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Wikno, 16–20 September 2025

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Part I

Invited speakers

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MODELLING OF IMMUNE RESPONSE WITH ECOLOGICAL FACTOR

Yaroslav Bihun[1], **Oleh Ukrainets**[2]

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ABSTRACT

In this paper, we investigate the G. Marchuk model [1] of an immune system with influence of the ecological factors $E(t)$ (air pollution, water quality, etc.), which can negatively affect the immune response to infectious diseases. We proposed an average indicator $E(t)$ of the ecological impact, which satisfies the general Hutchinson equation and is represented as follows:

$$\frac{dE(t)}{dt} = r\left(1 - \left(\frac{E(t-\Delta)}{E^*}\right)^n\right)E(t), t > 0, \tag{1}$$

where $r > 0$ denotes the linear growth rate, and $\Delta > 0$ represents the average time required to restore ecological balance, with the equilibrium level given by $E^* > 0$, $n \geq 1$.

A mathematical model of the immune response to infectious diseases was developed by G. Marchuk [1], was studied in the works of U. Forys and M. Bodnar, for example [2], and other authors. This report considers a mathematical model of the form:

$$\begin{aligned} \frac{dV}{dt} &= (\beta - \gamma F)V, \\ \frac{dC}{dt} &= \alpha\xi(m)V_\tau F_\tau - \mu_c(C - C^*) - \varepsilon_c E, \\ \frac{dF}{dt} &= \rho C - (\mu_f + \eta\gamma V)F, \quad \frac{dm}{dt} = \sigma V - \mu_m m + \varepsilon_m E, \end{aligned} \tag{2}$$

where $V(t), C(t), F(t)$ and $m(t)$ are the amounts of antigen population, cascade of plasma cells, antibodies and a generalized measure of organ damage caused by the infection accordingly, considering $0 \leq m \leq 1$, $V_\tau(t) = V(t-\tau), 0 < \tau$ – time of active immune response, coefficients of model (2) are non-negative numbers.

The existence of a non-negative solution to the system (1), (2) for $t > 0$ has been established. Conditions for the existence of stationary solutions corresponding to the healthy state and the chronic form of the disease have been determined. The local asymptotic stability of these solutions has been analyzed. Numerical simulations were performed to explore disease dynamics under varying model parameters and environmental influence.

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INCORPORATING BEHAVIORAL FEEDBACK VIA INFORMATION INDEX INTO EPIDEMIC INTEGRAL MODELS

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ABSTRACT

Epidemic modelling has traditionally relied on differential equations to describe the spread of infectious diseases. However, these models often overlook the complex feedback mechanisms introduced by human behavior in response to disease outbreaks. To address this gap, we propose an integral approach that incorporates behavioral feedback through an information index. The information index represents the delayed response of individuals to the evolving epidemic, capturing how public awareness and perception influence behavior over time. This delay is modelled using memory kernels, which characterize the persistence of information in the population's collective memory. Building upon the foundational model by Kermack and McKendrick, we formulate the force of infection as an integral equation, where the current infection rate depends on the entire history of past infections, weighted by the memory kernel. This approach allows for a more accurate representation of how past experiences and accumulated information influence current behaviors and, consequently, the dynamics of disease transmission. Our analysis demonstrates that the inclusion of memory effects can lead to new dynamical behaviors, such as oscillations, which are not captured by standard models. These behaviors have significant implications for understanding the long-term evolution of epidemics and for designing effective intervention strategies that consider the temporal aspects of behavioral responses. Numerical simulations illustrate how different memory kernels, such as Erlang distributions, influence the stability and oscillatory patterns of the epidemic. This research is conducted in collaboration with Eleonora Messina and Claudia Panico from the University of Naples Federico II [1,2, 3].

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MATHEMATICAL MODELING OF MALIGNANT GLIOMAS: TREATMENT DYNAMICS AND IN SILICO TRIALS

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ABSTRACT

Malignant gliomas (MGs), particularly glioblastoma, are among the most aggressive brain tumors, with limited treatment options and a poor prognosis. Current first-line therapy consists of maximal safe resection followed by the Stupp protocol—an intensive combination of radiotherapy and chemotherapy—which only modestly extends survival. This highlights the urgent need for new therapeutic strategies.

In this work, we present and validate an ordinary differential equation–based mathematical model that captures key features of MG dynamics, including cancer cell dormancy, phenotypic switching, drug persistence, and treatment-induced effects. The model was calibrated with in vivo data from animal studies and used to design and test alternative treatment schedules through in silico trials. Notably, we found that less aggressive, protracted dosing regimens may significantly outperform the standard protocol, potentially delaying resistance, reducing side effects, and extending survival. Extrapolating our findings to humans, our simulations suggest up to a fourfold increase in median survival with optimized regimens.

Although further experimental and clinical validation is required, this framework illustrates how mathematical modeling and in silico trials can guide the design of more effective and personalized treatment strategies for malignant gliomas and related cancers.

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THE CHANGING ROLE OF MATHEMATICS IN MEDICINE AND BIOLOGY IN THE 21ST CENTURY: AN ONCOLOGY PERSPECTIVE

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ABSTRACT

Mathematics has long provided the foundation for biomedical discovery — from dynamical systems and biostatistics to evidence-based medicine. In contemporary applications of mathematics, IT, and AI in medicine, the dominant challenge is increasingly one of **essential complexity** (in the sense of Frederick Brooks): the greatest difficulty lies not in the technology itself, but in accurately understanding and adequately modeling the intricacies of clinical reality. Modern tools such as machine learning (ML), retrieval-augmented generation (RAG), and MLOps practices reduce the *accidental complexity*, yet they cannot eliminate the intellectual effort required to design sound models. In other words, we have shifted from the era of asking "*how can we build it?*" to the era of asking "*what exactly should we build, and how should we model it correctly?*"

Breakthrough advances in AI and large language models (LLMs) are now delivering revolutionary tools that can raise diagnosis and therapy to unprecedented levels of quality. Examples such as the *Tsinghua AI Agent Hospital* demonstrate this transformative potential. Yet, the growing deployment of AI in medicine must confront the most critical challenge for contemporary AI: **trust in AI**.

In response, the University of Warmia and Mazury (UWM) and the National Oncology Institute (NIO–PIB) have launched a joint initiative, *OnkoBot* — an oncology-focused AI system with human-in-the-loop (HITL) supervision. OnkoBot is designed to support patients, enhance clinical decision-making, enable medical education and clinical auditing, and improve the overall safety of oncology care.

The OnkoBot project directly addresses two fundamental challenges for any non-trivial applications of mathematics, IT and AI to clinical medicine: *essential complexity* and *trust in AI*. OnkoBot is not just another chatbot; it ensures safe oncology use through uncertainty representation, justified reasoning, and HITL supervision.

This lecture outlines our framework for addressing these challenges in oncology, illustrated by the development of AI-based decision-support systems for prostate cancer diagnosis and treatment. Our objective is not to eliminate essential complexity or uncertainty in trust toward AI, but rather to *maintain them within acceptable bounds for clinical experts* through explicit representations of uncertainty, modular separation of concerns, verifiable reasoning, and human-in-the-loop collaboration. We propose mechanisms that simultaneously minimize uncertainty while maximizing explainability and ensuring alignment with regulatory requirements such as the MDR and AI Act, all under real-world clinical constraints.

The core of our approach lies in modeling medical knowledge via knowledge-representation systems based on granular computing (GrC) and, in particular, interactive granular computing (IGrC). These frameworks can also accommodate non-classical reasoning, including multi-valued, fuzzy, probabilistic, modal, and intuitionistic logics.

For especially complex applications, we recommend **IGrC**, which integrates informational and physical layers (e.g., clinical reality) through *composite granules (c-granules)* under explicit CONTROL — Risk Management (RM), Information Management (IM), Decision Management (DM), and Resource Management (ResM), i.e., the full spectrum of clinical decision contexts. This design grounds semantics in the physical domain and synchronizes language, reasoning, perception, and action. This continuous adaptation and synchronization of 'perception and action' takes place in a tight, iterative loop of collaboration with the medical expert, forming the core of the human-in-the-loop approach. From the perspective of rough sets, the focus shifts from approximating concepts to approximating *granules/solutions*, enabling approximate cognitive computations within real oncological workflows. Along these computations, approximate solutions to problems are constructed, e.g., concerning diagnosis or therapy. In this architecture, hallucinations are mitigated through evidence-linked granules, abstention policies, and provenance-based reasoning.

Based on the above considerations, we conclude that the core message of this lecture is a paradigm shift in the application of mathematics to 21st-century medicine. We are transitioning **from computational models that operate on numbers and aggregates (like vectors and matrices) to models of granular computing—particularly interactive ones—that work primarily with granular information (intuitively human-understandable knowledge units) and physical-world entities**. These models must undergo constant adaptation to meet the demands arising from the complexity of the modeled phenomena and concepts. This adaptability allows them to address the challenges of essential complexity and to build the trust demanded by modern medicine.

