem where the cost function measures the errors between the cell density, the concentration, and the desired given states; the cost of the control is also minimized.

We propose a new approach that utilizes the concept of weak solutions with energy inequalities to be the set of admissible sets, unlike classical approaches that assume a strong regularity of state solutions. This approach ensures the existence of an optimal control while simplifying both the mathematical analysis and the adjoint system formulation, particularly in the case of degenerate diffusion.

In our recent work [1], we proposed a pioneering approach to address the challenge of analyzing weak solutions for the optimal control of chemotaxis models with a two-sided degenerate diffusion function. In this context, we prove

the existence of solutions for both the direct and adjoint problems, despite the severe regularity issues induced by degeneracy.

The introduction of optimal control in such models presents numerical challenges. Indeed, handling optimal control in the weak solution framework remains particularly difficult. In the context of convection-diffusion equations with control, finite element methods have been employed to address control problems (see, for example, [2]). Additionally, in [3], the authors studied an optimal control problem for a two-dimensional attraction-repulsion chemotaxis.

In this work, we propose a novel numerical approach for optimal control of the isotropic degenerate Keller-Segel model using the finite elements method. Our goal is to numerically solve the optimal control problem associated with this parabolic PDE-constrained system.

The numerical resolution of such problems requires careful discretization and optimization strategies. Two main strategies exist: optimizing first or discretizing first, each leading to potentially different numerical results (see [4]).

We adopt the optimize-then-discretize approach, where we first derive the optimality conditions in the continuous model before discretizing and solving them. We begin by proving the existence and uniqueness of the discrete solution for the direct problem, followed by the adjoint problem.

For optimization problem, we use the gradient method, a first-order algorithm that relies on the cost function and its gradient at each step. Solving PDE-constrained optimal control problems remains challenging, requiring the storage of state, adjoint, and control variables at each time step.

Finally, we present numerical tests to assess the efficiency and stability of the gradient algorithm.

Keywords: chemotaxis, finite element method, optimal control, algorithm of gradient

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Impact of age-structure dependent control during the first two years of COVID-19 pandemic in the Basque country

Akhil Kumar Srivastav[1], Nico Stollenwerk[1], Maíra Aguiar[1,2]

[1]Mathematical theoretical biology,
Basque Center for Applied Mathematics, Spain
asrivastav@bcamath.org
nstollenwerk@bcamath.org

[2]Ikerbasque, Basque Foundation for Science, Spain
maguiar@bcamath.org

The age distribution of the population certainly impacts the spread and control of infectious diseases. In this article, we propose and analyze an infectious disease, Coronavirus disease 2019 (COVID-19), a viral disease declared a pandemic by WHO. It has posed the greatest threat to global public health. The proposed work is a phase wise retrospective study of the Basque country of Spain. Understanding the dynamic of the virus could help make future predictions on the evolution of epidemics.

Our goal is to study the dynamics of the COVID-19 disease over the first two years. Considering understanding the dynamics of disease severity between young and old population during the first two years of the pandemic, we propose a deterministic modeling framework stratifying the total human population into two groups: older and younger, assuming different risks for severe disease manifestation. In addition to analyzing the proposed model mathematically, a thorough sensitivity analysis was carried out using the PRCC method to pinpoint the crucial parameters impacting the transmission dynamics of COVID-19 in the overall hospitalized population.

We observed that the population younger than 70 would contribute more to the overall force of infection than the older population. However, unlike the current age-based models, the new models offer different perspectives on how population age impacts disease severity in the COVID-19 pandemic.

Keywords: epidemiology, COVID-19 modeling, data analysis, age-structure

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

On the practical stability of h-manifolds for impulsive fractional-order gene regulatory networks

Gani Stamov, Ivanka Stamova

Department of Mathematics,
The University of Texas at San Antonio,
San Antonio, TX 78249, USA
gani.stamov@utsa.edu
ivanka.stamova@utsa.edu

We study a fractional-order generalization of a class of impulsive gene regulatory networks (GRNs). The concept of stability with respect to a manifold is introduced. The stable behavior of specific manifolds defined by a function h with respect to the model is investigated, and sufficient conditions are proposed by constructing suitable Lyapunov-type functions. The control effects of impulsive perturbations at fixed times on the stability behavior are discussed.

