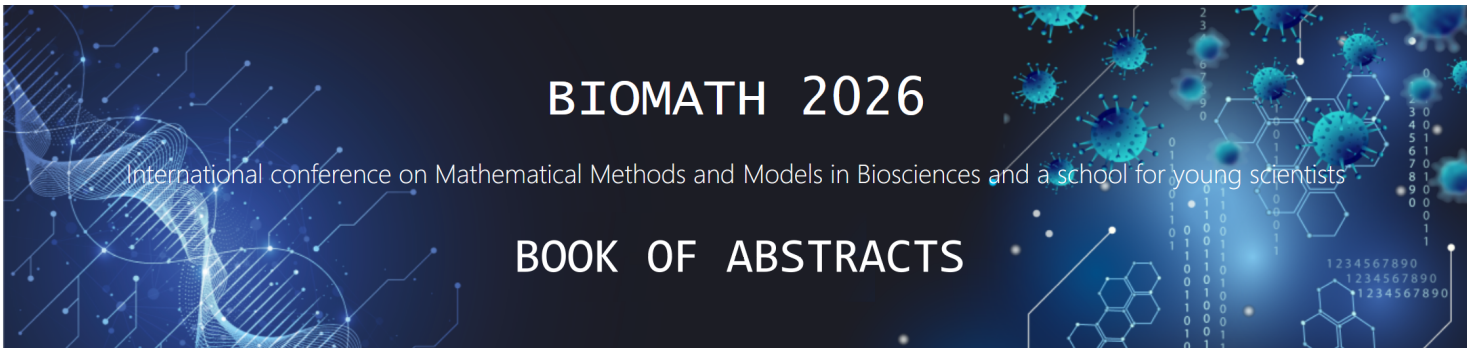
BIOMATH 2026
International conference on Mathematical Methods and Models in Biosciences and a school for young scientists
BOOK OF ABSTRACTS

DETAILED PROGRAM

Monday (June 15)

Morning

Plenary section **Chair: Gergely Röst**

08:50–09:00	**Opening ceremony**
09:00–10:00	**Wu, Jianhong:** Delay, feedback, and adaptation: a journey with Krisztin through ecology, epidemiology, physiology, and neural systems
10:00–10:30	**Sequeira, João:** Life science at big data scale: supercomputers for health

Coffee break

Section A **Chair: Kyeongah Nah**

11:00–11:30	**Ruiz-Herrera, Alfonso:** Dimension reduction and global attraction in delayed Wilson–Cowan neural networks
11:30–12:00	**Ivanov, Anatoly:** Periodicity in simple differential delay models from biological applications
12:00–12:30	**Nakata, Yukihiko:** A symmetric periodic solution for a class of distributed delay differential equations

Section B **Chair: Roumen Anguelov**

11:00–11:30	**Dumani, Phindile:** Dynamics of microbial communities exhibiting dormancy-driven oscillations
11:30–12:00	**Russo, Fabiana:** A thermodynamic model for water dynamics in subaerial biofilms
12:00–12:30	**Tenore, Alberto:** Modelling the role of phages in biofilm ecosystems and the spread of antimicrobial resistance

Afternoon

Plenary section **Chair: Ferenc Hartung**

14:00–15:00	**Kim, Yangjin:** Role of tumor-associated neutrophils and natural killer cells in regulation of the microenvironmental landscape of brain tumors: Delivery of nano-particles through BBB and STING pathways
15:00–15:30	**Walther, Hans-Otto:** On a protein synthesis model

Coffee break

Section A	**Chair: Hans-Otto Walther**
16:00–16:30	**Hartung, Ferenc:** On existence and uniqueness of solutions for impulsive differential equations with adaptive state-dependent delays
16:30–17:00	**Szczelina, Robert:** Periodic orbits in some delay differential equation modelling El Niño–Southern Oscillation
17:00–17:30	**Pituk, Mihály:** Linearized oscillation of delay differential equations
17:30–18:00	**Andò, Alessia:** Behavior-induced ocillations in epidemic outbreaks with distributed memory: Beyond the linear chain trick using numerical methods

Section B	**Chair: Sandip Banerjee**
16:00–16:30	**Srivastava, Pranjal:** A mathematical framework for per-read and per-sequence error characterization in single-molecule sequencing
16:30–17:00	**Khochman, Fatima:** Finite volume scheme and convergence analysis toward time-periodic solutions of the multidimensional monodomain model
17:00–17:30	**Didier, Francis:** Modeling STAT1–p53 cooperation under stress and p21/PUMA-mediated cell fate decisions
17:30–18:00	**Nali, Ibrahim:** Mushroom and isola bifurcations in a within-host bacterial infection model with Allee effect

18:30 Poster session and welcome reception

Tuesday (June 16)

Morning

Plenary section	**Chair: Gergely Röst**
09:00–10:00	**Nishiura, Hiroshi:** Balancing COVID-19 control and suicides: A unified modelling approach and challenges
10:00–10:30	**Oroszi, Beatrix:** When models meet reality: lessons from the COVID-19 pandemic

Coffee break

Section A	**Chair: Alfonso Ruiz-Herrera**
11:00–11:30	**Das, Bornali:** Inferring transmission regime shifts from population-level mortality data
11:30–12:00	**Nah, Kyeongah:** Impact of holiday mixing on influenza transmission: Why timing and preparedness matter
12:00–12:30	**Shi, Congjie:** Beyond vaccination coverage: A network model of vaccine attitude homophily and epidemic dynamics

Section B **Chair: Polly Yu**

11:00–11:30	**Rinas P R, Mohamed:** Impact of occupational noise exposure on diabetic control and psychological status in people with Type 2 diabetes mellitus
11:30–12:00	**Omer, Salaheldin:** Mutant p53 gain-of-function and immune suppression: Modeling the restoration of the STING–TBK1–IRF3 axis for enhanced cancer therapy
12:00–12:30	**Chapwanya, Michael:** A resource-limited phytoplankton growth model with nutrient recycling

Afternoon

Section A **Chair: József Farkas**

14:00–14:30	**Shillor, Meir:** On epidemiological models with state dependent infectivity, death and hospitalization
14:30–15:00	**Sensi, Mattia:** Avian flu modelling in poultry farms: case study of H5N1 HPAI in northern Italy in 2021–2022
15:00–15:30	**Kubik, Alicja B.:** Discovering the modes of action of antivirals from data and modelling: SARS-CoV-2 and Paxlovid as case study

Section B **Chair: Jacek Banasiak**

14:00–14:30	**Frunzo, Luigi:** Mathematical modelling of bioplastic degradation in marine environments
14:30–15:00	**Luongo, Vincenzo:** Modeling biofouling in microfiltration: A coupled filtration–biofilm model
15:00–15:30	**Bartha, Ferenc A.:** Multiscale modeling of viral infections and pharmacokinetics: from a generic hybrid framework to a Paxlovid case study

Coffee break

Section A **Chair: Mihály Pituk**

16:00–16:30	**Vizi, Zsolt:** Sensitivity analysis of social contact structures in epidemic models
16:30–17:00	**Garab, Ábel:** Evolution into chaos – implications of the trade-off between transmissibility and immune evasion
17:00–17:30	**Christopher, Julian:** The effect of time delay on the global stability of infectious disease models and other dynamical systems

Section B **Chair: Andrea Pugliese**

16:00–16:30	**Qwabe, Nkululeko:** Comparative dynamics of tuberculosis: The role of latency, treatment and relapse
16:30–17:00	**Balázs, István:** Discrete Lyapunov functional for systems of differential equations with time-variable delay
17:00–17:30	**Di Lenarda, Davide:** Extracting tent maps from the Mackey–Glass attractor

Wednesday (June 17)

Morning

Plenary section **Chair: Carsten Wiuf**

09:00–10:00	**Yu, Polly:** Non-monotonic dose-response curves in biochemical systems
10:00–10:30	**Hofbauer, Josef:** Lotka–Volterra systems

Coffee break

Section A **Chair: Josef Hofbauer**

11:00–11:30	**Boros, Balázs:** Codimension-three Andronov–Hopf bifurcation in infectious diseases affecting juveniles
11:30–12:00	**Kovács, Sándor:** Delay induced instability in system modelling COVID-19
12:00–12:30	**Anița, Sebastian:** Regional control of some reaction-diffusion systems in population dynamics

Section B **Chair: Yangjin Kim**

11:00–11:30	**De Reggi, Simone:** Stability analysis for a size-structured prey-predator model with self-regulation and resource dependent growth rates
11:30–12:00	**Olasz, Katalin:** Application of geometric modeling and optimal assignment algorithms in cell tracking
12:00–12:30	**Boldog, Péter:** The impact of programmed cell death on cell population dynamics: a stochastic and moment dynamics approach

Afternoon

Plenary section **Chair: Katerina Stankova**

14:00–15:30	**Wiuf, Carsten:** Molecular machines and the EM algortihm
15:00–15:30	**Banerjee, Sandip:** Modeling the dynamics of the Hepatitis C virus with a combined antiviral drug therapy: Interferon and Ribavirin

Coffee break

Section A **Chair: Michael Chapwanya**

16:00–16:30	**Ouifki, Rachid:** Modeling and optimal control of the ERβ paradox in TNBC: repurposing Tamoxifen for combination therapy
16:30–17:00	**Geretovszky, Anna:** When saboteur bacteria undermine chemotherapy: a mathematical model of cancer treatment dynamics
17:00–17:30	**Polner, Mónika:** Bistability and complex bifurcation diagrams generated by waning and boosting of immunity
17:30–18:00	**Kojouharov, Hristo:** Modeling competitive dynamics between healthy and cancerous liver cells under yes-associated protein (YAP) hyperactivation

Section B **Chair: Fabiana Russo**

16:00–16:30	**Régaisz, Olivér:** Real time modeling of the 2025 foot and mouth disease outbreak in Hungary and Slovakia
16:30–17:00	**Vásárhelyi, Bálint:** Genomic resolution of *Klebsiella pneumoniae* diversity enables scalable phage therapeutics
17:00–17:30	**Varga, Tamás:** Matrix games among full siblings in Mendelian populations
17:30–18:00	**Nyaweni, Fundile Sindy:** Comparative dynamics of tuberculosis:The role of latency, treatment and relapse

Thursday (June 18)

Morning

Plenary section **Chair: Bob Rink**

09:00–10:00	**Wodarz, Dominik:** Evolutionary dynamics of tissue and tumor cell populations: importance of spatial structure
10:00–10:30	**Pugliese, Andrea:** SEIR models with host heterogeneity

Coffee break

Section A **Chair: Meir Shillor**

11:00–11:30	**Banasiak, Jacek:** Metapopulations, delays and network transport with dynamics at the nodes
11:30–12:00	**Anguelov, Roumen:** On the mathematical models of time dependent inhibition of tumor growth
12:00–12:30	**Farkas, József:** Evolution of virulence in populations with a distributed parasite load

Section B **Chair: Yukihiko Nakata**

11:00–11:30	**Csuma-Kovács, Rita:** The mathematical analysis of transmission dynamics of varicella
11:30–12:00	**Glavosits, Villő:** Threshold dynamics in a time-delayed logistic model of cell populations
12:00–12:30	**Singh, Kanchan:** Dynamics and pattern formation in a prey–predator model with Allee effect and anti-predator behavior

14:00–19:00 Social programs

19:00–21:00 Gala dinner

Friday (June 19)

Morning

Plenary section **Chair: Yangjin Kim**

09:00–10:00	**Stankova, Katerina:** Combatting Darwinian diseases through Stackelberg evolutionary game theory
10:00–10:30	**Rink, Bob:** Reconstructing resonant interactions in oscillator networks from noisy time series

Coffee break

Section A **Chair: Hiroshi Nishiura**

11:00–11:30	**Dénes, Attila:** A two-patch SEIR model with prevalence-dependent behavioural response and mobility for Ebola dynamics
11:30–12:00	**Tekeli, Tamás:** What we saw was what we got? Correcting reported incidence data for testing intensity
12:00–12:30	**Röst, Gergely:** Behavioural dynamics in epidemic models: reversible and irreversible responses to infection risk

Section B **Chair: Alberto Tenore**

11:00–11:30	**Lee, Donggu:** Asthma-mediated control of optic glioma growth via T cell-microglia interactions: A mathematical model
11:30–12:00	**Devries, Kaylee Leslie:** Analysis of a general vector transmission model for infectious disease spread

ABSTRACTS

PLENARY TALKS

Role of tumor-associated neutrophils and natural killer cells in regulation of the microenvironmental landscape of brain tumors: Delivery of nano-particles through BBB and STING pathways

Yangjin Kim

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Glioblastoma multiforme (GBM) is the most aggressive form of brain cancer with the very poor survival and high recurrence rate. Tumor-associated neutrophils (TANs) play a pivotal role in regulation of the tumor microenvironment. In this study, we developed a new multi-scale model of the critical GBM-TAN interaction in the heterogeneous brain tissue. The model reveals that the dual and complex role of TANs (either anti-tumorigenic N1 and the pro-tumorigenic N2 type) regulates the phenotypic trajectory of the evolution of tumor growth and the invasive patterns in white and gray matter via mediators such as IFN-beta and TGF-beta. We investigated the effect of normalizing the immune environment on glioma growth by applying a therapeutic antibody and developed several strategies for eradication of tumor cells by neutrophil-mediated transport of nanoparticles. We also developed a strategy of combination therapy (surgery + Trojan neutrophils) for effective control of the infiltration of the glioma cells in one hemisphere before crossing the corpus callosum (CC) in order to prevent recurrence in the other hemisphere. This alternative approach compared to the extended resection of the glioma including CC or butterfly GBM may provide the greater anti-tumor efficacy and reduce side effects such as cognitive impairment. Natural Killer (NK) cells play an important role in mediating immune responses to a growing tumor and cancer treatment such as oncolytic virus and radiation therapies. NK cells controls a tumour microenvironment through the STING signaling pathway and therapeutic agents such as ADU-S100, a synthetic compound, were used to test anti-tumor efficacy of the immune therapy both in experiments and mathematical models. We suggest various therapeutic approaches such as agents overcoming brain blood barrier (BBB) and detailed BBB dynamics.