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RECONSTRUCTION AND MODULAR RESPONSE ANALYSIS OF INTRACELLULAR TRANSCRIPTIONAL NETWORKS

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ABSTRACT

Human cell contains around 20 thousand genes, and a change of transcription level of each gene can potentially change expression levels of all other genes. Thus, genes in human cells form a regulatory network which is responsible for the cell's behaviour. Current single-cell high-throughput technique, called perturb-seq, allows targeted perturbing expression levels of hundreds of genes and measured genome-wide transcriptional responses. Such data, being very informative, suffers from a number of essential problems, such as sparsity (drop-outs in measured data), noise, and inability to estimate extent of perturbation for some genes.

The Modular Response Analysis (MRA) method was specifically developed to infer the structure of the network from dense and high-quality perturbation data. In present work we have developed a pipeline to adapt MRA for perturb-seq data. We inferred regulatory networks for a numberof perturb-seq datasets, and analysed statistical properties of inferred networks. We have found that the importance of nodes and edges in the network is following lognormal or power-lognormal distributions that give us insight into the mathematical framework (differential equations) governing signal propagation within the network. Interestingly, the nodes that exert the highest impact on activity of all other nodes, tend to be the least affected by activity of other nodes, suggesting hierarchical structure of intra-cellular signalling. Clustering of MRA-predicted responses suggests that dynamics of inferred networks can be described as mutual inhibition between clusters of mutual co-activation. We assume that such clusters generate multiple steady nodes, and their basins of attraction are separated by multiple saddles.

In my talk, I'll show how applying MRA to perturb-seq data opens new avenues for research of dynamics of intra-cellular regulatory networks and I'll raise the number of open questions that our group is working on with a view on potential scientific collaboration.

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A POPULATION MODEL FOR THE RESPONSE OF PATIENTS WITH ADVANCED MELANOMA TO THE TREATMENT BY IMMUNE CHECKPOINT INHIBITORS, BASED ON THE REAL-WORLD DATA

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ABSTRACT

Immune checkpoint inhibitors (ICI) have brought an unprecedented improvement in the treatment of cancer, especially advanced melanoma, increasing 5-year survival rates to > 40% with anti-PD1-based monotherapy and > 50% for combined therapy. Yet, nearly half of the patients do not respond to ICI treatment, emphasizing the need to identify patients that have higher probability to benefit from it. Unfortunately, no single biomarker has been found that can define the subpopulation of likely responders.

Despite numerous clinical trials of various ICI treatments, there is no clear picture which combination of patients' characteristic and treatment protocols will be optimal. The number of possible experimental arms is limited, and extensive analysis is needed, in order to answer the important clinical questions. Usually the analysis of the clinical data is carried out using simple statistical models, such as logistic regression and Cox survival models. Even when augmented by modern learning techniques, these approaches oversimplify the complicated trajectories of the diseases interacting with the immune system and the treatment, representing them as static distributions of a single value of interest (e.g., Time to Progression).

We suggest using instead the dynamic models (e.g., implemented by ODEs) for representing these interactions and predicting the individual response (e.g., size of tumour lesions) as it develops in time, under the patient-specific conditions. This naturally leads to the concept of population model, where the individual patients are represented by vectors of parameters of the dynamic models, following a populational distribution, with possible dependence on known covariates. We have used real-world dataset of patients with advanced melanoma treated by Pembrolizumab, to develop such population model, using the mixed-effects model formalism. The model was fitted using a modification of SAEM algorithm that allows application of advanced machine learning for modelling the effect of covariates.

We report the results of fitting the population model, and show examples of clinical insights and questions that can be answered using simulations of this model.

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DEATH OF PATIENTS WITH COVID-19 AND THE ROLE OF MATHEMATICAL MODELS IN DECIPHERING ITS CAUSE

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ABSTRACT

The known causes of death in people with COVID-19 include acute respiratory distress syndrome (ARDS), multiple organ failure (MOF), pulmonary embolism, superinfection, and myocardial infarction. We hypothesize that all these conditions originate from a single cause – disrupted metabolism. We discuss various available methods for modeling metabolism and propose a comprehensive model that can be used to validate our hypothesis and help reduce COVID-19 mortality. The strength of this model lies in its ability to represent both healthy and disrupted tissue metabolism, along with pathological outcomes, within a simple system of nonlinear equations. Phase plane analysis shows different system behaviors in healthy, cancerous, and COVID-19 cases.

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INTERPRETING HIGH-FREQUENCY OSCILLATIONS IN THE BRAIN: MECHANISMS AND MEANINGS

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ABSTRACT

Establishing a link between brain activity recorded at the micro scale (at the level of single cells) and macro scale (whole brain dynamics) has been a long-standing challenge. High-frequency oscillations (HFOs, 80-250 Hz) visible in the electrical brain activity are a promising candidate for the missing bridge as they can be observed both in micro- and macroscopic recordings. Their interpretation is, however, complicated, as HFOs are a compound measure of various electrical processes in the brain, and their precise mechanism of generation still remains unknown. In my talk, I will first discuss the context of brain oscillations and then present results of my research group obtained from a publicly available dataset of recordings from the visual cortex of macaque monkeys in various behavioral states. Based on the shapes of recorded neuronal action potentials, we identified six classes of cells that exhibit a differential relationship to HFOs. Particularly, one class of cells shows a strong preference for spiking at the peak of the HFO, while most other classes prefer to spike at the trough. We hypothesize that the strongly peak-locking class acts as a generator of the locally observed oscillation, while other classes are recruited through synaptic coupling. Moreover, two classes of cells behave differently with respect to HFO when the eyes are open and closed, possibly reflecting dependence on brain-state-related external input. Finally, we compare the spatiotemporal dynamics of HFOs during the resting state and a visual task. In the resting state, HFOs appear as bursts of strong oscillatory activity, mostly when the eyes are closed, and horizontally propagate across the cortex. During visual tasks, HFOs reflect the structure of the visual experiment, but locally resemble the resting HFO activity. Altogether, our results bring novel insights into the mechanism of generation and possible function of HFOs.

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APPLICATION OF ADVANCED TECHNOLOGIES IN PREOPERATIVE PLANNING OF PAEDIATRIC NEUROSURGICAL AND CRANIOFACIAL PROCEDURES

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ABSTRACT

The lecture aims to present an interdisciplinary application of advanced technologies, such as Virtual Reality (VR) and Augmented Reality (AR), in the preoperative planning of complex neurosurgical and craniofacial procedures in paediatric patients, including those with rare diseases. Applied solutions, developed through close collaboration between medicine Biomedical engineering introduces a new standard in diagnostic and therapeutic processes by enhancing both the precision and safety of surgical interventions.

In the lecture, we will present innovative methods for generating personalised anatomical models using medical imaging technologies (CT, MRI) and their integration into virtual environments. These models enable detailed biomechanical analysis of cranial and cerebral structures, taking into account age-specific anatomical challenges. Particular emphasis will be placed on the role of computer simulations in identifying potential complications and optimising surgical techniques—an essential aspect in procedures requiring precise reconstruction and the minimisation of damage to adjacent tissues. We will also explore the real-time application of AR technologies in the operating room, which provides surgeons with access to holographic visualisation of anatomical structures during surgery.

Selected clinical cases will be presented to illustrate the practical implementation of these technologies, their impact on improving treatment outcomes, and their contribution to reducing hospitalisation time in paediatric patients.

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MATHEMATICAL MODELING AND SIMULATION – FROM A SINGLE CELL TO THE HUMAN POPULATION

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ABSTRACT

Mathematical modeling and computer simulations of created models allow for a better understanding of biological processes on many levels, from individual cells to entire populations. Using them, we can not only reproduce experimentally observable behaviors of biological systems, but also formulate and test hypotheses that would be time-consuming or costly to test under experimental conditions. This paper will present examples of the use of mathematical modeling and computer simulations to study and analyze various properties of systems at different levels of complexity. From studying the impact of input timing on the behavior of individual cells, through the impact of stochastics in gene switching on the pharmacodynamics of drugs in tissue, the impact of drug resistance management strategies on the survival of cancer patients, to the impact of the spread of information about an epidemic in a population on its course.

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MATHEMATICAL INSIGHTS INTO THE DYNAMICS OF ACUTE AND CHRONIC BACTERIAL INFECTIONS

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ABSTRACT

Bacteria are single-celled microorganisms and among the most basic forms of life, having emerged nearly a billion years ago. The human body contains trillions of bacteria, outnumbering our own cells by a ratio of approximately 10 to 1. Some bacteria are beneficial, such as those residing in the human intestine, while others can cause serious diseases, including pneumonia, cholera, and bacterial meningitis.

In the environment, bacteria can alternate between two distinct states: a planktonic state, in which they float freely, and an immobile state, in which they form biofilms—structured bacterial communities that act as a "fortress," protecting the bacteria from antibiotics, increasing multidrug resistance, and reducing the effectiveness of the immune response.