Keywords: gene regulatory networks, fractional derivatives, impulses, practical stability, h-manifolds

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Beyond the biting: a comparative study of dengue modeling approaches

Vanessa Steindorf[1], Nico Stollenwerk[1], Bob W. Kooi[1,2], Maíra Aguiar[1,3]

[1]Basque Center for Applied Mathematics, Spain
vsteindorf@bcamath.org
nstollenwerk@bcamath.org

[2]VU Amsterdam, The Netherlands
bob.kooi@vu.nl

[3]Ikerbasque-Basque Foundation for Science, Spain
maguiar@bcamath.org

Mathematical models play a crucial role in assisting public health authorities in disease control decision-making. For mosquito-borne diseases, integrating host and vector dynamics into models can be highly complex, particularly due to limited data availability, making system validation challenging.

In this study, extensions of SIR-type systems were proposed to model dengue fever transmission dynamics. The models differed in their treatment of mosquito dynamics: one incorporating it implicitly [1], while the other, explicitly modeling mosquito-host contact [2]. Both models considered temporary immunity after primary infection and disease enhancement in secondary infection, analogous to the temporary cross-immunity and the Antibody-dependent enhancement biological features observed in dengue epidemiology.

Qualitative analysis using bifurcation theory and numerical experiments revealed that the immunity period and disease enhancement outweighed the impact of explicit vector dynamics. Both models demonstrated similar bifurcation structures [3], that is, similar spread scenarios, indicating that explicit vector dynamics are only justified when assessing the effects of vector control methods. Otherwise, the additional complexity in the model is unnecessary, since both systems display similar dynamics.

The study underscores the importance of using simple models for mathematical analysis, initiating crucial discussions among the modeling community in vector-borne diseases.

Keywords: dengue fever, temporary cross-immunity protection, vector-host model, host-host model

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Modelling the effects of mosquito repellent in a two patch system with mobility

Kaloian Stoilov[1,2], Peter Rashkov[1]

[1]Institute of Mathematics and Informatics,
Bulgarian Academy of Sciences, Bulgaria
k.stoilov@math.bas.bg, p.rashkov@math.bas.bg

[2]Faculty of Mathematics and Informatics,
Sofia University "St. Kliment Ohridski"
kkstoilov@uni-sofa.bg

We study a malaria model with mobility between two patches subject to a control campaign based on mosquito repellents, based on previous work [1, 2]. The two control variables represent the proportion of repellent-protected population in each patch, and they are considered independent from one another. Each patch is assumed to have separate healthcare capacity. We address the question of limiting the sizes of infected populations at all future times in both patches below the respective capacities. This leads to a control problem of finding the viability kernel, which we translate to a variational problem using the level-set method [3]. A Hamilton-Jacobi-Bellman equation can be formulated and solved numerically [4]. Thus we determine how much the viability kernel is impacted by the effect of mobility between the patches, compared to the case when mobility is absent.

Keywords: ODE, malaria, mobility, control theory, HJB equation, level set

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Import driven large fluctuations in critical and subcritical percolation, state of the art and future perspectives

Nico Stollenwerk[1] & Maíra Aguiar[1]

[1]BCAM, Bilbao, Spain
nstollenwerk@bcamath.org

After introducing the notions of directed percolation (with a prime example in epidemiology being the SIS spatially extended stochastic system at and around the epidemiological threshold) and dynamical isotropic percolation (with the prime example being the SIR system), we show a simple renormalization scheme in the time domain to describe self-similarity at criticality and scaling near criticality.

Then we will charactrize the large fluctuations in subcritical epidemiological systems, which are driven by small import (in the limit of import vanishing), which is important in practical applications like invasion scenarios of vector-borne diseases [1], as well as prviosuly investigated during the COVID-19 pandemic after lock-down lifiting, avoiding supercitical explosion of infected but approaching the epidemiological threshold [2]. Technical aspects have been tackled since some time [3] (like Fock space representation of stochastic processes and path integrals), but now adjusted to the present scientific questions, relevant for the practical applications and data analysis.