Balancing COVID-19 control and suicides: A unified modelling approach and challenges

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During the coronavirus disease 2019 (COVID-19) pandemic, public health and social measures (PHSM) caused reduced mobility and contact, limiting secondary transmission. However, PHSM involved unintended societal costs, including an increase in the number of suicides in Japan, particularly among young adults. The present study examined the balance between COVID-19 deaths and suicides, modelling both outcomes as a unified mathematical system and taking the sum as the objective function. The transmission dynamics of COVID-19 were mechanistically modelled, and the number of excess suicides was predicted with a collaterally modelled statistical causal framework using unemployment statistics and social mood survey data as intermediate variables. Identifying the optimal additional control effort relative to existing control measures, we estimated that interventions 17% (95% confidence interval: 9%, 41%) more stringent than the interventions actually implemented would have minimized the total number of deaths. When applying greater weight to young adults via years of life lost, interventions with 10% (95% confidence interval: 9%, 43%) greater effort minimized the total disease burden. Using the proposed approach in real time could enable policymakers to choose a balanced choice of interventions in future pandemics, such as minimizing human life impact with slightly more stringent interventions in the case of the COVID-19 pandemic from 2020–2021.

When models meet reality: lessons from the COVID-19 pandemic

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The recent pandemic provided unprecedented opportunities and challenges in the use of quantitative methods for public policy. Models, projections, and epidemic curves became not only scientific tools but also key inputs to decision making affecting millions of people. Drawing on experiences from COVID-19 in Hungary, the talk examines the role of modelling in pandemic response. Particular attention will be given to the interpretation of surveillance data and epidemic trends, the communication of uncertainty, and the interplay between data, models, and expert judgment. The talk will also reflect on the limitations that became apparent when models were confronted with rapidly changing human behavior, varying interventions, and the emergence of new viral variants.

Combatting Darwinian diseases through Stackelberg evolutionary game theory

Katerina Stankova

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Darwinian diseases, such as cancer and antibiotic-resistant infections, evolve through natural selection in response to medical interventions, often leading to treatment failure. Traditional treatment strategies typically ignore this adaptive response, motivating game-theoretic models that explicitly account for interactions between strategic decision-makers and evolving populations. We introduce a general framework in which a rational leader interacts with evolutionary followers, whose strategies change through selection rather than deliberate optimization. This leader–follower interaction extends classical Stackelberg games by integrating evolutionary game dynamics with strategic optimization, allowing policies to anticipate both ecological and evolutionary feedback. Through this framework, we demonstrate how leader's evolutionarily informed strategies can outperform standard maximum tolerated dose approaches by stabilizing disease burden while reducing treatment-induced resistance. More broadly, this framework provides a unifying mathematical approach for strategic decision-making in evolving systems, which we term Stackelberg evolutionary games, opening new directions for applying game theory to biological, medical, and socio-ecological problems.

Molecular machines and the EM algortihm

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The implementation of abstract dynamical systems as molecular systems has gained scientific interest. Automated theoretical schemes can compile formal reaction networks into DNA oligonucleotide sequences; thereby providing a potential molecular implementation of the dynamics of the formal reaction network. In this context, we propose a novel algorithm for learning parameters of Hidden Markov Model (HMM), a flexible statistical framework widely used in Bioinformatics, Machine Learning and Data Science to model an underlying hidden structure.

Our algorithm is specified by a network of chemical reactions, and mimics the Baum-Welch algorithm which is the standard learning algorithm for HMMs. The Baum–Welch algorithm is an iterative Expectation-Maximization (EM) algorithm where one step is performed at a time in a prescribed sequence. The reaction network scheme is divided into four subnetworks that correspond to the forward, backward, expectation, and maximization steps of the Baum–Welch algorithm. Each subnetwork describes a system of ordinary differential equations

that might be run separately, exactly mimicking the steps of the Baum-Welch algorithm, or simultaneously, thereby obtaining a variant on the Baum-Welch algorithm.

Promising areas of application of this work come from cellular biology. In the future, a molecule-based HMM device might learn a molecular environment within an organism by sensing and interacting with the environment at the molecular level. It might take action according to the learning outcome, for example, choosing among different drug options, or a molecule-based HMM might be used as a building block in an artificial cell or population of cells, enabling cooperative behavior among cells or facilitating various tasks.

Joint work with Abhinav Singh, Abhishek Behera and Manoj Gopalkrishnan.

Evolutionary dynamics of tissue and tumor cell populations: importance of spatial structure

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Spatial organization is a fundamental feature of tumor architecture that profoundly shapes cellular evolution and selection. This lecture examines how spatial structure influences evolutionary dynamics, with implications for driver mutation selection, tumor progression, and therapeutic resistance. I will begin by surveying spatially explicit computational modeling approaches for cellular dynamics and evolution, emphasizing the relationship between continuous-space agent-based models and coarse-grained deme models that enable analytical tractability. Through selected studies, I will explore mutant evolution in spatially structured populations, first examining expanding populations across different dimensions, then investigating mutant invasion at steady state, which is relevant for both non-neoplastic tissue and tumors in growth plateau phases during multi-step carcinogenesis. I will close by discussing our recent finding that spatial structure can reverse conventional selection: mutants with increased reproductive output may experience negative selection when multiple kinetic parameters change simultaneously, for instance, concurrent increases in both division and death rates. This challenges the assumption that higher reproductive output generally confers a selective advantage. Overall, the lecture highlights how spatial population structure can fundamentally alter evolutionary principles in unexpected ways, deepening our understanding of tumor cell emergence during progression and therapy.

Delay, feedback, and adaptation: a journey with Krisztin through ecology, epidemiology, physiology, and neural systems

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This talk begins with a brief overview of earlier joint work with Tibor Krisztin on delay feedback systems with lossless feedback, focusing on their asymptotic behavior, including convergence to steady states and the emergence of periodic solutions. Building on these foundational results, we trace how the theory has evolved over the past four decades into a broader and more unified framework. This framework is applicable to a wide range of ecological and epidemiological models and captures intrinsic order-preserving dynamics with respect to both standard and non-standard high-rank cones.

Non-monotonic dose-response curves in biochemical systems

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A response curve measures the output of a biological system at equilibrium against an input parameter u, which could be a rate constant, or the dose of a stimulus (poison, drug, ligand, etc.). A non-monotonic response curve acts as a mechanism against overactivation. For example, it has been observed that a T-cell's response to antigen concentration is non-monotonic. We introduce the notions of feedback and feedforward loops for a general system of differential equations, and see how some of these network motifs are necessary for biphasic response. As application, we take a closer look at a model of T-cell response.

CONTRIBUTED TALKS

Behavior-induced ocillations in epidemic outbreaks with distributed memory: Beyond the linear chain trick using numerical methods

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We consider a model for an infectious disease outbreak, when the depletion of susceptible is negligible, and assume that individuals adapt their behavior according to the information they receive about the new cases. In line with the information index approach [1], we assume that individuals react to the past information according to a memory kernel that is continuously distributed in the past. Thanks to the recently developed pseudospectral approximation of delay equations [2], we study numerically the long-term dynamics of the model for memory kernels defined by Gamma distributions with general non-integer shape parameter, extending the analysis beyond what is allowed by the linear chain trick. In agreement with previous studies [3], we show that behavior adaptation alone can cause sustained waves of infections even in an outbreak scenario, and notably in the absence of other processes like demographic turnover, seasonality or waning of immunity. Our analysis gives a more general insight of how the period and peaks of the epidemic waves depend on the shape of the memory kernel and of how the level of minimal contact (essential service) impacts on the stability of outbreak disease equilibrium and behavior-induced positive equilibrium.

Acknowledgments:

The presenter is member of INdAM research group GNCS (Gruppo Nazionale per .il Calcolo Scientifico). Her research is partially supported by the PRIN 2022 SCORR project "Stochastic numerical modelling for sustainable innovation" (No. 20229P2HEA, CUP G53C24000710006) of the Italian Ministry of University and Research (MUR).

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On the mathematical models of time dependent inhibition of tumor growth

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The inhibition of tumor growth is typically modeled as a reduction of its natuaral growth rate, [5,6,9]. Using the so called "log-kill" pattern, [8], [**?**, **?**, 6, Eq.(7)] [9, Eq.21, Eq.22], the growth rate of the inhibited population is given in the form $r - h$, where r is the natural growth rate under optimal conditions and h represents the impact of the inhibitor. Hence, the basic model for the size of the population P of tumor cells is

$$\frac{\partial P}{\partial t} = (r - h)P. \tag{1}$$

Usually h is considered a function of the concentration x of the inhibitor, which is independent of the duration of the treatment t. In fact, when dependance on t is considered, it usually represents change of treatment/dose/concentration at certain times, [6]. For example, in [7] the dependence of h on t represents an "on-off" switch of treatment.

In our recent work on modelling and analysing of inhibition of B16-F10 melanoma cells with various inhibitors we established experimentally and theoretically that the inhibition rate may vary with time, specifically, it increases from 0 to some maximal value, [1–4]. It is well known that h exhibits similar behavior with respect to x.

In this talk we consider if and when the inhibition function h can be considered as a function of the product xt, that is, using a kind of a "mass action" principle. This question is relevant, because deriving h as a function of x and t may lead to involvement of many parameters in a setting in which the experimental data is usually scarce. Considering h as a function of xt is motivated by the following observations in the mentioned research:

- the saturation level of h when $t \to +\infty$ or $h \to +\infty$, or both, is independent of x and t,
- $\frac{\partial h(x,t)}{\partial t}$ is increasing on x, $\frac{\partial h(x,t)}{\partial x}$ is increasing on t.

We apply the stated modelling approach using the experimental data in [1–4] and use statistical analysis to show its advantages.

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Regional control of some reaction-diffusion systems in population dynamics

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We investigate some regional control problems for reaction-diffusion models in mathematical biology. The models describe the dynamics of interacting populations and contain local or nonlocal reaction and diffusion terms. A special attention is given to the necessary and sufficient conditions for stabilizability and to the structure of a stabilizing feedback control.

Discrete Lyapunov functional for systems of differential equations with time-variable delay

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We consider nonautonomous cyclic systems of delay differential equations with variable delay having various applications in biology. Under suitable feedback assumptions, we define an (integer valued) Lyapunov functional related to the number of sign changes of the coordinate functions of solutions. We prove that this functional possesses properties analogous to those established by Mallet-Paret and Sell for the constant delay case and by Krisztin and Arino for the scalar case. We also apply the results to equations with state-dependent delays.

Metapopulations, delays and network transport with dynamics at the nodes

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The talk's starting point is a linear metapopulation model, where the subpopulations can migrate between the nodes. Acknowledging that individuals appear at the target nodes some time after they depart from the home nodes, we arrive at a system of ordinary differential equations with delays. We aim to rephrase the model as a transport model on a digraph, where the delays result from the flow of individuals along the edges between the connected nodes. We show that such a model requires introducing specific dynamic conditions at the nodes relating the incoming and outgoing flows. The developed framework can be used to build a general model describing many metapopulation phenomena, e.g., disease spread through migrations. We present a preliminary qualitative analysis of the general model.