A large body of medical literature suggests that chronic infections are associated with biofilm formation, whereas acute infections are primarily driven by planktonic bacteria. But can these observations be explained mathematically?

The aim of our talk is to present a class of mathematical models that provide such an explanation. These models describe the dynamics of acute and chronic bacterial infections within a host. They incorporate the main components involved in the process—namely, the immune system, antibiotic treatments, bacterial communication via chemical signals, and biofilm formation—and explore how these elements interact. A wide range of numerical simulations will also be presented to illustrate the model's predictions.

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THE MATHEMATICAL HALLMARKS OF CANCER: YESTERDAY, TODAY, AND TOMORROW

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ABSTRACT

Cancer, a complex and multifaceted disease, is characterised by distinct biological capabilities often referred to as the Hallmarks of Cancer. These include sustaining proliferative signalling, evading growth suppressors, resisting cell death, enabling replicative immortality, inducing angiogenesis, activating invasion and metastasis, and, more recently, avoiding immune destruction, deregulating cellular energetics, and promoting genome instability.

Over the past five decades, Mathematical Oncology has focused on studying these hallmarks through various qualitative and quantitative approaches. Such models aim to capture the dynamics of tumour growth, metastasis, and potential treatment and have direct impact on our understanding of cancer biology and medical interventions.

In this talk, we will review the most important developments in the mathematical analysis of the Hallmarks of Cancer, from their initial conceptualisation to their applications in biology and medicine today. We will compare a range of modelling strategies and show how the incorporation of biological data helps to shed light on the interaction between tumour cells and their microenvironment. We will place particular attention on aspects of tumour growth, invasion, metastasis, therapeutic response, and drug resistance development.

We will also consider the challenges and opportunities in applying mathematical models to diverse cancer types and treatment contexts. These include addressing infection-related malignancies, exploring how disease progression and treatment efficacy vary under different clinical and environmental conditions, and highlighting the importance of robust data collection and computational tools. By emphasising context-specific approaches and studies, we will show the value of mathematical models in informing both policy decisions and patient care.

We will conclude by discussing avenues for future research, such as new modelling paradigms, the integration of artificial intelligence and virtual reality technologies, and the challenges of translating mathematical insights into clinical applications. Our aim is to illustrate both the progress made and the open questions that remain at the frontier of Mathematical Oncology, ultimately shedding light on how these advancements might lead to enhanced patient care and personalised medicine.

Part II

Contributed talks

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A MULTICOMPARTMENT PHENOTYPE-STRUCTURED MODEL OF TUMOR RESPONSE TO HYPOXIA AND RADIOTHERAPY

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ABSTRACT

Recent studies have highlighted the critical role of tumor–microenvironment interactions in shaping therapy outcomes. Hypoxia, in particular, acts as a key environmental stressor, fostering more aggressive phenotypes and affecting radiotherapy efficacy in two main ways. On one hand, hypoxia-adapted cells exhibit high resistance to environmental stresses, allowing them to survive in poorly oxygenated regions where ionizing radiation is less effective. On the other hand, their slower proliferation rates make them less vulnerable to treatments that primarily target dividing cells.

This work presents a continuous mathematical model to investigate how hypoxia drives the evolutionary dynamics of cancer cells and impacts radiotherapy. Building on [1], the model employs a phenotype-structured population framework and is formulated as a system of coupled nonlinear integro-differential equations, incorporating a second compartment to account for non-proliferating cells arising from radiation-induced damage, enabling a more realistic representation of tumor response.

The model integrates oxygen spatial heterogeneity and phenotypic traits to assess alternative radiotherapy schedules beyond the standard of care. Preliminary simulations suggest that exploiting tumor reoxygenation through adaptive treatment timing can substantially improve therapeutic outcomes and inform future clinical trial design.

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EXISTENCE OF WAVE SOLUTIONS OF A GLIOMA MODEL IN A POROUS MEDIUM

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ABSTRACT

In this study, we extend our previous results [1], where we investigated the dynamics of a glioma model with continuous chemotherapy administered to tumours using a reaction-diffusion system. As before, we assume that tumours evolve not only due to proliferation but also due to cell motility. However, in this work, cell motility is modelled by nonlinear diffusion in a porous medium, while tumour proliferation is described by a logistic source term. Our motivation for modelling cell motility via a diffusion term, rather than as active transport, stems from the observation that low-grade gliomas grow very slowly, making it less likely to find tumour cells far from the tumour bulk. Our main focus is on exploring the existence of travelling wave solutions in the extended model and comparing the results with those of previous models, [2].

This is joint work with Juan Belmonte Beitia, Marek Bodnar and Monika J. Piotrowska.

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WHY DO COMPUTERS LIKE LORENZ MAPS?

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ABSTRACT

Lorenz maps, initially inspired by the famous Lorenz attractor, have evolved into a rich family of one-dimensional dynamical systems that are simple to define yet capable of exhibiting highly complex behavior. These maps, including β-transformations and expanding Lorenz maps, arise naturally in diverse contexts - from symbolic dynamics to computational neuroscience. In this talk, we investigate why such maps are particularly appealing from a computational standpoint. We introduce the concepts of *numerical transitivity* and *numerical leo* (locally eventually onto), which offer practical tests to assess how thoroughly a map "explores" its domain under iteration. These notions serve as computational proxies for dynamical properties like chaos and mixing, allowing us to visualize and quantify behavior through finite-time simulations. We discuss algorithms for both properties and present illustrative examples using β-transformations, revealing surprising regions of apparent chaotic behavior even in seemingly simple systems. This exploration not only sheds light on the numerical behavior of Lorenz-type maps but also demonstrates their computational utility in modeling real-world phenomena. Finally, we show applications of our numerical methods to the analysis of the 1D Courbage-Nekorkin-Vdovin model of a single neuron (see [1–3]). This is joint work with Rudrakshala Kavya sri and Sishu Shankar Muni (School of Digital Sciences, Digital University Kerala, India).

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SHORT BRANCH SINGULARITIES IN PHYLOGENETIC COMPARATIVE METHODS

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ABSTRACT

It is often observed that estimation for phylogenetically structured datasets can seemingly unexpectedly fail or silently produce improbable parameter estimates. We explain here that this can be due to very short branch lengths in the phylogeny, causing a nearly singular covariance. We show ways of rectifying the situation either through appropriate data preprocessing or using possibilities of estimation software. We illustrate the situation with an analysis of morphometric measurements of the zygomatic arch in Caninae.

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ANALYZING THE IMPACT OF PROLIFERATION AND TREATMENT PARAMETERS ON LOW-GRADE GLIOMA GROWTH USING MATHEMATICAL MODELS

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ABSTRACT

Low-grade gliomas (LGGs) are characterized by their slow growth and infiltrative nature, making complete surgical resection challenging and often resulting in the need for adjunctive therapies. This study introduces a mathematical model appeared in [1] aimed at elucidating the growth patterns of LGGs and their response to chemotherapy. Our model undergoes validation against clinical data, demonstrating its efficacy in accurately describing real patient data. Through mathematical analysis, we establish the existence of a unique non-negative solution and delve into the stability of steady-state solutions. Notably, we establish the global stability of a tumor-free equilibrium under conditions of sufficiently robust constant and asymptotically dynamics in the case of periodic treatment. Additionally, a sensitivity analysis highlights the proliferation rate as the primary determinant of model outcomes. Finally, numerical simulations are employed to explore the stability of the fitting procedure. We compare results with our paper [2] where a slightly different model was proposed.

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A CONTINUOUS–TIME *SIS* CRISS-CROSS MODEL OF CO–INFECTION IN A HETEROGENEOUS POPULATION

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ABSTRACT

In a population we indicate two subpopulations, a low–risk (LS) and a high–risk (HS) subpopulation, that relate to the risk of getting infected. LS and HS have accordingly lower and higher susceptibility to each disease. For every variable and parameter we assign a subscript i equal to 1 and 2 for LS and HS, respectively. If i has no assigned value, then $i \in \{1, 2\}$. By S_1 and S_2 we denote a density of healthy people in LS and HS, respectively. The variables I_i mean a density of individuals from the given subpopulation that are infected by a pathogen of disease which we call disease A (DA). Similarly, we define J_i as a density of individuals suffering from disease B (DB). A density of a group infected by pathogens from both diseases is denoted by K_i.

Migrating and newborn individuals join each subpopulation through S_i class with a recruitment rate C_i. A natural death rate for each subpopulation is equal to μ_i. For DA we introduces transmission rates: $\beta_{11}, \beta_{22}, \beta_{12}, \beta_{21}$ reflecting transmission: among LS, among HS, from HS to LS and from LS to HS, respectively. Indicating four different rates means that DA differs in spreading and contracting a pathogen. To get a preliminary insight on co–infection dynamics for the heterogeneous population, for DB we assume that individuals differs only in contracting a pathogen. For this reason we take only two transmission coefficients for DB: σ_1 for LS and σ_2 for HS. By γ_i and g_i we denote a recovery rate for DA and DB, respectively. The disease–mortality rate for DA and DB is depicted by α_i and a_i.