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mathematical modeling of the chronic phase of Systemic Lupus Erythematosus

Vladimira Suvandjieva[1], Peter Rashkov[2], Ivanka Tsacheva[3]

[1]Institute of Mathematics and Informatics,
BAS, Bulgaria
vladimira.suvandjieva@math.bas.bg

[2]Institute of Mathematics and Informatics,
BAS, Bulgaria
p.rashkov@math.bas.bg

[3]Faculty of Biology,
Sofia University "St. Kliment Ohridski", Bulgaria
itsacheva@biofac.uni-sofia.bg

In this talk we will present a mathematical model for Systemic Lupus Erythematosus. The model consists of twelve ODE and represents the immune response during the chronic phase of SLE. It describes the interactions between immune cells, complement, complexes, antigens and cytokines during the adaptive immune response. We will show and analyze numerical results with several different sets of values for the parameters and initial conditions based on data from the literature, without going into detail about the analytical properties of the system. There is already a model concerning the initial phase of SLE in our article [2].

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Geometric nanoparticle model

Rebeka Szabó[1], Tímea Kégl[2], Gábor Lente[1]

[1]Department of Physical Chemistry and Materials Science,
University of Pécs, Hungary
rebekasz@gamma.ttk.pte.hu

[2]Department of General and Inorganic Chemistry,
University of Pécs, Hungary

Nanoparticles play an increasingly significant role in chemical research primarily in the catalytic processes of chemical reactions essential for sustainable energy management. The most crucial characteristic in the application of nanoparticles is their size, from which the surface-to-volume ratio can be inferred.

In the research summarized here, we have developed a new model extending across geometrical planes for nanoparticles, primarily for interpreting thermodynamic properties. The essence of the model lies in calculating the total internal energy of nanoparticles using the spatial arrangement of monomer units with the aid of the Lenard-Jones potential (which is inversely proportional to the sixth power of the distance between two monomer units, attractive, and to the twelfth power, repulsive).

By examining the internal energy based on the spatial coordinates of monomer units within the particle and seeking the energy minimum, the most favorable geometry can be determined, primarily needed for a small number of monomer units. For particles containing a larger number of monomer units, statistical considerations are more applicable. We also investigated the case of lattice structures. It was shown that any infinite lattice displaying translational symmetry is stable concerning the Lenard-Jones potential in the sense that the local energy minimum corresponds to the lattice's geometric arrangement.

Quantum mechanical calculations were also performed. We determined the total energy and geometry of palladium nanoparticles containing an increasing number of monomer units, comparing them with the expectations of the geometric model.

Keywords: geometric kernel, nanoparticle formation, Lenard-Jones potential

Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Oligooscillation in a closed system without autocatalysis

Rebeka Szabó, Gábor Lente

Department of Physical Chemistry and Materials Science,
University of Pécs, Hungary
rebekasz@gamma.ttk.pte.hu

Oscillatory chemical reactions are commonly associated with autocatalysis, where a product acelerates its own formation. This study presents a novel type of oscillation – termed *oligooscillation* – that occurs in a closed system without autocatalysis. The research focuses on a two-step consecutive reaction mechanism in which the second step is reversible, and an additional output reaction is included.

Through analytical modeling, we demonstrate that the concentration of a key reactant exhibits two maxima and one minimum over time, indicating oligooscillatory behavior despite the absence of autocatalysis. The findings suggest that oligooscillation emerges from the dynamic interplay between reaction rates and intermediate accumulation rather than self-catalyzing processes. This model introduces a new perspective on chemical kinetics in closed systems and provides insights into reaction mechanisms where oscillatory behavior can arise under previously unconsidered conditions. These results could have implications for understanding complex chemical and biochemical systems where oscillatory behavior is observed without an evident autocatalytic pathway.

Keywords: oligooscillation, general solution

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

A mathematical model of plasmid spread in microbial communities through horizontal gene transfer mechanisms

Julien Vincent[1], Alberto Tenore[2], Maria Rosaria Mattei[2], Luigi Frunzo[2]

[1]Microbial Ecology Laboratory,
University of Galway, Ireland
julien.vincent@universityofgalway.ie

[2]Department of Mathematics and Applications,
University of Naples, Italy
alberto.tenore@unina.it
mariarosaria.mattei@unina.it
luigi.frunzo@unina.it

Antimicrobial resistance (AMR) poses a critical global challenge with significant implications for public health and environmental sustainability. Antibiotic resistance genes (ARGs) are often carried within plasmids, mobile genetic elements capable of transferring between different microbial cells via horizontal gene transfer (HGT). This occurs primarily through conjugation, which enables direct cell-to-cell transfer, and natural transformation, where bacteria uptake extracellular DNA (eDNA). These processes, along with the presence of metal resistance genes (MRGs) on plasmids, are amplified by metal contamination, which increases selective pressure and facilitates the maintenance and dissemination of antibiotic resistance.