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Modeling the dynamics of the Hepatitis C virus with a combined antiviral drug therapy: interferon and ribavirin

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This talk introduces a mathematical model of the hepatitis C virus (HCV) dynamics and the effects of antiviral treatment. The model consists of four coupled ordinary differential equations that capture the interactions among target cells (hepatocytes), infected cells, infectious virions, and non-infectious virions. It combines ribavirin and interferon therapy and explains the observed biphasic and triphasic patterns of viral load decline. A critical drug-efficacy threshold is identified, indicating that HCV can be eliminated when treatment efficacy exceeds it. In contrast, when efficacy remains below the critical level, the system converges to a new equilibrium characterized by a reduced, yet persistent, population of infectious virions compared with the pre-treatment steady state.

Multiscale modeling of viral infections and pharmacokinetics: from a generic hybrid framework to a Paxlovid case study

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Mathematical models are indispensable tools for understanding viral dynamics and assessing the efficacy of antiviral therapies. We present a hybrid multiscale framework that merges continuous partial differential equations (PDEs) with discrete agent-based modeling (ABM) to capture the spatiotemporal progression of viral infections within lung tissue. By representing epithelial cells as individual discrete agents and both virus and drug concentrations as continuous variables, the model effectively bridges distinct biological and physical scales.

First, we outline the generic architecture and mathematical foundations of this framework. We explore varying drug delivery methods and integrating interventions that increase viral clearance, induce infected cell cytotoxicity, reduce viral budding, and inhibit target cell infection. Then, we apply the generalized foundation to a specific clinical scenario: an in silico evaluation of Paxlovid (nirmatrelvir and ritonavir) against SARS-CoV-2. The computational simulations successfully replicate clinical in vitro data and verify the biological necessity of ritonavir as a pharmacokinetic enhancer for simplified in vivo cases.

Joint work with N. Juhász, S. Marzban, R. Han, G. Röst, D. Zs. Gálfi

The impact of programmed cell death on cell population dynamics: a stochastic and moment dynamics approach

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Classical mean-field models of cell population dynamics, including cancer progression, often rely on the "well-mixed" assumption and neglect the role of cell death. In this work, we demonstrate how these simplifications lead to a significant overestimation of growth rates and saturation levels, with critical implications for tumor therapy design.

First, we present a stochastic modeling framework comparing mean-field approximations with Agent-Based Models (ABM) to investigate the "Ghost Effect" – a phenomenon where apoptotic cells do not vanish instantly but act as static barriers. These structures preserve spatial "memories" of former clusters, persistently inhibiting the motility and proliferation of living cells. Our results show that spatial correlations and volume exclusion consistently predict a lower carrying capacity than classical models.

Then, to bridge the gap between computationally expensive simulations and overly simplistic ODEs, we use a Moment Dynamics approach. By tracking higher-order moments,

we derive a system of coupled ODEs that captures crowding effects and correlation-induced inhibition at a fraction of the computational cost.

Finally, we discuss applications in clinical oncology, highlighting how realistic modeling can help determine minimal effective chemotherapy doses by accounting for self-crowding.

Joint work with Márk Veres.

Codimension-three Andronov–Hopf bifurcation in infectious diseases affecting juveniles

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We present a three-compartment infectious disease model with a few transitions that, despite its simplicity, admits multiple stable limit cycles when modeled with ordinary differential equations. In fact, we show that the unique endemic equilibrium undergoes a codimension-three Andronov–Hopf bifurcation (a.k.a. a Takens–Hopf bifurcation). The rigorous analysis requires us to compute the first, second, and third focal values (a.k.a. Lyapunov coefficients).

The key feature of the model is that juveniles are affected by the disease disproportionately seriously: after contracting the disease, they die before they can transmit it further. At the same time, adults recover from the illness and gain lifelong immunity. The number of limit cycles that bifurcate from the endemic equilibrium depends on how much more easily a juvenile can contract the disease, and also on the basic reproduction number.

Finally, we draw a connection between our model and the standard SIRWS model. The latter is known to admit a codimension-two Andronov–Hopf bifurcation (a.k.a. a Bautin bifurcation). We discuss how this fact follows immediately from our new results by invoking the recently developed theory of inheritance.

Surrogate-assisted virtual population generation in QSP models

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Background Quantitative Systems Pharmacology (QSP) integrates systems biology and pharmacology to describe and predict how drugs interact with biological systems. It relies on mathematical models, often formulated as systems of ordinary differential equations, that encode the underlying biological knowledge of the system. Sparse population-level data

and model non-identifiability often yield multiple plausible parameterizations, motivating the use of virtual populations (VPops) to represent uncertainty and inter-individual phenotypic variability [1,2]. Among the available generation strategies [3,4,5,6], widely used approaches follow the Allen et al. framework [3]. However, generating such populations remains computationally demanding for complex QSP models, as the algorithms require repeated evaluation of the model across many parameter sets. Here, we extend the Allen et al. framework by introducing a surrogate-assisted strategy, in which model evaluations are replaced by a surrogate model, and we assess its impact across multiple VPop generation algorithms.

Methods The framework proposed by Allen et al. [3] assumes a model together with a set of observable quantities described by the model and measured experimentally. The algorithms consist of two main steps: first, the generation of plausible patients (PPs), i.e., a set of model parameterizations that produce biologically realistic model simulations; and second, the selection of a Virtual Population (VPop), whose goal is to reproduce the distribution of the observed data. To extend this framework, we introduced a surrogate-assisted approach in which a Gaussian process surrogate was trained to approximate the mapping from the parameter space to corresponding model observables, to avoid the numerical integration of the dynamical system during the PPs generation. Evaluations were performed on three QSP models of increasing dimension: plasma cholesterol regulation [8] (9 variables), colonic motility [9] (15 variables) and Gaucher's disease type 1 (GD1) [10] (82 variables)—implemented in MATLAB R2025b. In all test cases, the systems were calibrated using parameter values from the literature. The VPop generation methods were compared using established metrics of efficiency, diversity, convergence to empirical target distributions (Kolmogorov–Smirnov (KS) distance in marginal distributions) and computational cost [4].

Results Surrogates noticeably improved the speed of Markov Chain Monte Carlo (MCMC), Simulated Annealing (SA), and Nested Simulated Annealing (NSA) algorithms [**?**] for the two higher-dimension models (GD1 and colon motility). For the lower-dimensional plasma cholesterol model, this improvement was only observed with SA, for the other two methods, the original simulation approach remained more efficient. In the colon motility system the approach reduced the time required to obtain one virtual patient by 2.70×, 6.09×, and 5.38× relative to the corresponding full simulations with MCMC, SA, and NSA, respectively (Table 1). Similarly, for the GD1 model, the corresponding speedups were 1.21×, 1.25×, and 3.36× (Table 2). Finally, for the plasma cholesterol model, a speedup was achieved with SA 1.14×, while efficiency decreased for MCMC 0.55× and NSA 0.69× (Table 3). Among the tested algorithms, MCMC showed convergence difficulties and reduced diversity relative to SA and NSA, consistent with previous observations [4]. For the remaining metrics, namely diversity and goodness of fit, we observed no significant differences between the full simulated system and the surrogate approach.

Conclusion Our results show that surrogate-assisted optimization significantly accelerates VPop generation in high-dimensional QSP models without compromising the resulting goodness of fit, diversity, or parameter distribution. Ultimately, the success of this strategy depends on the trade-off between training overhead and the surrogate's ability to identify the cost function's minima, rather than its ability to replicate the full dynamical system. While direct simulation is still better for low-dimensional models like the plasma cholesterol case, surrogate-assisted optimization is a promising scalable strategy for VPop generation in more

Colon Motility Model				
	Simulated		Surrogate	
(lr)2-3 (lr)4-5 Method	Time [sec/N_{Vpop}]	GoF	Time [sec/N_{Vpop}]	GoF
MCMC	36.45 ± 28.60	0.62 ± 0.01	13.49 ± 8.99	0.562 ± 0.01
SA	135.40 ± 45.91	0.456 ± 0.02	22.25 ± 18.38	0.4095 ± 0.04
NSA	148.74 ± 148.63	0.5819 ± 0.04	27.66 ± 8.55	0.5858 ± 0.02

Table 1: Comparison of VPop generation methods for the colon motility model. All measurements were repeated six times, and results are reported as mean values. Reported times correspond to the mean time required to generate one virtual patient, while goodness of fit (GoF) was evaluated using the Kolmogorov–Smirnov test.

Gaucher disease type 1 Model				
	Simulated		Surrogate	
(lr)2-3 (lr)4-5 Method	Time [sec/N_{Vpop}]	GoF	Time [sec/N_{Vpop}]	GoF
MCMC	2.3584 ± 0.84	1.5560 ± 0.02	1.9474 ± 0.39	1.5737 ± 0.02
SA	9.8694 ± 1.88	3.2590 ± 0.03	7.8889 ± 1.36	3.2819 ± 0.03
NSA	55.108 ± 9.06	1.8619 ± 0.03	16.384 ± 1.31	1.7954 ± 0.04

Table 2: Comparison of VPop generation methods for the Gaucher disease type 1 model. All measurements were repeated six times, and results are reported as mean values. Reported times correspond to the mean time required to generate one virtual patient, while goodness of fit (GoF) was evaluated using the Kolmogorov–Smirnov test.

complex QSP applications.

Joint work with Stefano Giampiccolo and Luca Marchetti.

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	Plasma Cholesterol Model			
	Simulated		Surrogate	
(lr)2-3 (lr)4-5 Method	Time [sec/N_{Vpop}]	GoF	Time [sec/N_{Vpop}]	GoF
MCMC	0.1736 ± 0.08	0.0677 ± 0.01	0.31709 ± 0.12	0.0832 ± 0.01
SA	8.4828 ± 1.72	0.0657 ± 0.01	7.4588 ± 1.27	0.0628 ± 0.01
NSA	3.8619 ± 1.09	0.0569 ± 0.03	5.6283 ± 1.39	0.0608 ± 0.04

Table 3: Comparison of VPop generation methods for the Plasma Cholesterol model. All measurements were repeated six times, and results are reported as mean values. Reported times correspond to the mean time required to generate one virtual patient, while goodness of fit (GoF) was evaluated using the Kolmogorov–Smirnov test.

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A resource-limited phytoplankton growth model with nutrient recycling

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Phytoplankton are central to aquatic food webs and global biogeochemical cycles, yet their recurrent bloom dynamics and coexistence patterns challenge classical ecological theory. We propose a spatially explicit, resource-limited nutrient-phytoplankton-zooplankton model that incorporates nutrient recycling, general functional responses, and self-diffusion. Bifurcation analysis reveals conditions for the emergence of stationary and sustained oscillatory patterns driven by the interplay between nutrient utilisation and diffusion. Numerical simulations are provided.

The effect of time delay on the global stability of infectious disease models and other dynamical systems

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When studying mathematical models of infectious disease, one characteristic of great interest is the long term persistence of the disease: given an initial infection rate, will it become

endemic? or die out? Mathematically this is a question about the stability of an endemic equilibrium. Since the initial conditions of an outbreak are not under our control, local stability results are often insufficient: one would like to know whether the conditions present in a specific outbreak would lead the system to the endemic equilibrium, or to disease extinction. For this reason, global stability results play an important role in the analysis of epidemic models.

In this talk we examine the effect of delayed variables on the global stability of systems of ordinary differential equations. This problem arises naturally in mathematical models of infectious disease, where delays may represent vector-borne transmission, incubation periods, temporary immunity, or other biological processes that prevent instantaneous responses in the system. Our approach is based on Lyapunov's Direct Method. Specifically, we construct Lyapunov functionals for the delayed system by modifying the Lyapunov functions used for the corresponding ODE model. This approach allows us to extend stability results from the non-delayed system to the delayed system, and provides a framework for analyzing the effect of delays in a broad class of dynamic models.

The mathematical analysis of transmission dynamics of varicella

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Varicella (chickenpox) is a highly transmissible childhood infection caused by the varicella-zoster virus (VZV). In Hungary, varicella vaccination has been available for several years and was incorporated into the national routine immunization programme in September 2019. We analyse VZV transmission using a compartmental model ex- tended with a realistic age structure (RAS) comprising 66 age groups. The model is used to assess the impact of the implemented two-dose vaccination schedule on VZV circulation. As the introduction of routine vaccination coincided with the onset of the COVID-19 pandemic in Hungary, we also examine how pandemic-related behavioural and contact-pattern changes may have influenced VZV transmission dynamics. The results highlight the combined effects of vaccination and pandemic disruptions on the epidemiology of VZV.

Joint work with Gergely Röst.