The proposed model of co–infection reads

$$\dot{S}_1 = C_1 - \beta_{11} S_1 I_1 - \beta_{12} S_1 I_2 + \gamma_1 I_1 - \mu_1 S_1 - \sigma_1 S_1 (J_1 + J_2) + g_1 J_1, \tag{1a}$$

$$\dot{I}_1 = \beta_{11} S_1 I_1 + \beta_{12} S_1 I_2 - (\gamma_1 + \alpha_1 + \mu_1) I_1 - \sigma_1 I_1 (J_1 + J_2) + g_1 K_1, \tag{1b}$$

$$\dot{J}_1 = \sigma_1 S_1 (J_1 + J_2) - (g_1 + a_1 + \mu_1) J_1 - \beta_{11} J_1 I_1 - \beta_{12} J_1 I_2 + \gamma_1 K_1, \tag{1c}$$

$$\dot{K}_1 = \sigma_1 I_1 (J_1 + J_2) + \beta_{11} J_1 I_1 + \beta_{12} J_1 I_2 - (g_1 + a_1 + \gamma_1 + \alpha_1 + \mu_1) K_1, \tag{1d}$$

$$\dot{S}_2 = C_2 - \beta_{22} S_2 I_2 - \beta_{21} S_2 I_1 + \gamma_2 I_2 - \mu_2 S_2 - \sigma_2 S_2 (J_1 + J_2) + g_2 J_2, \tag{1e}$$

$$\dot{I}_2 = \beta_{22} S_2 I_2 + \beta_{21} S_2 I_1 - (\gamma_2 + \alpha_2 + \mu_2) I_2 - \sigma_2 I_2 (J_1 + J_2) + g_2 K_2, \tag{1f}$$

$$\dot{J}_2 = \sigma_2 S_2 (J_1 + J_2) - (g_2 + a_2 + \mu_2) J_2 - \beta_{22} J_2 I_2 - \beta_{21} J_2 I_1 + \gamma_2 K_2, \tag{1g}$$

$$\dot{K}_2 = \sigma_2 I_2 (J_1 + J_2) + \beta_{22} J_2 I_2 + \beta_{21} J_2 I_1 - (g_2 + a_2 + \gamma_2 + \alpha_2 + \mu_2) K_2. \tag{1h}$$

Each parameter is fixed and positive. In particular, every parameter besides C_i is in the range $(0, 1)$. Figure 1 is a schematic drawing of the proposed model.

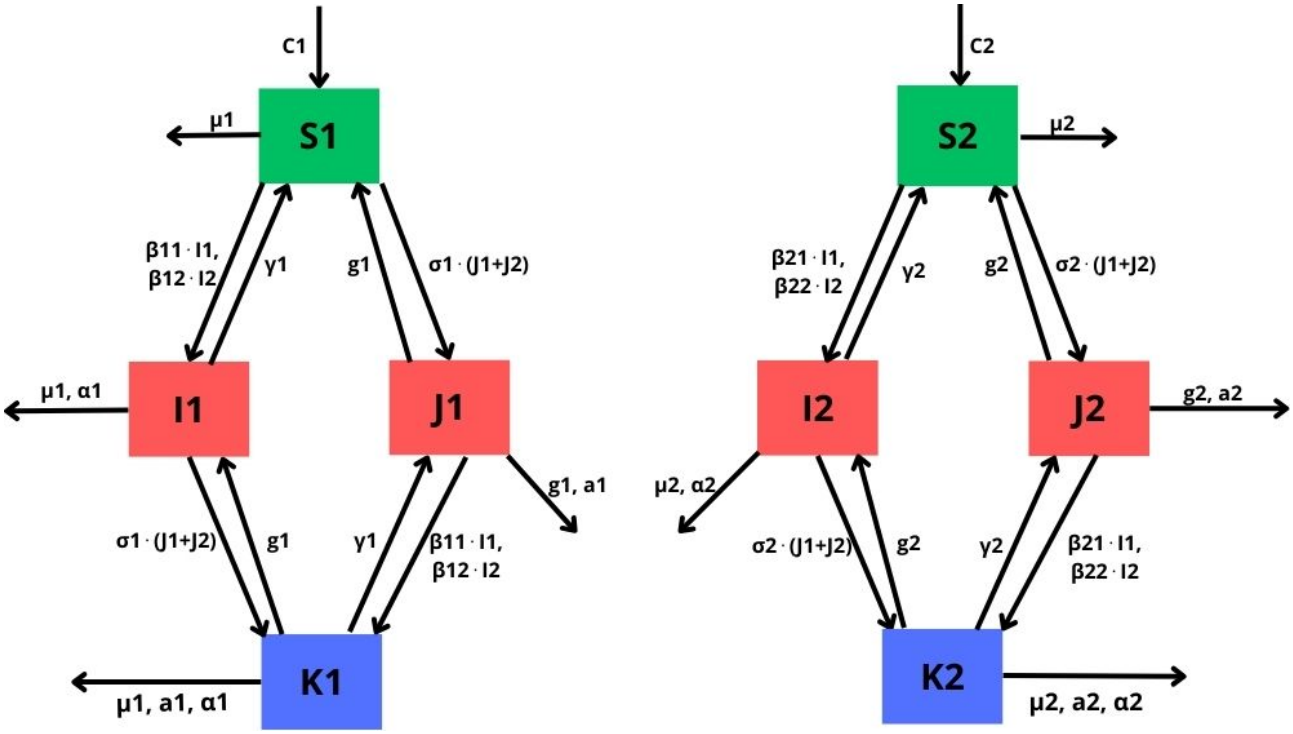

Figure 1. Possible movements between particular classes from system (1).

System (1) has four stationary states: disease–free (E_{df}), with sole DA or DB (E_A and E_B). We also suspect that there exists the endemic state (E_e), with two diseases present, exists, but we did not manage to prove it because of complicated computations. State E_{df} has the form

$$E_{df} = \left(\widehat{S}_1, 0, 0, 0, \widehat{S}_2, 0, 0, 0\right), \quad \text{where} \quad \widehat{S}_1 = \frac{C_1}{\mu_1}, \quad \widehat{S}_2 = \frac{C_2}{\mu_2}.$$

It exits unconditionally, while provided conditions determine the existence of E_A and E_B. For state E_e we only gave insight into its existence because of the complexity of the computations. For system (1) we computed the basic reproduction number $\mathcal{R}_0$. This number can be written as

$$\mathcal{R}_0 = \max(\lambda_1, \lambda_2),$$

where

$$\lambda_1 = \tfrac{\sigma_1}{q_1}\widehat{S}_1 + \tfrac{\sigma_2}{q_2}\widehat{S}_2, \qquad q_i := g_i + a_i + \mu_i$$

and

$$\lambda_2 = \frac{1}{2k_1k_2}\left(k_2\beta_{11}\widehat{S}_1 + k_1\beta_{22}\widehat{S}_2 + \sqrt{(k_2\beta_{11}\widehat{S}_1 - k_1\beta_{22}\widehat{S}_2)^2 + 4k_1k_2\beta_{12}\beta_{21}\widehat{S}_1\widehat{S}_2}\right),$$

where $k_i := \gamma_i + \alpha_i + \mu_i$. Later we investigated the local stability of the stationary state. State E_{df} is locally stable if $\mathcal{R}_0 < 1$, what is expected. Analysis of the local stability for E_A and E_B provided the list of conditions. What is important is that the parameters from both diseases affect the local stability of both states.

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2024–2025: SEVERAL ANNIVERSARIES IMPORTANT TO ME

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ABSTRACT

During this conference, we will be celebrating two anniversaries. It will be the 30th conference in the series of National Conferences on Mathematics Applied to Biology ana Medicine, and also my birthday (18th, as is customary for every adult woman).

The first conference took place in September 1995 in Zakopane and was organized on the initiative of Prof. Mariusz Ziółko, as a continuation of the schools of mathematical modeling in biology organized in Zawoja by Prof. Adam Łomnicki. The main idea was and still is to unite the community dealing with mathematical modeling of broadly understood natural phenomena in Poland. We meet every year, with a break due to the pandemic in 2020 – that is why we are celebrating our 30th anniversary only this year. We visited many interesting places, from the sea to the mountains. For the first five conferences, Professor Łomnicki chaired the conference's scientific committee. Then, until 2024, Professor Ziółko served as chairman. Professor Łomnicki served as honorary chairman until his death in 2021. Last year, this role was entrusted to me. I hope to maintain the scientific level of the conference in the years to come.