This study presents a multidimensional continuum model for plasmid dissemination in microbial communities via horizontal gene transfer. The model is formulated as a system of nonlocal partial differential equations derived from mass conservation laws and reaction kinetics principles. The microbial domain is modeled as a homogeneous, viscous, incompressible fluid with a velocity given by Darcy's law. The model considers plasmid-carrying cells as distinct volume fractions and their horizontal gene transfer via conjugation and natural transformation. Conjugation is modeled as a density-dependent process, due to the necessity of contact between a donor and a recipient cell to occur. A convolution integral regulates the gene transfer expression to account for its dependence on the presence of potential receptors around a donor, called recipient-sensing. A promotion function is also introduced to account for the burst in conjugation

due to the presence of trace metals. Transformation is modeled as a frequency-dependent process, considering the availability of natural eDNA as the primary factor affecting the process.

The model is solved numerically, and simulations are performed to examine how transformation and conjugation shape the dynamics and ecology of plasmid spread in a two-dimensional system, emphasizing their distinct ecological roles. Additionally, the study investigates how the microbial community regulates, and is in turn influenced by, metal dynamics. Model results confirm relevant experimentally observed evidences in plasmid spread, such as the respective intensity of different horizontal gene transfer mechanisms and the importance of selective pressure.

Keywords: horizontal gene transfer, plasmid dissemination, nonlocal PDEs, metal resistance

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Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Asymptotic analysis for a class of heat diffusion problems in composites with non-standard imperfect contact conditions

Micol Amar[1], Daniele Andreucci[1], Claudia Timofte[2]

[1]Department of Basic and Applied Sciences for Engineering,
Sapienza Università di Roma, Italy
micol.amar@uniroma1.it
daniele.andreucci@uniroma1.it

[2]University of Bucharest, Faculty of Physics, Romania
claudia.timofte@g.unibuc.ro

In this talk, we shall present some recent homogenization results for a class of heat diffusion problems in an ε-periodic two-phase composite material with imperfect contact conditions between its constituents. Here, ε is a small parameter related to the characteristic dimension of the underlying microstructure. On the interface separating the two phases, inspired by [1], we impose several non-standard transmission conditions of non-local type, obtained through a concentration procedure, by assuming that the interface is the limit of a thin anisotropic layer. By using periodic homogenization techniques, various macroscopic models are obtained at the limit (see [2, 3]).

Our setting might have applications in the analysis of diffusion processes in biological composite materials and, also, in the study of the electrical conduction in living tissues.

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Spatial patterning of bacterial colonization on leaf surfaces

Romina Travaglini[1,2], Marzia Bisi[2], Davide Cusseddu[3], Ana Jacinta Soares[4]

[1]INDAM – Istituto Nazionale di Alta Matematica Francesco Severi, Italy
travaglini@altamatematica.it

[2]Dipartimento di scienze Mathematihe, Fisiche e Informatiche,
Università di Parma, Italy
marzia.bisi@unipr.it

[3]Dipartimento di Scienze Matematiche G. L. Lagrange,
Politecnico di Torino, Italy
davide.cusseddu@polito.it

[4]Centro de Matemática,
Universidade do Minho, Portugal
ajsoares@math.uminho.pt

We present a mathematical model applied to bacterial aggregation on leaf surfaces, a phenomenon influenced by spatial heterogeneity in water and nutrient availability, and interactions among bacterial populations. These interactions, which may be cooperative or competitive, can result in diverse spatial patterns. By leveraging insights from the kinetic theory of active particles and classical macroscopic models, we derive a reaction-diffusion system for two interacting bacterial populations on a leaf surface. We perform numerical simulations that contribute to the understanding of microbial spatial organization and pattern formation.