Inferring transmission regime shifts from population-level mortality data

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Infectious disease dynamics emerge from complex interactions between transmission pathways and host behavior, yet identifying shifts in transmission regimes is often limited by the lack of detailed case-level data. Here, we show that population-level mortality trajectories can contain sufficient information to detect discrete changes in transmission dynamics. Using a spatially explicit metapopulation model, we analyze mortality records from seven settlements during the 1878–1879 plague outbreak in the Lower Volga region. We demonstrate that the observed epidemic trajectories cannot be reproduced by models assuming smoothly varying transmission, but instead require distinct temporal regimes. In particular, we identify an early amplification phase characterized by an order-of-magnitude increase in effective transmission, followed by a rapid transition to a suppressed regime consistent with strong behavioral feedbacks. These results indicate a reorganization of underlying transmission processes, potentially reflecting a shift toward more efficient human-to-human transmission, although the specific mechanisms cannot be uniquely identified from mortality data alone. More broadly, our findings show that epidemic trajectories can encode discrete regime shifts arising from ecological and behavioral feedbacks, and that such transitions can be inferred from aggregate data. This provides a generalizable framework for detecting hidden changes in transmission dynamics in both historical and contemporary outbreaks where detailed clinical data are unavailable.

Stability analysis for a size-structured prey-predator model with self-regulation and resource dependent growth rates

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We investigate the dynamics of a size-structured predator-prey model with nonlinear growth rates. We assume that the prey growth rate decreases with prey population density, while the predator growth rate depends on predation. By appropriate scaling, let 0 denote the size at birth, and 1 denote the maximal size of both prey and predators. Furthermore, let $u(t, s)$

and $v(t,s)$, for $t \geq 0$ and $s \in (0,1)$, denote the prey and predator size-densities. In its most general form, the model is described by the following system of quasi-linear equations:

$$\begin{cases} \dfrac{\partial}{\partial t}u(t,s) + \dfrac{\partial}{\partial s}\left[g_1(U(t),s)u(t,s)\right] = -\left[d_1(s) + (Hv(t,\cdot))(s)\right]u(t,s), \\ \dfrac{\partial}{\partial t}v(t,s) + \dfrac{\partial}{\partial s}\left[g_2\left((Ku(t,\cdot))(s),s\right)v(t,s)\right] = -d_2(s)v(t,s), \\ g_1(U(t),0)u(t,0) = \displaystyle\int_0^1 \beta_1(s)u(t,s)\,ds, \\ g_2\left((Ku(t,\cdot))(0),0\right)v(t,0) = \displaystyle\int_0^1 \beta_2(s)v(t,s)\,ds, \end{cases}$$

where, denoting with $h(s,z)$ the attack rate of predators of size z on prey of size s, with $h \in C([0,1],\mathbb{R})$,

$$H(t,s) = \int_0^{\bar{s}} h(s,z)v(t,z)\,dz$$

is the *total attack rate* on prey of size s,

$$K(t,s) = \int_0^{\bar{s}} zh(z,s)u(t,z)\,dz$$

is the *gain* to predators of size s, and

$$U(t) = \int_0^1 u(t,s)\,ds, \qquad t \geq 0$$

is the *prey total size* at time $t \geq 0$. Existence and uniqueness of solutions are proved under weak conditions. A threshold is established for the stability of the predator-free equilibrium and the existence of a positive equilbrium. When restricted only to the prey, the model is a special case of the one studied in "Farkas and Hagen, *J. Math. Anal. Appl.*, 328(1), 2007". In this case it is shown that the positive equilibrium may undergo Hopf bifurcation, a novel feature in this class of models. Finally, numerical exploration of bifurcations is perfomed through pseudospectral collocation methods as in "Scarabel et al., *Vietnam J. Math.*, 49(1), 2021".

Joint work with Shangjiang Guo, Mimmo Iannelli, Andrea Pugliese, and Xuan Tian.

A two-patch SEIR model with prevalence-dependent behavioural response and mobility for Ebola dynamics

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We develop a two-patch SEIR model for Ebola transmission that incorporates human behaviour and mobility. We consider two patches representing urban and rural environments,

and in each patch, the population is further divided into two groups based on their willingness to adhere to intervention measures. Both adherence and travel is influenced by disease prevalence. Unlike traditional approaches assuming permanent migration, we adopt a more realistic framework where individuals retain residency in their home region while spending time in the other region. We analyse key model properties, including the control reproduction number, and show that the disease dies out when this threshold is below one. Parameters are estimated by fitting the model to epidemiological data from the 2018–2020 outbreak in the Democratic Republic of Congo. We then conduct scenario-based analyses to investigate the impact of behavioural responses, misinformation, regional resource allocation, and travel duration on epidemic dynamics. The results highlight the importance of adaptive behaviour and mobility in shaping disease spread and control strategies.

Joint work with Abba B. Gumel.

Analysis of a general vector transmission model for infectious disease spread

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As an extension of the framework developed by Earn and McCluskey (PNAS 2025 Vol. 122 No. 49), we consider a very general vector transmission model for the spread of an infectious disease. The human and vector populations each contain a single susceptible class and an arbitrary number of post-infection compartments, allowing for general stage structure (e.g., exposed, infectious, treated or quarantined classes).

Key model assumptions:

- no return from the infected classes to the susceptible classes in both populations
- each infected class can be reached from the respective susceptible class
- a mass action incidence function (with a criss-cross structure: infected vectors infect susceptible humans, and infected humans infect susceptible vectors)

For the resulting system of ordinary differential equations, we explicitly determine the disease-free and endemic equilibria and derive a closed-form expression for the basic reproduction number.

Using techniques similar to those developed by McCluskey and Earn, we study the global stability of the disease-free equilibrium when $R_0 \leq 1$ and of the endemic equilibrium when $R_0 > 1$.

Extracting tent maps from the Mackey–Glass attractor

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Since its appearance in the celebrated paper [3], the Mackey–Glass equation has become an essential reference in the field of delay differential equations (DDEs). Its importance goes well beyond being a prototype model for investigating dynamical diseases in biology and medicine or for investigating the effects of delayed feedback in control and relevant applications. Even from a strictly mathematical point of view, it represents a cornerstone benchmark to understand emerging analytical techniques or to test advanced computational methods. Despite the great attention it has received in almost half a century, a rigorous mathematical proof of chaos in the Mackey-Glass equation is still an open problem. However, several numerical simulations highlight the chaotic nature of the Mackey-Glass system.

Inspired by the pioneering work of Lorenz [2], in this talk we present several computational results showing the presence of tent-like scalar maps in the dynamics of the Mackey-Glass equation. Up to our knowledge, an in-depth study on tent maps in the dynamics of this system has not been provided yet. The numerical evidence of the presence of such maps can be a strong indicator of chaotic behavior, since their iteration gives rise to chaotic dynamics. We provide an interpretation of the adopted tools on the basis of the arguments proposed by Siegberg in [4] to reduce the dynamics of simpler DDEs to tent maps in order to apply standard results on chaotic maps [1]. The emerging key mechanism is that of a double reduction: first from continuous to discrete time, second from infinite to finite dimensional state stapce.

This is a joint work with Alessia Andò and Dimitri Breda (University of Udine), supported by FSE+ grant: "Computational and datadriven models for advanced sustainable processes", CUP: G23C25000620008.

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Modeling STAT1–p53 cooperation under stress and p21/PUMA-mediated cell fate decisions

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Cell-fate decisions under stress are governed by the dynamic interplay between the tumour suppressor p53, its negative regulator Mdm2, and downstream effectors such as p21 and PUMA. While stress-induced oscillations of p53 is well established, the quantitative impact of Signal Transducer and Activator of Transcription 1 (STAT1)—which both represses Mdm2 transcription and co-activates p53 target genes—has remained largely unexplored. We present a mathematical model that explicitly couples stress and STAT1 signals to the canonical p53-Mdm2 loop and to the p21 and PUMA branches. Depending on the stress intensity and on the level of STAT1, p53 displays oscillatory, damped, or plateau dynamics. A sensitivity analysis is performed to assess the impact of kinetic parameters on the dynamics. Decision rules are then established to map p53-driven dynamics onto cell-fate outcomes. Sustained moderate oscillations correlate with reversible arrest of the cell cycle, damped intermediate responses with senescence, and high plateaus with apoptosis. Simulations of heterogeneous cell populations reproduce experimental fate distributions for archetypal cell lines (MCF-7, HCT116, U2OS), highlighting cell-type-specific sensitivity to p21 versus PUMA. Our model establishes a quantitative link between stress intensity, STAT1 signalling, and downstream fate control. It provides a predictive, dynamical basis for interpreting how cytokine signalling and DNA damage jointly govern p53 responses, and thereby cell fate across cell types.

Dynamics of microbial communities exhibiting dormancy-driven oscillations

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The physiological structure of microbial communities in natural environments is typically a response to changes in internal and external conditions. External conditions may include the availability of nutrients, the presence of inhibiting or toxic substances while internal conditions may include cell to cell interactions. Microbial communities play critical roles in numerous ecosystems and bio-geochemical processes, however, there is still limited understanding of their interactions and how these interactions collectively generate community-level behaviors. In this talk, we present and investigate a bacterioplankton-nutrient interaction model that takes into account the quiescent stage. We establish conditions under which microbial

population oscillations (boom and bust) may occur. Numerical simulations will be presented to support the theoretical results.

Evolution of virulence in populations with a distributed parasite load

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Modelling evolution of virulence in host-parasite systems is of great importance. It is often the case that individuals within an infected population will have a variable infection load, i.e., the infected population is naturally structured with respect to the parasite burden. We formulate and analyse an SI-type model, where the infected subpopulation is structured with respect to infection load. We show that such distributed infection load has important consequences for the eventual evolution of virulence.

Mathematical modelling of bioplastic degradation in marine environments

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The degradation of bioplastics in marine environments is governed by complex interactions between microbial communities, polymer properties, and environmental conditions. In this work, we propose a mathematical framework to describe the dynamics of microbial-mediated bioplastic degradation, with particular attention to deep-sea environments.

The model accounts for key processes including biofilm formation, enzyme production, polymer breakdown, and uptake of soluble degradation products. Microbial populations are structured into functional groups to capture their distinct metabolic roles in the degradation process.

The system is formulated through a set of nonlinear differential equations, combining hyperbolic equations for microbial population dynamics, parabolic equations for enzymes and dissolved compounds, and an ordinary differential equation describing biofilm thickness evolution. Spatial heterogeneity is incorporated via a one-dimensional two-layer diffusion model with moving boundaries, representing the coupled dynamics of biofilm growth and polymer degradation.

Numerical simulations illustrate how microbial activity and biofilm development regulate degradation rates and influence community structure over time. The model provides a predictive tool for assessing the fate of bioplastics in marine environments and contributes to a better understanding of biodegradation processes under realistic ocean conditions.

Joint work with V. Luongo, M. R. Mattei, F. Russo, A. Tenore.

Evolution into chaos – implications of the trade-off between transmissibility and immune evasion

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Predicting viral evolution presents a significant challenge and is a critical public health priority. We develop a novel model that selects for a new strain with the highest invasion fitness, assuming a trade-off between immune evasion and transmissibility. In case the trade-off function is linear, we can describe the evolutionary patterns following the emergence of subsequent strains by a non-linear difference equation. Revisiting Cull's enveloping technique, we provide necessary and sufficient criteria for when evolution converges to a unique equilibrium state. We also identify scenarios characterized by a two-periodic pattern in upcoming strains, indicating a situation where a highly transmissible but not immune-evasive strain is replaced by a less transmissible but highly immune-evasive strain, and vice versa, creating a cyclic pattern. Finally, we show that under certain conditions, viral evolution becomes chaotic and thus future transmissibility rates become unpredictable in the long run.

This is a joint work with Gréta Kutas, Gergely Röst (University of Szeged), and Golsa Sayyar (University of Manchester).

Evolution into chaos – implications of the trade-off between transmissibility and immune evasion

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When saboteur bacteria undermine chemotherapy: a mathematical model of cancer treatment dynamics

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We construct a mathematical model of cancer dynamics with chemotherapeutic treatment, in the presence of bacteria that are capable of metabolizing the chemotherapeutic drug, hence sabotaging the therapy. We investigate the possibility of complementing the cancer treatment with antibiotic drugs, thus eradicating the bacteria or at least mitigating their negative impact on the prospects of therapy. Our model is a system of nonlinear differential equations, for which we perform a complete analysis, explicitly characterizing the four possible outcomes, depending on whether the cancer cells or the bacteria become extinct or persist. Global stability results are proven by the iterative application of a comparison principle, and a bifurcation diagram is created to show the transitions between scenarios with respect to the controllable parameters. We apply our model to an experiment on mice with colon cancer and the drug Gemcitabine. We also examine the phenomenon from a control theory perspective, where we consider the chemotherapy and the antibiotics as controls and thus seek the optimal combined therapy.