In terms of anniversaries related to me, I began working at the University of Warsaw in 1989. However, due to a leave of absence for a project at the Institute for Medical Biomathematics (IMBM) at the turn of 2019 and 2020, I formally celebrated my 35th anniversary this year. Moreover, in 2004 I visited IMBM for the first time, which means that last year I celebrated the 20th anniversary of my collaboration with Prof. Zvia Agur (founder of IMBM and the president of this institution) and her team. This is a very fruitful collaboration that has resulted in important and interesting publications (cf. [1–5]), and thanks to which I had the opportunity to receive the Hugo Steinhaus Prize (the main prize of the Polish Mathematical Society in the field of applied mathematics) this year. I hope for many more years of such fruitful cooperation.

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CREATION OF SPOTS ON MELTING SNOW — A SIMPLE MATHEMATICAL MODEL

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ABSTRACT

Snow that fell in winter melts in spring. Usually, the speed of snow melting on a given surface is uniform. This causes the thickness of the snow layer to be a decreasing function of time but a constant function of spatial variables. However, in special conditions, even in the case when the initial layer of snow is more or less uniform on the surface, after some time the melting speed and at the same time the thickness of the snow are different in different areas. This leads to the formation of spots on the snow.

Such a phenomenon can be observed in areas where there is high dustiness and the snow that fell in winter contains a large admixture of dust.

The presented work contains a proposal for a new mathematical model of the reaction-diffusion type, which describes the described phenomenon well.

Of course, the model has one, zero, stationary point. However, an appropriately defined measure of the diversity (in space) of snow thickness can increase or decrease over time before reaching a stationary state.

The results of a computer simulation of this model are presented. It is shown that for different values of the model parameters, spots on the snow appear or do not appear during melting.

Further analysis of the model should lead to the determination of the conditions under which the diversity measure increases and snow spots appear.

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DYNAMICS OF AGE-RELATED DEGRADATION IN THE HUMAN CARDIAC CONDUCTION SYSTEM: A CELLULAR AUTOMATA APPROACH

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ABSTRACT

In this contribution, we present a simplified numerical model of the human cardiac conduction system that accounts for age-related structural and functional deterioration using a cellular automata-based framework. The sinoatrial node (SAN), atrial conduction pathways, and atrioventricular node (AVN) are modeled as coupled two-dimensional cellular automata governed by modified Greenberg-Hastings dynamics. This approach enables the simulation and analysis of action potential propagation under physiological and pathological conditions, with a particular focus on age-related degradation in cardiomyocyte function.

Cardiac aging is characterized by a gradual decline in the renewal capacity of cardiomyocytes, with turnover rates decreasing from 0.8% in early adulthood to 0.3% in individuals over 75 years of age [1]. As a result, many cardiac muscle cells lose their ability to generate or transmit electrical impulses, contributing to arrhythmias such as bradycardia and tachycardia [2]. Our model incorporates two pathological cellular states: inactive cells, which are unable to conduct or respond to stimuli, and fibrotic cells, which display altered action potential characteristics, including prolonged depolarization-repolarization phases and reduced amplitude.

The numerical results confirm that degeneration of cardiac conduction structures—either through inactivity or fibrosis—leads to loss of synchronization, rhythm disturbances, and impaired impulse propagation. The simulations reproduce clinically relevant features such as the emergence of ectopic rhythms, decreased pacing rates, and unstable excitation patterns, in line with known mechanisms of arrhythmia in the aging heart [3, 4].

The presented model offers a computationally efficient and biologically plausible tool to study age-associated changes in cardiac electrophysiology. Due to its modularity, it can be extended to analyze specific structural alterations, regional dysfunction, or stimulus-response abnormalities. Future work will explore the integration of therapeutic strategies into the model, with the goal of assessing their potential effectiveness in mitigating the progression of age-related cardiac conditions and supporting the development of targeted treatments aimed at improving cardiovascular function and quality of life in elderly patients.

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INTEGER PROGRAMMING FRAMEWORK FOR RNA SECONDARY STRUCTURE PREDICTION

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ABSTRACT

The prediction of RNA secondary structure is a fundamental task in bioinformatics and structural biology due to the crucial roles RNA molecules play in diverse biological processes. To carry out its functions, RNA must fold into a well-defined structure. RNA exhibits a naturally hierarchical organization. Its primary structure refers to the linear sequence of nucleotides, the secondary structure is formed through canonical base pairings (Watson-Crick-Franklin and Wobble), and the tertiary structure corresponds to the molecule's three-dimensional atomic arrangement. Since secondary structure contacts are typically stronger and form more rapidly than tertiary interactions, secondary structures can often be predicted independently and serve as a critical intermediate step toward solving the more complex problem of tertiary structure prediction.

Traditional computational methods for RNA secondary structure prediction, guided by a thermodynamic hypothesis and Turner's nearest-neighbor parameters [1], aim to identify the most stable conformation of an RNA molecule by minimizing its overall free energy. These methods decompose RNA structure into well-defined substructures – such as stems, hairpins, internal loops, bulges, and multibranch loops – and assign empirically derived free energy values to each component based on its sequence and structural context. Despite dynamic programming algorithms, such as those implemented in RNAstructure [2] or ViennaRNA [3], allow for finding the minimum free energy (MFE) structures efficiently, there is still a wide margin for improvement in predicting accuracy.

In this work, we present a novel energy-based integer programming (IP) framework to predict RNA secondary structure via loop decomposition from a single input sequence. We provide a formal mathematical definition of loops and integrate them into our optimization model via binary variables, which indicate whether to include a particular loop in the solution. The search space of all feasible loop decompositions is defined by a set of linear constraints. The integer programming model obtains optimal secondary structure by minimizing the sum of energies over all possible loops for a given RNA sequence. Since RNA molecules can populate an ensemble of structures, we also introduce an extended parameterized model that generates suboptimal structures to provide alternative conformations to the MFE structure. Additionally, we address scalability challenges by exploring the influence of initial feasible solutions on overall computation time.

The proposed IP model was benchmarked on the archive II dataset of sequences with experimentally determined reference secondary structures. It was implemented in Python 3 and solved with

a state-of-the-art optimizer that employs the branch-and-cut technique. Model's predictions were compared to references and structures produced by the dynamic programming methods using standard metrics, including Interaction Network Fidelity (INF) and F_β score. The results show that the IP-based approach generates biologically meaningful structures and, in some cases, outperforms dynamic programming algorithms in predictive accuracy. Therefore, the IP framework provides a valuable supplementary tool for identifying alternative secondary structures.

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A MATHEMATICAL MODEL OF THE INTERACTIONS BETWEEN IMMUNE SYSTEM AND INFECTIOUS AGENTS

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ABSTRACT

Infectious diseases infections are widely distributed throughout the world. In this talk I present a mathematical model describing the response of the immune system to infections. A preliminary analysis of the model as well as results of simulations are performed. A brief discussion on the biological meaning of the numerical results is presented.

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IDENTIFIABILITY AND OBSERVABILITY OF SOME EPIDEMIOLOGICAL SYSTEMS: SIR VS. SIRS

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ABSTRACT

Compartmental models based on ODEs are widely used for the study of infectious diseases. A typical methodology when applying these models to a real epidemic is (1) setting a model based on the known features of the disease, (2) looking for parameters available in the literature and collecting real data series, and (3) calibrating the remaining unknown parameters and initial conditions using these data. However, before performing (3), one can wonder if these unknowns are uniquely determined by the known data. This is addressed by studying the observability and identifiability properties of the system. In the first part of the talk, we present some theoretical results about these properties in general nonlinear ODE systems [1]. Then, we illustrate these results by applying them to the case of an SIRS model along with the observation of a portion of infectious individuals [2]]. Furthermore, when performing (1), it may not be clear which model suits better when there is little information available; for example, if the population will lose their acquired immunity after some time. Regarding this problem, we also study an SIR model with the same observation and compare both cases. This comparison yields a novel methodology for model discrimination, allowing us to determine whether these observed data come from an SIR or an SIRS model when the observations are available for a short period of time.

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HOSPITAL COMPETITION WITH AGE-STRUCTURED PATIENTS AND CONGESTION EFFECTS: A DIFFERENTIAL GAME APPROACH

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ABSTRACT

We explore a noncooperative game framework involving two hospitals, where treatment quality suffers under congestion. Recognizing that healthcare demand is significantly influenced by patient age, we incorporate a continuous age distribution into our model. Each hospital aims to determine the optimal treatment (age-structured) intensity that maximizes its objective: for a public hospital, this involves enhancing the cross life-expectancy as measure for the number and quality of treated patients (public hospital); for a private hospital, the goal is to maximize profits based on public payments for treatment. The resulting problem leads to the introduction of differential games with the closed-loop information structure. The paper formulates conditions for verifying whether a given strategy profile constitutes an ε-Nash equilibrium with the dual closed-loop information structure. The verification theorem is then used to develop a numerical algorithm for determining ε-Nash equilibria in a finite number of steps. The numerical simulations demonstrate how the Nash equilibrium can shift in response to varying socio-economic factors.