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June 15–20, 2025, Sofia, Bulgaria
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QSAR modeling of arylsulfonylhydrazones as potential anti-breast cancer agents

Boris Vasilev, Mariyana Atanasova

Drug Design and Bioinformatics Lab, Faculty of Pharmacy,
Medical University of Sofia, Bulgaria
120588@students.mu-sofia.bg

Breast cancer is the most common cancer among women worldwide. Despite progress in early detection and treatment, there is still a pressing need for more effective drugs with fewer side effects. Arylsulfonylhydrazones exhibit a range of pharmacological properties, with their anticancer potential being of particular interest. Computational approaches, such as in silico analysis, play a crucial role in the early stages of drug discovery, significantly reducing the time and resources required for preliminary evaluations. In this study, a Quantitative Structure–Activity Relationship (QSAR) analysis, a widely used ligand-based drug design (LBDD) method, was applied to a series of arylsulfonylhydrazone derivatives to investigate the relationship between their chemical structures and anticancer activity against human breast cancer. The developed models can support the design of novel, promising compounds for further research and development as potential anticancer agents.

Keywords: QSAR, arylsulfonylhydrazones, anti-breast cancer agents

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Modelling spike frequency adaptation through higher-order fractional leaky integrate and fire model

Yash Vats[1,3], Mani Mehra[2], Dietmar Oelz[3]

[1]UQIDRA (UQ-IITD Research Academy),
Indian Institute of Technology Delhi (IIT-Delhi), India
yashvats425@gmail.com

[2]Department of Mathematics,
Indian Institute of Technology Delhi (IIT-Delhi), India
mmehra@maths.iitd.ac.in

[3]School of Mathematics and Physics,
University of Queensland, Australia
d.oelz@uq.edu.au

Spike frequency adaptation is a key characteristic of spiking neurons [1]. To examine this form of adaptation, we introduce a higher-order fractional leaky integrate and fire model. In this model, the exponent of the fractional derivative can range between one (representing an ordinary first order derivative) and two. In this regime, the impact of the past membrane potential on the present potential is inhibitory leading to spike frequency adaptation. We also analyze spike frequency adaptation in response to noisy input current and show that spike frequency adaptation is reinforced as the intensity of noisy input increases.

Keywords: spike frequency adaptation, neuron, fractional differential equation

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https://biomath.math.bas.bg/biomath/index.php/bmcs

Statistical approach for quantifying the evolution of tumor heterogeneity in chronic lymphocytic leukemia (CLL)

Vidhi Vidhi, Ulysse Herbach, Coralie Fritsch, Nicolas Champagnat

SIMBA team, Inria Center of University of Lorraine,
IECL, University of Lorraine, CNRS, France
vidhi.vidhi@inria.fr
ulysse.herbach@inria.fr
coralie.fritsch@inria.fr
nicolas.champagnat@inria.fr

Intra-tumor heterogeneity, a significant challenge in targeted cancer therapy, is particularly pronounced in CLL. Clonal evolution, driven by VDJ recombination and somatic hypermutation, generates a heterogeneous population of subclones that can confer resistance. Thus, phylogenetic tree reconstruction is key to understanding this process.

Using the weighted uniform distribution [1], we present a probabilistic framework for clonal reconstruction, generating a phylogenetic graph to better account for biological noise and allow sampling of multiple evolutionary trajectories, offering a more flexible and realistic model of tumor evolution than tree-based methods [2, 3]. To further refine this construction, we developed a Variational Expectation-Maximization algorithm, which systematically adds an optimal number of unobserved clones. This improves resolution, leading to a more complete and accurate representation of tumor evolution.

Future work will integrate longitudinal cancer gene mutation data (VCF) into our existing VDJ-based evolutionary graphs, creating a unified graph. This will provide a more comprehensive model of clonal evolution, improving insights into tumor progression and resistance for precision oncology.

Keywords: phylogenetic tree, VDJ sequencing, somatic hypermutation, leukemia, intraclonal heterogeneity, variational expectation maximization

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Migration in branching processes: An overview with open problems

Tsvetomira A. Zlatkova, Vessela K. Stoimenova

Faculty of Mathematics and Informatics,
Sofia University "St. Kliment Ohridski", Bulgaria
czlatkova@fmi.uni-sofia.bg
stoimenova@fmi.uni-sofia.bg

Branching processes with migration and control mechanisms play a fundamental role in modeling population dynamics, genetic evolution, and stochastic processes in various applied fields. While a lot is known about their theoretical properties, incorporating migration and control functions introduces significant complexity, particularly in statistical inference. Estimating key parameters remains a challenge due to data limitations and structural dependencies within the process.

We will review key developments in the study of controlled branching processes with migration, emphasizing probabilistic results and statistical challenges. Open questions and potential directions for future research are also discussed, highlighting gaps in existing methods and the need for new approaches.

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