Joint work with Gergely Röst.

Threshold dynamics in a time-delayed logistic model of cell populations

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We extend the delayed logistic cell-population model of Baker and Röst [1], building on the general theory of delay differential equations [2, 3]. The generalized equation incorporates distributed delays expressed via both discrete and integral terms, and explicitly features the death rates of dividing and motile cells as parameters.

We first establish well-posedness, along with the nonnegativity and boundedness of biologically relevant solutions. We then derive an explicit threshold parameter that determines the stability of the zero equilibrium and the existence of a positive equilibrium. When the zero equilibrium is stable, no positive equilibrium exists and the cell population goes extinct. When the zero equilibrium is unstable, there exists exactly one positive equilibrium, which is stable; in this system we prove uniform strong persistence of the population.

Our results quantify how the death rates of dividing and motile cells, as well as the delay representing the duration of the division process, shape the system's global dynamics.

Joint work with Gergely Röst.

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On existence and uniqueness of solutions for impulsive differential equations with adaptive state-dependent delays

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In this talk we consider a class of impulsive nonlinear differential equations with adaptive state-dependent delays. We discuss the existence and uniqueness of solutions of the initial value problem using a Picard–Lindelöf type argument where we define approximate solutions with the help of equations with piecewise-constant arguments (EPCAs). Moreover, we show that the solutions of the associated EPCAs approximate the solutions of the original impulsive DDE with adaptive state-dependent delay uniformly on compact time intervals. The key

assumption underlying both results is that the delayed time function is monotone, or piecewise strictly monotone.

Lotka–Volterra systems

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I plan to present some old and new results on Lotka-Volterra systems

$$\dot{x}_i = x_i \left(r_i + \sum_j a_{ij} x_j \right), \quad i = 1, \ldots, n$$

and mention some open problems.

Periodicity in simple differential delay models from biological applications

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Finite volume scheme and convergence analysis toward time-periodic solutions of the multidimensional monodomain model

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The monodomain model is widely used in cardiac electrophysiology to describe the propagation of the electrical potential responsible for heart contraction. Mathematically, it is a

system of partial differential equations consisting of a nonlinear parabolic equation coupled with a system of ordinary differential equations.

Since the cardiac activity involves regular heartbeat it is crucial to explore numerical simulations preserving the time-periodic nature of the solutions. Thus, the main objective of this work is to analyze the periodic behavior of the solution from both theoretical and numerical perspectives. To this end, we employ the cell-centered finite volume method (FVM) for the spatial discretization coupled with an implicit time integration scheme.

On the theoretical side, we search for a discrete initial condition that will ensure the periodicity of the solution. Then, given this initial condition, we construct a time-periodic discrete sequence generated by the finite volume scheme and prove the convergence of this discrete periodic sequence toward a weak time-periodic solution of the multidimensional monodomain model.

On the numerical side, we investigate the qualitative behavior of the solution in two space dimensions and propose three different ionic models.

This work provides a rigorous discrete framework for the study of time-periodic solutions to the monodomain system and contributes to a deeper numerical understanding of periodic cardiac electrical activity.

Modeling competitive dynamics between healthy and cancerous liver cells under yes-associated protein (YAP) hyperactivation

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Partial hepatectomy (PH), which removes two-thirds of the liver, is a common treatment for hepatocellular carcinoma (HCC). When cancerous cells remain after PH, they compete with regenerating healthy cells for limited resources. Recent studies suggest that hyperactivation of Yes-associated protein (YAP) may serve as a non-invasive therapeutic option. We develop two ordinary differential equation models describing post-PH competition, with and without YAP hyperactivation therapy, and analyze them using experimental data. Simulations show that effective treatment schedules depend on tumor aggressiveness. While high YAP doses can clear tumors, moderate activation combined with other therapies may offer more practical, patient-specific outcomes.

Delay induced instability in system modelling COVID-19

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This talk is about a model describing the spread of COVID-19 in the workplace. To delay the spread of the infection, fragrances are sprayed into the air. We investigate how the stability of the originally globally stable equilibrium changes under the effect of the delay.

Discovering the modes of action of antivirals from data and modelling: SARS-CoV-2 and Paxlovid as case study

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The use of antiviral drugs to treat SARS-CoV-2 infection has been widely extended and several antiviral treatments have been tested, involving different modes of action (MOAs). These drugs may be either newly developed treatments or repurposed drugs and, though a positive effect may be observed from the application of these treatments, it may not always be clear what is the driving mechanism underneath. Moreover, testing these drugs involves great amounts of human, animal and material resources that limit the obtained results. The use of mathematical models is imperative to reduce these costs, to assess possible strategies of application of the treatments, and to uncover unknown behaviors.

One of the most widely used SARS-CoV-2 antiviral treatments is Paxlovid (nirmatrelvir/ritonavir), which is known to reduce viral replication. Here we present a methodology to validate this behavior and to find other possible hidden modes of action of the treatment. We consider a classical TIV model and clinical data from patients infected with the Omicron variant, both patients treated with Paxlovid and untreated patients. Given these data, we explore what parameters can capture the effect of the treatment and, hence, potential hidden mechanisms of action. Furthermore, taking into account that there is some delay between administration of a drug and its effect, we also explore what this delay is when Paxlovid is administered to treat the infection with Omicron.

This work is in collaboration with Stanca M. Ciupe and Gergely Röst.

Asthma-mediated control of optic glioma growth via T cell-microglia interactions: A mathematical model

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Optic glioma, a slow-growing tumor, is associated with Neurofibromatosis type 1 (NF1) mutations and increased midkine (MDK) production. A connection between asthma and optic glioma has previously been observed, but the mechanisms are unclear. To elucidate the role of asthma in the regulation of glioma formation, we investigated the role of T cells and the subsequent pathways in the regulation of microglia, a key player in the glioma tumor microenvironment (TME). While asthma is often linked to chronic inflammation, our mathematical analysis and experimental evidence suggest that inflammation can play a key role in suppressing the proliferation of optic glioma cells via immune reprogramming of T cells and the delicate control of signaling networks in microglia. Our mathematical model unveils the complex interactions between tumor and immune cells in optic glioma. Our results indicate that asthma-induced T cell reprogramming inhibits tumor growth by promoting the release of decorin and a subsequent suppression of CCR8 and the intercellular binding kinetics in microglia, followed by blocking of CCL5 production in TME via suppression of NFkB. We developed anti-cancer strategies by leveraging this asthma-induced immune regulation.

Modeling biofouling in microfiltration: A coupled filtration–biofilm model

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Recently, microfiltration has emerged as an effective technology for both water production and wastewater treatment applications. Nevertheless, its performance is significantly hindered by membrane fouling, which is predominantly driven by the accumulation of organic constituents, including microbial cells and extracellular polymeric substances (EPS). The formation of these fouling layers results in increased hydraulic resistance and a progressive reduction in permeate flux. In the context of wastewater treatment, this biologically mediated fouling—referred to as biofouling—represents a major operational burden, owing to the substantial energy demand and chemical consumption associated with membrane cleaning protocols. Given that biofouling is inherently governed by biofilm formation processes, the capability to accurately predict biofilm growth and structural evolution on membrane surfaces is of critical importance for improving membrane system efficiency and optimizing backwashing operations across varying filtration regimes. In this study, a one-dimensional

mathematical model is proposed, formulated as a free-boundary problem to capture the spatiotemporal dynamics of biofilm development and EPS production during microfiltration. The modeling framework integrates classical resistance-in-series filtration theory, grounded in Darcy-type formulations, with a multispecies description of biofilm growth. The model provides a quantitative tool for investigating biofouling kinetics and assessing the impact of backwashing strategies in microfiltration systems. This approach offers valuable support for the design, optimization, and operational control of wastewater treatment processes.

Impact of holiday mixing on influenza transmission: Why timing and preparedness matter

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Despite massive population movements during holidays in South Korea, their actual impact on influenza transmission remains obscure, suggesting that the specific timing of these events relative to the epidemic cycle may be a critical but overlooked factor. In this study, we provide an explanation for why these holiday effects may have been systematically underestimated by utilizing a mechanistic model integrated with empirical data on observed contact patterns during holidays.

We argue that this phenomenon is not due to a lack of effect, but rather a structural suppression driven by the intersection of climatic factors, declining population susceptibility following the epidemic peak, and age-specific vaccine-induced immunity. Our findings suggest that as climate change shifts epidemic timings, strategic preparedness will be essential to manage the evolving risks of holiday mixing.

A symmetric periodic solution for a class of distributed delay differential equations

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A logistic type delay differential equation, with both instantaneous feedback and distributed delay is derived from an SIRS type epidemic model with constant immunity period. It is shown that the equation has a periodic solution with period equal to twice the maximum delay for a special case. The periodic solution has a certatin symmetry. Numerical simulations suggest that the periodic solution is stable. I will show the recent results concerning the

existence of a symmetric periodic solution for a class of distributed delay differential equations.

Mushroom and isola bifurcations in a within-host bacterial infection model with Allee effect

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The interplay between nonlinear bacterial growth and host cell regulation can generate complex dynamics in within-host infection models. This work presents a model for a self-replicating bacterial infection incorporating an Allee effect, under both constant host cell turnover and density-dependent (logistic) proliferation. The analysis establishes well-posedness and identifies the basic reproduction number as a threshold governing the transition between bacteria-free and infection states. A detailed study of the equilibrium equation reveals how the Allee threshold ε shapes the number and feasibility of steady states, leading to multiple infection equilibria. In the logistic formulation, this interplay gives rise to intricate bifurcation structures, including mushroom and isola configurations, both of which exhibit bistability, and a cusp catastrophe, where two branches of the fold curve meet tangentially, highlighting the strong nonlinear effects induced by the Allee mechanism. The system undergoes a transcritical bifurcation at $\mathcal{R}_0 = 1$, with explicitly determined direction, while the logistic model further exhibits oscillatory dynamics through a Hopf bifurcation, as supported by numerical simulations. These results demonstrate how Allee effects and host cell regulation jointly enhance the dynamical complexity of within-host bacterial systems.

Comparative dynamics of tuberculosis: The role of latency, treatment and relapse

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Tuberculosis (TB), which poses a severe threat to global health, is a multifaceted problem influenced by a number of factors including treatment, relapse, and infection dynamics. In this study, we develop a mathematical model for the transmission of TB to investigate the impact of treatment, latent infection, and relapse on the spread of TB in a community. We formulate the mathematical model by adopting a compartmental approach that divides the total population into susceptible latent infectious, and recovered individuals. Qualitative

analysis is also carried out to understand the effect of various epidemiological parameters on TB infection dynamics in a population. The study revealed that TB infection is endemic in a population under untreated conditions, with a constant level being a result of continuous infection and latent infection development. When treatment is initiated, the study revealed that TB infection is reduced in a population because the treatment period is shortened, reducing the infection period and the resulting infection rate. The study also revealed that TB infection cannot be eradicated completely because of the high rate of relapses and development of latent infection. The study also revealed that the treatment rate should be increased to reduce the peak infection rate in a population and to reduce the active infection rate in a population. On the other hand, the study revealed that the high rate of relapses and development of latent infection counteracts the effect of increased treatment rate in a population, making it impossible to eradicate TB infection completely.

Application of geometric modeling and optimal assignment algorithms in cell tracking

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Background and introduction:

Quantitative analysis of intracellular bacterial infections is essential for understanding host–pathogen interactions and the progression of infection-induced cellular damage. In particular, tracking the temporal behavior of macrophages infected with Salmonella enterica serovar Typhimurium can provide valuable information about infection dynamics and cell lysis. Manual analysis of large microscopy datasets is highly time-consuming; therefore, automated segmentation and cell-tracking methods are required. The aim of this thesis was to develop a mathematical and computational framework for the automatic detection, geometric characterization, and temporal tracking of cell nuclei in fluorescence microscopy image sequences.

Methods:

The study was performed on RAW 264.7 macrophages labeled with Cy5 fluorescent dye, while bacteria were labeled with TRITC fluorescence. The dataset consisted of more than 37,000 microscopy images obtained from three independent experiments. Images were acquired over a 20-hour observation period at 20-minute intervals, across 21 microscopic fields with a resolution of 1024×1024 pixels. Cell nuclei were segmented using the deep learning–based Cellpose algorithm. The resulting binary masks were approximated by inertia ellipses derived from second-order geometric moments. Geometric descriptors including centroid position, major and minor axis lengths, orientation, and axis ratios were extracted for each nucleus. Cell tracking between consecutive frames was formulated as an optimal assignment problem. A weighted cost function combining spatial displacement, size variation, shape differences, and orientation changes was minimized using the Hungarian algorithm. Phantom assignments were introduced to handle temporary segmentation errors and missing detections.