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HOW NOT TO TRIM THE BRANCH YOU ARE SITTING ON: TWO MODELS OF A MYOPIC MARINE ECONOMY WITH A REALISTIC FISH DYNAMICS

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ABSTRACT

Markets are variable. If firms in a market face losses, they gradually disappear. It is also widely assumed in economic theory that copies of profitable firms are established proportionally to the profit. This process is usually considered in a market environment which is constant and any changes of the environment are examined as a jump with consequences illustrated by a comparative statics. This cannot be applied to firms operating in industries based on common renewable resources, like e.g. fishing in open access marine fisheries. First of all, the biomass of the caught species evolves as a result of fishing. Besides, interactions between various species constituting its ecosystem have to be taken into account, which substantially increases the complexity of the problem even if the firms considered are myopic. In this paper, we model such a market, with the firms fishing the top predator in a tritrophic food chain. The dynamics of the number of firms is proportional to single firm's profit. The firms interact within the structure of two different economic organizations of the market: the perfect competition, in which firms do not take into account their influence on the market, and the Cournot oligopoly, in which each of the firms knows how its decisions influence the price. Both dynamic models are analysed with various dynamical tools such as stability and bifurcation analysis. We are especially interested in the case when the population without the top predator results in a stable steady state or a stable limit cycle while introduction of the top predator results in chaotic dynamics, which corresponds to introduction of an invasive species. We answer the question how changes of the model parameters can result in stabilizing the three species system and how those changes can be obtained by various constant over time policies of a regulatory institution. Due to multiple bifurcations, controlling the resulting chaos to a stable steady state was possible within either intervals of policy parameters or even a sum of disjoint intervals.

Wikno, 16th–20th September 2025

BIOMATHEMATICS — USER GUIDE

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ABSTRACT

It is worth considering what biomathematics is, that is, what mathematics applied in life sciences is. It is also worth considering whether it is developing in the right direction. I have a strong opinion on this matter that I would like to share. I hope what I say provokes some disapproval from the audience.

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Wikno, 16th–20th September 2025

SENSITIVITY ANALYSIS OF THE P53 SIGNALING PATHWAY MODEL

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ABSTRACT

The p53 protein is involved in many cellular processes, while the most important are: detection of DNA damage and induction of apoptosis (the so-called programmed cell death). Therefore, the role of p53 protein in cancer progress has been widely studied during many years [1]. The p53 signaling pathway in the cell is quite complex and involves many other proteins, like: MDM2, PTEN, PIP3, AKT [2]. To better understand the role of p53 in cancer disease one can use the mathematical modeling approach. Due to its complexity, dynamical models which try to simulate the dynamics of this pathway is often described by large numbers of nonlinear equations. For example model from work [2] include system of 12 nonlinear differential equations and 43 parameters. To study these complex models one can use the different sensitivity analysis methods. The classical approach of sensitivity analysis for dynamical systems include calculation of the so-called sensitivity function for different parameters of the system [3]. Other approach involve calculation of the Green's function to study the behaviour of particular dynamical system [4]. The Green's function can be used to study how change of non-stationary parameters of the model at different times affect the system behaviour.

In this work we used Green's function approach to analyse the model from work [2]. Obtained results shows the impact of how change at different times of one model variable (representing the effect of ionizing irradiation to the cell) affect the change of other variables in the system (responsible for level of DNA damage and quantities of different proteins involved in the p53 pathway).

ACKNOWLEDGMENTS

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Wikno, 16th–20th September 2025

MECHANOCHEMICAL PATTERNING: A NEW STRAIN-MORPHOGEN PDE MODELING FRAMEWORK

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ABSTRACT

In this talk, I present a new mechanochemical framework for morphogenesis in regenerating epithelia, providing mechanistic insight into how physical forces and biochemical signalling interact to control pattern formation in living tissues. Focusing on Hydra morphogenesis, the model couples morphogen dynamics with tissue mechanics through a positive feedback loop: mechanical stretching promotes morphogen production, while morphogen concentration regulates tissue elasticity. Through bifurcation and stability analysis, we explain symmetry breaking and the emergence of single-peaked patterns without invoking a second diffusible inhibitor. This mechanochemical model is further contrasted with classical pattern formation theory, demonstrating how mechanical feedback offers an alternative mechanism for long-range inhibition. Theoretical predictions are supported by experimental validation.

Wikno, 16th–20th September 2025

PERCEPTUAL BINARY DECISION-MAKING MODEL WITH TIME DELAY AND HILL FUNCTION

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ABSTRACT

The results from a paper by Morawski & Czartoszewska [1] about a neural mass perceptual decision-making model introduced by Piskała et al. [2] are presented. The model describes the activity of two neuron populations influenced by each other and external signals. The groups' activities correspond to the process of making a perceptual binary decision and are modeled through a system of delay differential equations. Existing results are generalized by investigating the impact of both a delay in the self-inhibition and a generic Hill coefficient on solutions to the system of differential equations, with the focus on stability and the Hopf bifurcation. Several versions of the model with various assumptions are compared using analytical and numerical methods, providing insight into the impact of the modifications.

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Wikno, 16th–20th September 2025

PREDICTION OF ALZHEIMER'S DISEASE USING NEURAL CDE AND OPTIMAL CONTROL TOOLS

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ABSTRACT

Alzheimer's disease (AD) is one of the reason of causing dementia. Dementia is mostly an aging disease and touches large group of older part each community. It could cause serious damage to memory. AD is pervaded by localized brain atrophies. It deteriorates the key biological functions of neurons, such as communication, metabolism, repair, remodelling, and regeneration. The typical symptoms of the disease are accumulation of amyloid-β ($A\beta$) plaques composed of $A\beta$ peptides, and neu-rofibrillary tangles (NFT) composed of hyperphosphorylated tau proteins. PET scans of the brain of people with AD show accumulation of $A\beta$ and NFT. Some of the scans prove high $A\beta$ and low tau, while others show low $A\beta$ and high tau. This gave rise to two different hypotheses. Based on PET scan patterns of high $A\beta$ and low tau, the amyloid hypothesis states that $A\beta$ aggregation triggers a chain of events that ultimately results in AD pathology, while based on patterns of low $A\beta$ and high tau, the tau hypothesis postulates that tau tangle pathology precedes the $A\beta$ plaques formation and that tau phosphorylation and aggregation are the main cause of AD. There exist several mathematical model that can produce patterns of $A\beta$ and τ as seen in PET scans of AD patients. We consider a certain simplified version of the known models, with parameter estimates based on, and validated by, clinical data for $A\beta$, tau proteins, microglia and neurons following [1]. We use this mathematical model described by five partial differential equations to derive a kind of Neural CDE (neural controller differential equation). It will serve as fundament to derive a new methodology (machine learning) to predict appearance of AD for patience with PET scan at the begging stage of observed dementia. Trying to predict next step in time series (in our case observed dementia) is still a challenging problem. Different type of machine learning methodologies are proposed. We suggest a novel approach to processing data, which have description by mathematical model. It is a kind of neural-controlled differential equation to evaluate time series. We develop a different learning methodology supported by optimal control tools to formulate a kind of verification theorem to predict the next step in the time series.

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Wikno, 16th–20th September 2025

MODELLING BEHAVIOURAL CHANGES AND VACCINATION IN THE TRANSMISSION OF RESPIRATORY VIRUSES WITH CO–INFECTION

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joint work with Bruno Buonomo

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ABSTRACT

Co-infection of two respiratory viruses occurs when an individual's respiratory system is simultaneously infected by two genetically different viral diseases. In the recent literature, several models can be found that provide useful insights into the co-infection dynamics [2, 3]. However, a crucial aspect remains neglected: the influence of information-driven changes in human behaviour. Indeed, it is well known that human behaviour plays a pivotal role in determining the course of an epidemic and the effectiveness of any containment measures. We propose a behavioural co-infection compartmental model to investigate the effects of the behavioural changes induced by the information about the epidemic status [1]. First, we consider the case where the containment measures are purely non-pharmaceutical and model the contact rate as a decreasing function of the information index, defined as a distributed delay that quantifies the level of information and rumours about the disease status [4, 5]. We perform a qualitative analysis of the model through stability and bifurcation theory, in order to analyse the existence and stability of both endemic and co–endemic equilibria. Second, we extend the model to incorporate vaccination. The vaccination rates are assumed to increase with information about the prevalence of the diseases, and the contact rate to increase with the number of vaccinated individuals. Three information indexes are employed to quantify the information about the disease prevalence and vaccinated individuals. Among the main results, we show that behavioural changes may have a stabilising effect when only non-pharmaceutical measures are considered. In this case, sustained oscillations may turn into damped oscillations converging towards a steady state in which co-infection is endemic. Conversely, when both vaccination and non-pharmaceutical measures are considered, the effect of behavioural changes in contact patterns may have a destabilising effect.

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Wikno, 16th–20th September 2025

ON INSTABILITY OF PREY-PREDATOR SYSTEM

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ABSTRACT

In this paper, we consider a specific prey–predator system with convective terms in one spatial dimension, $x \in [0, L]$

$$\begin{aligned} N_t + (NV)_x &= -\alpha N n, \\ n_t + (nv)_x &= \beta N n. \end{aligned} \tag{1}$$

We assume that there exists $a \in [0, L]$ such that $v_x < 0$ on $[0, a)$ and $v_x > 0$ on $(a, L]$, so that $v(a) = 0$. For simplicity, we assume that V is constant. Under these conditions we need only one boundary condition at $x = 0$, i.e.

$$N_t(0) = N_0.$$

Assuming high typical mobility of the predator, we can separate the evolution time scales and introduce a small parameter. Roughly speaking, this means that $1/\alpha$ is large. We show that, to good approximation, the system can be reduced to a single linear partial differential equation for N and an ordinary differential equation for $J(t)$:

$$\begin{aligned} N_t + (NV)_x &= -R(x)N, \\ \frac{d}{dt}J(t) &= \lambda J(t), \end{aligned} \tag{2}$$

where $-\lambda$ is an eigenvalue of the operator

$$\mathcal{L}(t) = v(x)\frac{d}{dx} + v_x + N(t, x),$$

which depends parametrically on t.

The system (2) is much easier to analyze. In general, it has oscillatory solutions. For large β it is possible to find an analytical form of these solutions.

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MATHEMATICAL MODELING OF THE CORROSION PROCESS OF BIODEGRADABLE MAGNESIUM ALLOY IMPLANTS

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ABSTRACT

Magnesium, due to its properties, is an excellent material for the production of biodegradable implants. These implants have a wide range of applications, including pediatric orthopedics. Thanks to mathematical modelling we are able to estimate the rate of implant degradation.

To model the corrosion process of implants made from magnesium alloys, different approaches were applied, including models based on the works of P. Bajger et al. [1] and N. Pohl et al. [2]. An analysis was conducted to determine which of the mathematical models best represents the nature of the process. A simulation of a PDE model with a moving interface was performed. The model evaluation was based on data from the literature (e.g., [3]) as well as experimental data.

ACKNOWLEDGMENTS

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Wikno, 16th–20th September 2025

PANGRAPHS AS MODELS OF HIGHER-ORDER INTERACTIONS

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ABSTRACT

Graphs have long been effective models for pairwise interactions, providing valuable insights into the fundamental properties of trophic and mutualistic networks. However, it is now increasingly recognized that non-pairwise (higher-order) interactions play a crucial role in influencing the stability of underlying dynamic systems. Hypergraphs, which allow edges to connect arbitrary subsets of vertices, have been proposed as models capable of incorporating these interactions. Despite this, their application often obscures the roles of individual vertices and magnifies centrality measures.

In this work [1], we propose an extension of the hypergraph concept that more effectively captures complex higher-order interactions, including the modification of information. We introduce the concept of a pangraph, an extension of the ubergraph [3] into directed graphs. In a pangraph, edges can start and/or end at other edges, with arbitrary levels of nesting. This framework enables a more consistent representation of complex interactions. In this talk, we will explore the properties of pangraphs, their relationship to classical directed graphs through the Levi representation, and propose centrality measures tailored to these structures. We will also discuss potential methods for extending the pangraph concept to the dynamics, mainly transport equation, on metric graphs.

Finally, we highlight two compelling applications of pangraphs. The first applies the pangraph framework to structure the theory of Petri nets with catalysts. The second revisits a hypothesis about the significance of interaction modifications, as presented in [2]. Using a real-world coffee ecosystem database, we show that the results in [2] can be interpreted as an amplification of centrality measures in the hypergraph model.

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The work was conducted in the collaboration with M. Iskrzyński (Polish Academy of Sciences, Poland), A. Grzelik (Polish Academy of Sciences, Poland) and G. Mütlu (Gazi University, Turkey).

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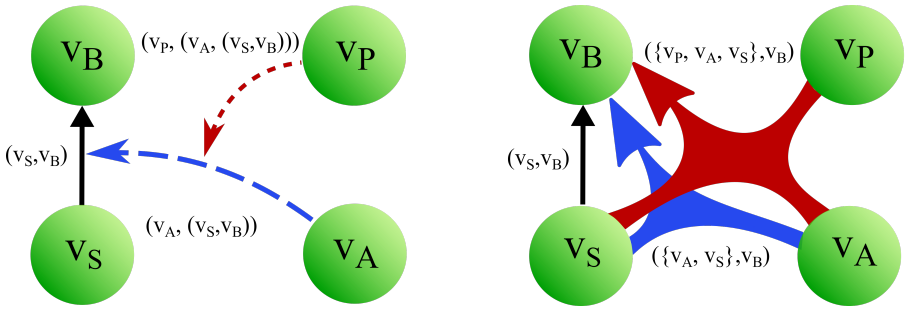

Figure 1. A 4-node subgraph of the coffee agroecosystem model from [1] is presented here in two representations: as a pangraph (on the left) and as a hypergraph (on the right). In this diagram, the nodes v_P, v_A, v_S and v_B correspond to Phorid, Azteca, Scale, and Beetle, respectively, as described in [2]. The colours in the pangraph indicate the depth of objects within it: fundamental vertices (with zero depth) are shown in green, one-depth edges are black, two-depth panedges are blue, and three-depth panedges are red.

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Wikno, 16th–20th September 2025

TWO-STRAIN DENGUE MODEL WITH A CONSTANT RECRUITMENT RATE

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ABSTRACT

In this talk, we examine a two–strain dengue model that captures the interactions between human and mosquito populations. The model incorporates vertical transmission of the virus from adult mosquitoes to their offspring and possibility of reinfection with another dengue strain. We assume that the recruitment rate for susceptible larval mosquitoes is constant which allows us to show the local stability of the disease-free and endemic equilibria, the existence of different two–strain stationary states and global stability of disease–free equilibrium. Additionally, we present numerical simulations to support our findings.

Wikno, 16th–20th September 2025

PROGRAMMABLE BIOMOLECULAR COMPUTING BASED ON CRISPR-CAS: CONCEPS, COMPUTATIONAL PERSPECRIVES, AND POTENTIAL APPLICATIONS

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ABSTRACT

The CRISPR-Cas system represents an advanced platform for programmable genome editing that enables precise control of DNA cleavage in prokaryotic and eukaryotic cells. Initially demonstrated by programmable in vitro DNA cleavage by Cas9 endonuclease [1], this RNA-guided technology has enabled a wide range of applications in biotechnology and medicine. A notable advancement includes the combination of Cas9 with the *Fok*I restriction enzyme, creating dimeric RNA-guided nucleases with enhanced specificity for targeted genome modification [2].

Currently, DNA computing provides innovative approaches for applying the mathematical foundations of computer science to medicine [3], and enhances the programmability of biological systems [4]. This report introduces conceptual directions for the integration of biomolecular computing technologies [3,4] with CRISPR-Cas systems [1]. Special emphasis is placed on how current biomolecular computation frameworks can guide mathematical modelling and enhance the programmable capabilities of CRISPR-Cas systems. This interdisciplinary integration promises novel applications and innovative solutions, highlighting the role of computational and mathematical approaches in advancing precision medicine.

ACKNOWLEDGMENTS

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Wikno, 16th–20th September 2025

DYNAMIC THRESHOLD CURVES AND RESPONSE PRECISION IN FORCED EXCITABLE SYSTEMS

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ABSTRACT

Phase-locking of ongoing oscillations to a periodic signal is a well-studied phenomenon that can be explored with a variety of analytical approaches. Much less is known about what factors determine the response precision of excitable units that are intrinsically at rest but are activated by periodic forcing and noise. One motivation for considering this issue comes from the behavior of auditory neurons, which fire spikes in a precise range of phases relative to incoming sound waves, a behavior for which the mechanism is unknown. We shed light on this coding precision by introducing a new tool, the dynamic threshold curve (DTC), designed to study the responses of an excitable system to a subthreshold signal. The DTC provides an effective instantaneous threshold that takes into account how the intrinsic dynamics and the input combine with noise or perturbations to generate a response. The DTC effectively summarizes, in a single curve, the information of response precision of the excitable model, as we exhibit showing that the distribution of spike times of the excitable system is well captured by the first passage time of a simple, Gaussian stochastic process to the distance to the DTC. This shows that peaks and troughs of the DTC, but also their slope, convey fine information about spike timings in response to noise. In particular, it captures properties of type 2 and type 3 excitable cells studied previously, and provide a framework to predict the DTC properties necessary to support auditory neurons' response precision, which we show to arise in a well-established auditory neuron model.

This is a joint work with J. Rubin (University of Pittsburgh) and J. Touboul (Brandeis University).