Results:

The implemented framework successfully reconstructed stable cell trajectories over 60 consecutive time points and enabled quantitative analysis of temporal morphological changes. The extracted geometric parameters allowed the identification of characteristic trajectory types, including healthy non-dividing cells, dividing cells, and infection-associated abnormal behaviors. Infected cells showed significant morphological alterations before lysis, including nucleus shrinkage and changes in shape descriptors. The tracking method proved robust against temporary detection failures due to the integration of phantom assignments and gap handling mechanisms.

Discussion:

The results demonstrate that geometric modeling based on inertia ellipses combined with optimal assignment algorithms provides an effective and interpretable framework for large-scale cell tracking tasks. The proposed approach enables automated quantitative analysis of infection-induced cellular processes and supports the detection of biologically relevant morphological trends associated with cell death. The methodology may contribute to future studies investigating intracellular bacterial infections and could be extended with improved segmentation correction and predictive modeling techniques for earlier lysis detection.

Mutant p53 gain-of-function and immune suppression: Modeling the restoration of the STING–TBK1–IRF3 axis for enhanced cancer therapy

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Cancer progression is frequently driven by mutations in the tumor suppressor gene *TP53*. These mutations cause the protein to lose its normal growth-inhibitory functions and acquire new properties that promote tumor development and immune evasion. Recent experimental studies show that mutant p53 (mutp53) suppresses the immune system by binding to TANK-binding kinase 1 (TBK1). This interaction blocks the formation of the Stimulator of Interferon Genes (STING)–TBK1–interferon regulatory factor 3 (IRF3) signaling complex, which is essential for inducing Type I interferon (IFN-I) production. Consequently, the anti-tumor immune response is weakened.

Despite increasing experimental research on for the mutp53–TBK1 interaction, the quantitative impact of this axis on tumor–immune dynamics remains poorly understood. In particular, it is unclear how modulation of mutp53 or restoration of TBK1 activity influences long-term tumor control at the systems level.

To investigate the potential benefits of mutp53–TBK1 based therapeutic interventions, we developed a mathematical model based on a system of ordinary differential equations (ODEs). This proposed model captures the dynamic interplay between tumor growth, immune effector cells, IFN-I, and the intracellular STING–TBK1–IRF3 signaling axis regulated

by mutp53. Parameter uncertainty was explored using Latin Hypercube Sampling, and the resulting model outputs were analyzed using Partial Rank Correlation Coefficient to evaluate parameter significance and model robustness.

Numerical simulations indicate that in the absence of therapeutic intervention, mutp53-mediated suppression of innate signaling facilitates immune escape and sustained tumor progression. Furthermore, simulations demonstrate that while both single-agent interventions reduce tumor burden, shRNA-mediated knockdown of mutp53 elicits a more pronounced antitumor response compared to ectopic overexpression of TBK1 Most importantly, the combination therapy exhibits a significantly stronger antitumor effect than either monotherapy, leading to the greatest reduction in tumor burden and demonstrating superior therapeutic efficacy. These results are consistent with recent experimental evidence supporting mutp53 modulation and TBK1 restoration.

Joint work with R. Ouifki.

Modeling and optimal control of the ERβ paradox in TNBC: Repurposing Tamoxifen for combination therapy

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Triple-negative breast cancer (TNBC) is one of the most aggressive subtypes of breast cancer and is characterized by the absence of estrogen receptors, progesterone receptors, and human epidermal growth factor receptor 2. Due to the lack of these therapeutic targets, TNBC does not respond to hormone-based therapies such as Tamoxifen.

Recent studies indicate that Tamoxifen can be repurposed for TNBC by binding to ERβ, sequestering the mutant p53 (mp53) from the mp53–p73 complex and thereby freeing p73 to activate tumor-suppressive pathways. This interaction reactivates p73-dependent apoptosis and, in a predator–prey-like manner, drives coupled decreases in p73 and mp53. Consequently, therapeutic efficacy depends on the relative proportions of mp53 and released p73. This mechanistic duality provides a plausible explanation for the ERβ paradox reported in several studies, whereby ERβ may mediate either tumor suppression or tumor promotion. These observations underscore the need to better understand the quantitative interplay between Tamoxifen- and ERβ-based interventions and the balance between p73 and mp53.

In this study, we develop a mathematical model to assess the therapeutic impact of combining Tamoxifen with ERβ-targeted therapy. An optimal control framework based on the Pontryagin Maximum Principle is employed to determine time-dependent strategies that minimize tumor burden and treatment cost. Robustness and parameter uncertainty are evaluated using Latin Hypercube Sampling and Partial Rank Correlation Coefficient sensitivity analysis.

Simulations reveal an ERβ dose–response relationship consistent with the ERβ paradox under both monotherapy and combination therapy. The optimal control analysis demonstrates significant tumor reduction when Tamoxifen is combined with sufficiently elevated ERβ levels.

Joint work with S. Omer.

Linearized oscillation of delay differential equations

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Several model equations from population dynamics can be transformed into the nonlinear first order delay differential equation

$$x'(t) + \sum_{j=1}^{N} p_j(t) f_j(x(t - r_j)) = 0,$$

where $p_j \colon [0, \infty) \to \mathbb{R}$ and $f_j \colon \mathbb{R} \to \mathbb{R}$, $1 \le j \le N$, are continuous functions satisfying

$$\lim_{x \to 0} \frac{f_j(x)}{x} = 1, \qquad 1 \le j \le N,$$

and $0 = r_1 < r_2 < \cdots < r_N$, where $N \ge 2$ is an integer. The biologically meaningful equilibria of the model equations are transformed into the zero equilibrium.

It is known that, in contrast to the autonomous case, the oscillation of the linearized equation

$$x'(t) + \sum_{j=1}^{N} p_j(t) x(t - r_j) = 0,$$

does not imply the oscillation of the solutions of the above nonlinear equation near its zero equilibrium. In this talk, we present new linearized oscillation criteria in terms of the asymptotic hull of the linearized equation. This is a joint work with Professors Josef Diblík (Brno University of Technology, Czech Republic) and Iren Jadlovská (Slovak Academy of Sciences, Slovakia).

Bistability and complex bifurcation diagrams generated by waning and boosting of immunity

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We investigate an epidemiological model that incorporates waning immunity at the individual level and immune boosting upon re-exposure to the pathogen. When immunity is fully restored upon boosting, the system can be expressed as an SIRS-type model with discrete and distributed delays. We conduct a numerical bifurcation analysis varying the boosting force and the maximum period of immunity (in the absence of boosting), while keeping other parameters fixed at values representative of a highly infectious disease like pertussis. The stability switches of the endemic equilibrium, identified numerically, are validated using an established analytical approach, confirming that the equilibrium is unstable in a bounded parameter region and stable outside this region.

Using recently developed continuation methods for models with discrete and distributed delays, we explore periodic solutions and their bifurcations. Our analysis significantly extends previous findings and reveals a rich dynamical landscape, including catastrophic bifurcations of limit cycles, torus bifurcations, and bistability regions where two stable periodic solutions coexist, differing in amplitude and period.

These complex bifurcations have critical public health implications: perturbations—such as non-pharmaceutical interventions—can shift the system between attractors, leading to long-term consequences from short-term measures.

SEIR models with host heterogeneity

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Population heterogeneity is a key factor in epidemic dynamics, influencing both transmission and final epidemic size. While heterogeneity is often modelled through age structure, spatial location, or contact patterns, differences in host susceptibility have recently gained attention, particularly during the COVID-19 pandemic.

Several recent papers [1,2,4,5] have examined the effect of heterogeneity in susceptibility on epidemid dynamics, especially on the epidemic final size. In [4] a criterion was obtained to compare the epidemic final size yielded by different distributions of susceptibility. In particular, it was shown that, for the same value of R_0, the epidemic final size is smaller with any distribution of heterogeneity than with a homogeneous susceptibility; more generally,

restricting to some specific families of distributions, as the gamma distribution, it was shown that the higher is the variance the smaller is the epidemic final size, if R_0 is kept constant.

Recently, some authors [3,6] have considered the case in which susceptibility and infectiousness are correlated, positively or negatively. In this talk we analyse this case, building on the framework of Diekmann and Inaba [2], we focus on the special case of SEIR epidemic models, assuming that at the epidemic start there is no pre-existing immunity. Using as fundamental quantity $g(x)$, the average infectiousness conditional on susceptibility equal to x, one obtains a closed system of three ODEs, that can be easily simulated and for which some analytical results are obtained. We prove that when $g(x)$ is increasing, then with any distribution of heterogeneity the epidemic final size is smaller than with the homogeneous model with the same value of R_0; the opposite may hold when $g(x)$ is a decreasing function. Specializing to the case where susceptibility is distributed according to a Gamma or extended Beta distribution, we obtain stronger results on the dependence of the epidemic final size on the variance and the shape of $g(x)$.

Assuming a Gamma-distributed susceptibility and a simple form for $g(x)$, the resulting model consists of a system of ODEs with one or two parameters more than the classical SEIR model; this makes it practical for fitting epidemic data. We illustrate its use by fitting data on seasonal influenza in Italy, and comparing the results to those obtained with simple SEIR models with pre-existing immunity.

Joint work with Tamás Tekeli and Cinzia Soresina.

Acknowledgments

This work was supported by the project "One Health Basic and Translational Actions Addressing Unmet Needs on Emerging Infectious Diseases" (INF-ACT), BaC "Behaviour and sentiment monitoring and modelling for outbreak control/BEHAVE-MOD" (No. PE00000007, CUP I83C22001810007) funded by the NextGenerationEU.

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A mathematical analysis of the signalling pathway of p53 and its influence on the expression of the transcription factors E2F and NF–Y in the CycA/Cdk2 subsystem in cancer cells

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The CycA/CDK2 protein kinase complex plays a significant role in regulating cellular processes. These processes form part of the G_1 phase, the S phase, and the M phase. These represent different developmental stages of a cell. Moreover, the CycA/CDK2 complex is responsible for facilitating the cell's exit from the G_1 phase. This study aims to evaluate the impact of p53 protein production in the CycA/CDK2 subsystem. Furthermore, we examine the expression of the p53 protein and its supervisory role in cellular machinery. This protein is very well studied in terms of its function although the exact nature of its expression is not fully understood, it is known to occur in a pulsatile manner and is triggered by DNA damage. Consequently, the severity of DNA damage directly correlates with the level of p53 protein expression in cellular systems. We develop a mathematical model to gain a deeper understanding of this subsystem. The primary objective of this investigation is to analyse the effect of p53 protein expression on cancerous cells via the transcription factors E2F and NF–Y in this subsystem. We further conduct mathematical simulations of the subsystem to replicate the expected cellular biology and the impact of this inhibitor. Finally, we employ sensitivity analysis to understand the effects of reaction parameters and components on the subsystem. The ultimate goal is to develop a model that provides us with an understanding of the p53 protein cellular defence mechanism. Our analysis reveals a potential mechanism by which this integrated subsystem can filter noise and respond robustly to varying levels of DNA damage.

Real time modeling of the 2025 foot and mouth disease outbreak in Hungary and Slovakia

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In spring 2025, a foot-and-mouth disease (FMD) outbreak occurred along the Hungary—Slovakia border region, affecting only 10 farms before being contained. While the small number of cases is encouraging from a control perspective, it poses a major statistical challenge: standard likelihood-based methods for inferring transmission parameters and evaluating control measures are not suitable for such limited data. Nevertheless, timely and quantitative

estimates – such as the probability of epidemic fade-out or the effectiveness of implemented interventions—are crucial for guiding contingency planning and resource allocation.

To address this challenge, we developed a streamlined, simulation-based inference framework built on a farm-level branching-process model. The approach employs approximate Bayesian computation (ABC): rather than deriving an explicit likelihood, we generate a large ensemble of simulated outbreaks under a range of plausible parameter sets and retain those that closely match the observed epidemic. These "look-alike" epidemics allow us to construct posterior distributions for key epidemiological quantities of interest.

Our method is transparent, biologically grounded, and computationally efficient, making it suitable for real-time decision support during small outbreaks. This work demonstrates how modern simulation and Bayesian tools can extract meaningful insights from sparse data, even in high-stakes epidemic situations.

Joint work with Gergely Röst.

Impact of occupational noise exposure on diabetic control and psychological status in people with Type 2 diabetes mellitus

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This study develops and analyses a nonlinear eco-metabolic delay differential model to investigate the regulatory dynamics of glucose (G), insulin (I), β-cell mass (M), and amount of fat cells (F), with particular emphasis on delay-induced destabilisation in metabolic processes. The model incorporates key physiological feedback mechanisms, along with a discrete-time delay representing insulin response and cellular adaptation lags. We examine fundamental properties of the system, including positivity and boundedness of solutions, existence of multiple biologically feasible equilibria, and their local stability. A metabolic threshold is derived that governs the transition between metabolically controlled and dysregulated states. It is shown that the inclusion of delay can significantly alter system dynamics, leading to stability switching and the emergence of oscillatory behaviour. In particular, we establish that a Hopf bifurcation occurs when the delay parameter crosses a critical value, and explicit conditions for its existence are obtained. The direction and stability of the bifurcating periodic solutions are further characterised near the interior equilibrium point.

To account for environmental and physiological variability, a stochastic version of the model is formulated, and its robustness is assessed under random perturbations. Additionally, sensitivity analysis is performed to identify key parameters influencing metabolic transitions and threshold dynamics. To reduce hyperglycemia and treatment-related costs, a finite-time optimal control problem is formulated within the glucose–insulin system. Using Pontryagin's Maximum Principle, the Hamiltonian and adjoint equations are derived to characterise optimal interventions. The results identify strategies that lower glucose levels while minimising overall treatment costs. Numerical simulations are carried out using MATLAB to validate the analytical results and illustrate delay-induced oscillations, stochastic effects, and regime

shifts. The findings provide deeper insight into the role of delayed feedback in metabolic regulation and offer a quantitative framework for understanding the onset and control of metabolic dysregulation.

Reconstructing resonant interactions in oscillator networks from noisy time series

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Networks of coupled oscillators (think of neurons, chemicals, animal species) arise abundantly in biology. I will discuss the problem of inferring the differential equations that govern such oscillatory processes from time series observations: the so-called reconstruction problem. This reconstruction is typically done by first extracting phase signals from the time series, and subsequently fitting phase equations to these signals. The fundamental problem inhibiting the reliable reconstruction of phase equations is that these equations are not unique: distinct phase equations may generate the same or highly similar time series. As a result, classical reconstruction methods such as SINDy are ill-posed in this context, and their outcomes hard to interpret. Our solution to this problem is to reconstruct a "representative" differential equation, the so-called resonant normal form, from the data. We prove that our method reconstructs this normal form correctly, and can hence "learn" the true dynamics of the oscillator network. This is joint work with Bengi Dönmez.

Behavioural dynamics in epidemic models: reversible and irreversible responses to infection risk

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Human behaviour is both a driver and a consequence of epidemic spread. During outbreaks, individuals adapt their contacts, mobility, and protective practices in response to perceived risk, public health interventions, and social norms. While some behavioural changes are temporary and quickly reversed when the perceived threat declines, others, such as vaccination, are irreversible, leading to lasting changes in population-level epidemic patterns.

This talk explores mathematical approaches for incorporating behavioural adaptation into infectious disease models, with a particular focus on distinguishing reversible and irreversible

behavioural responses; risk awareness and imitation driven behaviours. We examine in details the counter-intuitive phenomenon of non-monotone attack rates: sometimes a more transmissible pathogen creates a smaller outbreak, when behavioural response has a specific form.

Joint work with Seyed M. Moghadas

Dimension reduction and global attraction in delayed Wilson–Cowan neural networks

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Networks of Wilson–Cowan oscillators provide a powerful mathematical framework for modeling neural dynamics. However, despite significant advances, the global behavior of these networks remains poorly understood. In this paper, we develop a systematic methodology to establish criteria for global attraction in networks of Wilson–Cowan oscillators with both intra- and inter-node delays, as well as time-dependent external inputs. Our approach reduces this problem to verifying the uniqueness of solutions to an associated system of inequalities in $\mathbb{R}^2$. This methodology applies to arbitrary network architectures, accommodates both excitatory and inhibitory interactions, and allows general time dependencies in external inputs beyond the T-periodic case. Furthermore, we characterize the global attraction in some classes of networks. From an applied perspective, we identify several stabilizing mechanisms in neural systems: appropriate external inputs or a balance between excitatory and inhibitory connections can effectively stabilize the network dynamics.

A thermodynamic model for water dynamics in subaerial biofilms

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Subaerial biofilms (SABs) are microbial communities that colonize air-exposed surfaces in both natural and engineered environments, forming self-sustaining ecosystems wherever direct exposure to the atmosphere and solar radiation occurs. SABs microbial activities are regulated by multiple external drivers, including atmospheric humidity, temperature, solar radiation, and the deposition of organic and inorganic matter, with water availability representing the primary constraint. While precipitation, dew, and fog contribute to SAB hydration,

evaporation and condensation processes, closely linked to the fluctuating temperature and humidity they experience, are key determinants of water availability and constitute the main focus of this study. Therefore, SABs form an interfacial layer between the air atmosphere and the mineral substrate, interacting directly with both compartments.

In this framework, a thermodynamic mathematical model is developed to describe water dynamics within the SAB, the surrounding atmospheric air, and the underlying mineral substrate. The model captures variations in water content and availability by explicitly accounting for phase exchange at liquid–gas interfaces through gradients of water chemical potential. It also captures the role of the SAB in delaying water loss while sustaining water uptake from the stone pore network to compensate for atmospheric evaporation. In addition, under highly hydrated conditions, the SAB may act as a barrier for the stone layer to water transport.

The key components of the model are validated against experimental data reported in the literature, with particular reference to the laboratory study where water evaporation is measured from limestone samples with and without SAB under controlled environmental conditions. This comparison supports the modeling assumptions and enables parameter identification. Finally, numerical simulations under variable environmental conditions, including daily fluctuations, are performed to assess the role of evaporation and condensation in controlling water availability and transport within the SAB–stone system. Different scenarios are considered by varying the permeability of the stone and the presence or absence of the biofilm layer.

Avian flu modelling in poultry farms: case study of H5N1 HPAI in northern Italy in 2021–2022

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We provide an overview of the mechanisms behind the spreading of avian flu in farms, focusing in particular on the H5N1 Highly Pathogenic Avian Influenza (HPAI) epidemic which occurred in northern Italy in 2021–2022 [3].

We present unpublished data on the spread of HPAI among a network of hundreds of farms, visualizing the possible infection routes of the epidemic. We then define a stochastic SEUDR (Susceptible – Exposed – Undetected – Detected – Removed) model, based in part on [1].

We identify three main sources of infection (wildlife, same poultry company, and geographical distance), and estimate the parameters of our probabilistic model through the available data. We then proceed to the identification of the most likely date and source of infection for each farm involved in the epidemic wave under analysis, and provide a model which can be adapted to any other avian flu epidemic which involves both wildlife and domestic poultry.

Joint work with Andrea Pugliese, Paolo Mulatti, and Sara Sottile.

Acknowledgments

This work in progress is sponsored by Fondazione Caritro [2] as part of the 2024 post-doc project "Modelli matematici di malattie infettive più ospiti e popolazioni eterogenee: applicazioni all'influenza aviaria" ("Mathematical models of infectious disease spreading in multi-host and heterogeneous populations: applications to avian flu").

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Life science at big data scale: supercomputers for health

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Over the past decades, advances in computing have fundamentally transformed the life sciences, enabling researchers to address biological and medical questions at unprecedented scales. From the sequencing and analysis efforts of the Human Genome Project to modern artificial intelligence systems capable of identifying patterns in complex clinical and molecular data, computational power has become an indispensable driver of discovery in health research.

This presentation explores several landmark moments in which large-scale computing reshaped our understanding of human health and disease. Historical examples include the role of computation in genomics, the contrasting epidemiological responses to pandemics from the past and nowadays, and distributed computing initiatives that mobilized computational and human resources to tackle fundamental problems in protein structure and function.

By tracing the parallel growth of computational capabilities and biological knowledge, we discover how advances in high-performance computing have repeatedly expanded the boundaries of what is scientifically possible.

The history of health research is, in many ways, a history of increasingly powerful computational tools. As biological data continue to grow in volume and complexity, supercomputing is no longer merely an enabling technology but a central component of scientific discovery, shaping both the future of medicine and the way society responds to global health challenges.

Beyond vaccination coverage: A network model of vaccine attitude homophily and epidemic dynamics

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Homophily, the tendency of individuals to associate with others who share similar characteristics, plays an important role in shaping contact patterns, yet its impact on vaccination dynamics and epidemic outcomes remains incompletely understood. While some studies suggest that homophily can cluster unvaccinated individuals and exacerbate outbreaks, others show that, under certain network structures, it may mitigate transmission. Here, we develop a network-based modelling framework that integrates three vaccination attitudes (i.e., pro-vaccine, hesitant, and anti-vaccine) with dynamic opinion formation to investigate how homophily and behavioural responses jointly influence vaccine uptake and epidemic spread. Our results show that final vaccination coverage does not translate linearly into epidemic attack rates. Notably, similar levels of overall coverage can lead to markedly different epidemic sizes depending on the spatial and network distribution of vaccinated individuals. We further show that homophily within the vaccine attitude network amplifies heterogeneity in vaccine adoption, leading to the emergence and persistence of unvaccinated clusters. These localised structures play a decisive role in transmission dynamics, highlighting the limitations of population-level models that assume homogenous mixing. To explore the robustness of these findings, we analyse a range of network topologies, including scale-free, small-world, modular, and empirical networks, and quantify how varying levels of homophily influence local uptake behaviours and infection spread.

Joint work with Silvio C. Ferreira, Seyed M. Moghadas, and Jianhong Wu.

On epidemiological models with state dependent infectivity, death and hospitalization

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This talk describes recent results on modified epidemiological models in which the infectivity, the death and the hospitalization rates are system dependent. We present the the three models, describe shortly their analysis and show typical and interesting computer simulations.

Dynamics and pattern formation in a prey–predator model with Allee effect and anti-predator behavior

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In this talk, we present a prey-predator model incorporating a strong Allee effect in prey growth and anti-predator behavior affecting predator mortality. We discuss the temporal dynamics by establishing positivity, boundedness, permanence, and stability of equilibrium points, and derive conditions ensuring long-term coexistence of both species. The model is extended to a reaction-diffusion framework to explore spatial dynamics in one-dimensional and two-dimensional domains. Conditions for diffusion-driven instability are obtained, and numerical simulations demonstrate the emergence of spatial patterns such as stripes and spots. The results show how variations in the Allee threshold and predation parameters, together with diffusion, influence species persistence and spatial organization.

A mathematical framework for per-read and per-sequence error characterization in single-molecule sequencing

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We present a mathematical framework for quantifying basecalling error at multiple scales in single-molecule (nanopore) sequencing, from individual bases to whole-sequence classification.

We define hierarchical Phred-like quality scores — per-base, per-read, and per-sequence — and prove via Jensen's inequality that averaging in the Phred domain systematically overestimates accuracy relative to the Phred transform of the mean error. This concavity-driven bias has direct consequences for quality reporting. We address it with an alignment-based correctness score incorporating predicted basecaller confidence and empirical accuracy into a single Phred-scale summary.

We then lift the analysis to sequences by constructing a confusion matrix indexed by true targets and basecaller assignments. Row-normalization produces a stochastic matrix of pair-wise misclassification probabilities; its Frobenius distance from the identity yields a Phred-like scalar of classifier fidelity. Clopper–Pearson confidence intervals from the multinomial row structure, with minimum read-count bounds, ensure reliable estimation of rare confusions. A bridge between scales is provided by per-base reliability zones: under conditional independence, the product of position-specific error rates at discriminating sites predicts which off-diagonal entries dominate, enabling anticipation of sequence-level misclassification from basewise profiles.

Periodic orbits in some delay differential equation modelling El Niño–Southern Oscillation

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El Niño–Southern Oscillation (ENSO) is a global climate phenomenon that emerges from oscillations in atmospheric pressure and sea surface temperatures over the tropical Pacific Ocean. It has a great impact on the climate not only in the equatorial region of the Pacific, but also in the rest of the world, therefore understanding its oscillation patters is of great importance.

Here, we deal with the phenomenological model of ENSO in form of a non-autonomous delay differential equation:

$$x'(t) = -a \cdot \tanh\big(\kappa \cdot x(t-\tau)\big) + b \cdot \cos(2\pi t), \tag{1}$$

with $a, b, \kappa, \tau > 0$ are some parameters. An extensive study of the (apparently) stable solutions of (1) was done numerically in [1]. In this work, we want to provide rigorous proofs of some of the results there, in particular, we show existence of periodic orbits for various values of parameters, and we show bi-stability in form of two co-existing periodic solutions, for $\kappa \to \infty$. The proofs are computer-assisted.

This is a joint work with Jakub Kural, Anna Gierzkiewicz and Jean Philippe Lessard. This work was supported by National Science Centre, Poland (grant no. 2023/49/B/ST6/02801) and Polish national strategic program for the excellence of science "Inicjatywa Doskonalosci - Uniwersytet Jagiellonski" (ID.UJ).

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What we saw was what we got? Correcting reported incidence data for testing intensity

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During the COVID-19 pandemic, non-pharmaceutical interventions were employed to limit the spread of the SARS-CoV-2 virus. In some countries, this included large-scale voluntary testing of non-symptomatic individuals to gauge the prevalence in the general population and

to identify asymptomatic and pre-symptomatic infections in order to reduce disease spread. Differences between the intensity of testing means that comparing case-counts across borders may be deceptive.

In this work, we use mathematical modelling to investigate the dynamics of both observed and unobserved infections as a function of the rate of voluntary testing. The model indicates that increasing the rate of testing causes the number of observed cases to increase, despite a decrease in prevalence due to testing. For larger testing rates, the observed case-counts also decrease. The non-monotonicity of the observed cases explains some discrepancies seen when comparing uncorrected case-counts between countries. One such example was observed during the winter 2020/2021 COVID-19 epidemics in Denmark and Hungary, where reported case-counts were comparable, despite differences in prevalence.

We determine a quantitative measure for the ascertainment ratio between observed cases and all infections, allowing for test-intensity correction of case-counts. This measure allows us to correct case-counts for testing intensity during the winter 2021/2022 epidemic of the Omicron variant (BA.1 and BA.2) in Denmark, showing good agreement with results from serology-studies.

Joint work with Rasmus Kristoffer Pedersen, Christian Berrig, Gergely Röst and Viggo Andreasen.

Modelling the role of phages in biofilm ecosystems and the spread of antimicrobial resistance

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The spread and control of antimicrobial resistance represent a major public health challenge. This has led to increasing interest in the use of bacteriophages, either alone or in combination with antibiotics, as a strategy to treat antimicrobial-resistant biofilms. Assessing the potential of phage therapy requires a detailed understanding of phage-microbe interactions, including both their lytic activity and their ability to mediate the transfer of resistance genes via transduction.

In this work, we present a modelling framework that captures these processes within a spatially structured biofilm. The model is formulated as a system of non-local partial differential equations defined on a one-dimensional free-boundary domain. The solid phase of the biofilm is described by hyperbolic PDEs with reaction terms accounting for biomass growth, decay, and genotype changes due to plasmid acquisition. Bacterial subpopulations are distinguished based on plasmid carriage, conjugative ability, and compatibility with plasmid uptake. The framework incorporates the main mechanisms of horizontal gene transfer – conjugation, natural transformation, and generalised transduction – as well as selective pressures arising from antibiotics and heavy metals. Conjugation is modelled through density-dependent mass-action kinetics, whereas transformation follows a frequency-dependent formulation. Phage infection and generalised transduction are represented as saturation processes depending on

the rate of the phage adsorption. The model also includes biomass decay and extracellular polymeric substance production, with all active components assumed to depend on a single limiting nutrient. Substrate dynamics are described by a system of nonlinear parabolic PDEs governing diffusion-reaction processes. Multiple soluble compounds are considered, each interacting differently with the biomass. The limiting nutrient is consumed during bacterial growth, metals inhibit growth and may be reduced by plasmid-carrying cells, and antibiotics exert a bactericidal effect by converting active biomass into inert material. The release of extracellular DNA during cell lysis and its uptake by competent cells via natural transformation are explicitly modelled. In addition, both lytic and transducing bacteriophages are included, with lytic phages inducing cell death and transducing phages enabling the conversion of plasmid-free cells into plasmid carriers.

Numerical simulations investigate the impact of phage predation on bacterial population dynamics and plasmid spread. We further assess the relative contributions of different horizontal gene transfer mechanisms, with particular emphasis on generalised transduction. Finally, we explore the potential of phage therapy for eradicating antibiotic-resistant biofilms, both as a standalone treatment and in combination with antibiotics. The results highlight how phage–antibiotic synergy can substantially reduce the antibiotic concentrations required to eliminate even highly resistant biofilm communities.

Matrix games among full siblings in Mendelian populations

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We introduce a mathematical framework that combines tools from Mendelian genetics and evolutionary matrix game theory. Within this framework, we define the genotype dynamics that describes the temporal evolution of genotype frequencies in a diploid population. We show that, in this model, the evolutionary stability of a genotype distribution implies its dynamical stability.

We apply the framework to a model of familial selection in which offspring survival is determined by interactions among full siblings that can be described by a prisoner's dilemma game. We investigate the conditions under which a homozygous population is evolutionarily stable. Our analysis demonstrates that the evolutionary stability of a given genotype is jointly determined by the payoff matrix and the genotype–phenotype mapping (e.g., dominant–recessive or intermediate inheritance).

Genomic resolution of *Klebsiella pneumoniae* diversity enables scalable phage therapeutics

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The genetic diversity of *Klebsiella pneumoniae* poses a major challenge to the development of broadly applicable phage therapeutics. To identify a scalable design strategy, we integrated an incidence-weighted phylogenetic model of the European carbapenem-resistant K. pneumoniae population with large-scale phage host-range profiling. Despite substantial diversity, only 16 strain types account for 70% of carbapenem-resistant infections across Europe. These form persistent transmission lineages that are endemic in Southern and Eastern Europe, whereas new intercontinental introductions gradually increase the strain diversity responsible for the infections. Guided by this population structure, we assembled an international panel of ~ 400 isolates representing 13 dominant strain types and systematically evaluated phage activity across them. Phylogeny-guided phage selection and training enabled the development of lineage-specific cocktails of two to three phages that suppressed over 90% of isolates within their target lineages. These cocktails control intra-lineage heterogeneity driven by frequent capsule loss while limiting the emergence of resistance. Overall, we establish a surveillance-informed framework for scalable phage therapy against carbapenem-resistant *K. pneumoniae*.

Sensitivity analysis of social contact structures in epidemic models

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Understanding how variations in contact patterns affect epidemic outcomes is crucial for identifying the age groups that drive uncertainty in disease transmission models, thereby improving model accuracy and informing targeted interventions. Sensitivity analysis provides a structured approach to quantify how changes in parameters, such as age-specific contact rates, affect key metrics like the basic reproduction number, and clinical outcomes such as hospitalizations, ICU admissions, and mortality.

In this talk, we present an eigenvector-based approach that uses the left and right eigenvectors of the Next Generation Matrix to quantify changes in age-specific contact rates affecting $\mathcal{R}_0$ [1]. This method identifies which interactions between age groups contribute most to disease transmission. Compared to simulation-based techniques [2], it is both computationally efficient and interpretable, especially when applied to structured compartmental models.

Joint work with Evans Kiptoo Korir.

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On a protein synthesis model

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The lecture reports about a differential-algebraic system modeling protein synthesis, with state dependent delays due to transcription and translation which are implicitly defined by threshold conditions.

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Age Group Sensitivity Analysis in age stratified epidemic models: Investigating the impact of contact matrix structure

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Understanding the role of different age groups in disease transmission is crucial for designing effective intervention strategies. Age-structured epidemic models capture these dynamics through contact matrices, which describe interactions between subpopulations. However, empirical contact estimation is inherently prone to measurement noise, as survey responses vary systematically across age groups and are collected through heterogeneous channels. This imprecision introduces substantial uncertainty into epidemic predictions. In this study, we present the Age Group Sensitivity Analysis (AGSA) framework for quantifying how structural perturbations in age-specific contact patterns propagate to epidemic outcomes. AGSA integrates age-stratified epidemic models with Latin Hypercube Sampling (LHS) and Partial Rank Correlation Coefficient (PRCC) analysis to perform a systematic sensitivity assessment of age-specific interactions. A key novelty of our approach is a sensitivity aggregation technique that attributes the overall dispersion in epidemic outcomes to individual age groups. By identifying the groups whose contact variations contribute most to model variability, AGSA highlights where refined empirical data are most urgently needed. This provides a principled basis for targeted data collection efforts, thereby constraining epidemic forecasts and supporting the robust evaluation of age-specific public health interventions.

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Comparison of agent-based, mean-field, and pairwise models of a predator-prey ecosystem

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Stochasticity and spatial structure significantly influence predator-prey dynamics yet are often overlooked in traditional mean-field models. We conduct a comprehensive comparison of three modeling methodologies for a spatially explicit stochastic predator-prey system: agent-based Monte Carlo simulations, mean field approximation, and pairwise models.

We implement an agent-based model in which sheeps (preys) and wolves (predators) experience stochastic movement, reproduction, and mortality.

We use this agent-based framework to systematically derive the relevant mean-field equations assuming spatial homogeneity, as well as the pairwise model that incorporates nearest-neighbor correlations via moment closure approximations. We analyze the three techniques under different parameter regimes, extinction events, and oscillatory dynamics.

Our results show that, while the mean field approximation qualitatively represents coexistence regimes, it fails to accurately recreate stochastic extinction processes. The pairwise model improves agreement with agent-based Monte Carlo simulations by accounting for local correlation effects, although discrepancies remain in substantially fluctuation-dominated regimes.

Joint work with István Balázs.

Modeling STAT1–p53 cooperation under stress and p21/PUMA-mediated cell fate decisions

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Cell-fate decisions under stress are governed by the dynamic interplay between the tumour suppressor p53, its negative regulator Mdm2, and downstream effectors such as p21 and PUMA. While stress-induced oscillations of p53 is well established, the quantitative impact of Signal Transducer and Activator of Transcription 1 (STAT1)—which both represses Mdm2 transcription and co-activates p53 target genes—has remained largely unexplored. We present a mathematical model that explicitly couples stress and STAT1 signals to the canonical p53-Mdm2 loop and to the p21 and PUMA branches. Depending on the stress intensity and on the level of STAT1, p53 displays oscillatory, damped, or plateau dynamics. A sensitivity analysis is performed to assess the impact of kinetic parameters on the dynamics. Decision rules are then established to map p53-driven dynamics onto cell-fate outcomes. Sustained

moderate oscillations correlate with reversible arrest of the cell cycle, damped intermediate responses with senescence, and high plateaus with apoptosis. Simulations of heterogeneous cell populations reproduce experimental fate distributions for archetypal cell lines (MCF-7, HCT116, U2OS), highlighting cell-type-specific sensitivity to p21 versus PUMA. Our model establishes a quantitative link between stress intensity, STAT1 signalling, and downstream fate control. It provides a predictive, dynamical basis for interpreting how cytokine signalling and DNA damage jointly govern p53 responses, and thereby cell fate across cell types.

Analysis of predator-prey models with infection in both species and human intervention

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This study examined how infectious diseases affect predator-prey dynamics and evaluated the role of human intervention through treatment and vaccination. Four mathematical models were developed to represent different intervention strategies, with populations classified as susceptible, infected, vaccinated, or treated. We proved model positivity and boundedness, determined equilibrium points, and analysed their stability using Jacobian eigenvalues and Routh-Hurwitz criteria. MATLAB simulations validated the analytical findings. Without intervention, predators went extinct, while intervention in prey populations enabled coexistence—highlighting the critical role of human actions in preserving species.

Modelling of diabetes mellitus with time delay

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This study investigates the effect of time delay in a system describing type 1 diabetes mellitus treated with exogenous insulin administration. We show that delay in the regulation of blood glucose level can lead to oscillatory behavior in the system.

A mathematical framework for per-read and per-sequence error characterization in single-molecule sequencing

Pranjal Srivastava
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We present a mathematical framework for quantifying basecalling error at multiple scales in single-molecule (nanopore) sequencing, from individual bases to whole-sequence classification.

We define hierarchical Phred-like quality scores — per-base, per-read, and per-sequence — and prove via Jensen's inequality that averaging in the Phred domain systematically overestimates accuracy relative to the Phred transform of the mean error. This concavity-driven bias has direct consequences for quality reporting. We address it with an alignment-based correctness score incorporating predicted basecaller confidence and empirical accuracy into a single Phred-scale summary.

We then lift the analysis to sequences by constructing a confusion matrix indexed by true targets and basecaller assignments. Row-normalization produces a stochastic matrix of pairwise misclassification probabilities; its Frobenius distance from the identity yields a Phred-like scalar of classifier fidelity. Clopper–Pearson confidence intervals from the multinomial row structure, with minimum read-count bounds, ensure reliable estimation of rare confusions. A bridge between scales is provided by per-base reliability zones: under conditional independence, the product of position-specific error rates at discriminating sites predicts which off-diagonal entries dominate, enabling anticipation of sequence-level misclassification from basewise profiles

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