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Wikno, 16th–20th September 2025

IMPACT OF AGE-STRUCTURE DEPENDENT CONTROL DURING THE FIRST TWO YEARS OF COVID-19 PANDEMIC IN THE BASQUE COUNTRY

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ABSTRACT

The age distribution of the population certainly impacts the spread and control of infectious diseases [1, 2]. In this article, we propose and analyze an infectious disease, Coronavirus disease 2019 (COVID-19), a viral disease declared apandemic by WHO. It has posed the greatest threat to global public health.The proposed work is a phase wise retrospective study of the Basque country of Spain. Understanding the dynamic of the virus could help make future predictions on the evolution of epidemics. Our goal is to study the dynamics of the COVID-19 disease over the firsttwo years. Considering understanding the dynamics of disease severity betweenyoung and old population during the first two years of the pandemic, we propose a deterministic modeling framework stratifying the total human population into two groups: older and younger, assuming different risks for severe disease manifestation. In addition to analyzing the proposed model mathematically, athorough sensitivity analysis was carried out using the PRCC method to pin-point the crucial parameters impacting the transmission dynamics of COVID-19 in the overall hospitalized population.We observed that the population younger than 70 would contribute more to the overall force of infection than the older population. However, unlike the current age-based models, the new models offer different perspectives on how population age impacts disease severity in the COVID-19 pandemic.

Keywords: Deterministic COVID-19 model, Stability analysis, data analysis, age-structure, sensitivity analysis

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Wikno, 16th–20th September 2025

KOLMOGOROV GENERALIZED PREDATOR-PREY MODELS

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ABSTRACT

The existence of Lyapunov function is proved for some general dynamical system in Kolmogorov framework

$$x' = g(x)G(x,y), \quad y' = h(y)H(x,y)$$

with nonzero stationary solution under some monotonicity assumptions imposed on nonlinearities. The applications include different variations of predator-prey models. Moreover, some optimal control problem of fishing in Ghana is considered. The results were obtained in collaboration with Dorota Bors from University of Lodz and students from University of Wrocław, including Łukasz Rębisz, partially based on a generalization of the method applied successfully to astrophysical models.

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MATHEMATICAL MODEL OF CAR-T CELL THERAPY FOR GLIOBLASTOMA WITH THE LOGISTIC CANCER GROWTH WITH TIME DELAY

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ABSTRACT

In this work, I present an analysis of a mathematical model for CAR-T cell therapy in the treatment of glioblastoma multiforme, with a particular focus on the role of time delay. The analysis follows the approach outlined in [1].

CAR-T cell therapy involves the infusion of genetically engineered T cells designed to more effectively recognize and eliminate cancer cells. Based on multiple studies—primarily [5] and [3]—the model is formulated as a system of differential equations.

I begin by introducing the model and explaining the role of each component in the equations. The main focus of the poster, however, lies in the analysis of the model's steady states and their stability in relation to the presence of time delays. I also briefly explore how various treatment strategies can be incorporated into the model, with the aim of identifying the most effective therapeutic approaches for glioblastoma multiforme.Through numerical simulations presented in the poster, I demonstrate how time delay influences the model's dynamics. The parameter values used in these simulations were estimated based on data from [2] and [4].

This model offers a promising framework for optimizing cancer treatment strategies. By running simulations, we can investigate a range of therapeutic scenarios and identify the most effective approaches—such as adjusting dosages, combining therapies, or tailoring treatment plans to individual patient profiles.

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MATHEMATICAL MODELLING OF CANCER INVASION: PHENOTYPIC TRANSITIONING PROVIDES INSIGHT INTO MULTIFOCAL FOCI FORMATION

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ABSTRACT

The transition from the epithelial to mesenchymal phenotype and its reverse (from mesenchymal to epithelial) are crucial processes necessary for the progression and spread of cancer. We investigate how phenotypic switching at the cancer cell level impacts the behaviour at the tissue level, specifically on the emergence of isolated foci of the invading solid tumour mass leading to a multifocal tumour. To this end, we propose a new mathematical model of cancer invasion that includes the influence of cancer cell phenotype on the rate of invasion and metastasis. The implications of the model are explored through numerical simulations revealing that the plasticity of tumour cell phenotypes appears crucial for disease progression and local invasive spread [1]. The computational simulations show the progression of the invasive spread of primary cancer reminiscent of in vivo multifocal breast carcinomas, where multiple, synchronous neoplastic foci are frequently observed and are associated with a poorer patient prognosis.

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A HYBRID STOCHASTIC MODEL OF RETINAL ANGIOGENESIS

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ABSTRACT

Understanding the biological principles that govern blood vessel growth in the retina has important clinical implications, for the prevention of possible retinopathies, which may eventually lead to blindness. We present a mathematical model that describes vessel formation by branching diffusion of Langevin type with chemotaxis due to fields of concentrations governed by PDEs. There are two types of cells in the model, the cells undergo proliferation and can change their type. The movement of vessel tips is given by the following Langevin type stochatic equation

$$\begin{cases} d\mathbf{X}_i^2(t) = & \mathbf{V}_i^2(t)dt \\ d\mathbf{V}_i^2(t) = & [-k\,\mathbf{V}_i^2(t) + F(g, \nabla g, u, \nabla u)]dt + \sigma dW_i(t), \end{cases}$$

where u and u are concentration fields of vascular growth factor and oxygen, that evolve according to the following PDEs

$$\frac{\partial u(t,\mathbf{x})}{\partial t} = -d_u u(t,\mathbf{x}) + D_u \Delta u(t,\mathbf{x}) + \alpha_u \eta(t,\mathbf{x}, Q^{[1]}(t)),$$

$$\frac{\partial g(t,\mathbf{x})}{\partial t} = -d_g g(t,\mathbf{x}) + D_g \Delta g(t,\mathbf{x}) + S\,(u(t,\mathbf{x})) - \alpha_g g(t,\mathbf{x})\eta(t,\mathbf{x}, Q^{[1]}(t)),$$

We call our model hybrid since it includes the coupling of a fully stochastic model for the construction of a vessel network in the retina, with continuum underlying fields describing relevant factors, such as growth factors and oxygen.

The model leads to numerical simulations that somehow reproduce normal vascularization, and predict possible pathologies.

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FEEDBACK-FEEDFORWARD CONTROL IN EMT SIGNALLING PATHWAY MODEL

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ABSTRACT

Introduction

Positive and negative feedback loops are well-established concepts in building and analysis of cell signalling pathways' models. However, control theory and engineering experience have led to the development of advanced structures as more viable options in many problems. The complexity of biological interactions suggests that more complex control structures may be found in their models.

One of the basic structures, used widely in industrial applications, is a feedback-feedforward structure, which joins the benefits of standard feedback control with feedforward's ability to quickly react to disturbances in the system. It includes two controllers: one responsible for standard feedback reaction and the second for filtering the input signal and directly supplying it to the plant. One of the key features of such a structure is the high sensitivity of its output to changes in the feedforward path when compared to changes in the feedback. Should such a structure be found in a signalling pathway model, this characteristic can be used for preliminary filtering of parameters for sensitivity analysis, as more potent drug targets will be present in the feedforward path.

Epithelial-mesenchymal transition (EMT) is considered crucial in the process of acquiring metastatic capabilities by the tumour, therefore finding effective therapy targets in its signalling pathway can be of great merit. Model of EMT developed by Lu, et al. [1] was chosen to search for components structurally and functionally similar to the technical feedback-feedforward control structure. It describes interaction between 2 proteins - Snail and Zeb, their mRNAs and 2 microRNAs - miR-34 and miR-200. The main advantage of that model, in the context of this work, was its small size (only 6 differential equations) however, the model being well verified in the literature is not without significance.

Methods

The search for a given structure can be divided into stages: representing interactions between molecules (variables) as a directed graph of connections, searching for preliminary candidates based on the graph of connections, verifying candidates by checking if key summing junctions are represented in the equations. As an additional, final verification of the method, sensitivity analysis is performed to check the key behavioural trait of the structure - high sensitivity to changes in the feedforward path. Sensitivity was checked using two methods - time domain based [2] and frequency domain based [3].

Results

First stage of the analysis found 14 candidates for a feedback-feedforward structure, based solely on the similarity of connections' graph. All candidate structures were built on 6 core feedback loops, though for each core feedback loop, pairs of candidates are found, for which molecules assigned to the roles of feedback controller and plant are switched.

Next stage of analysis - verification of key summing junctions - led to the rejection of 8 out of 14 candidates. Those 6 candidates that passed the stage are similar to each other in terms of roles assigned to types of molecules, i.e. protein levels act as input signal, and feedback loop is based on interactions between mRNA and miRNA.

Final stage - sensitivity analysis - took into account 6 parameters for each candidate, paired in such a way that for each parameter in the feedback path there was a parameter with the same interpretation (e.g. production rate, or degradation rate) in the feedforward path. Verification of the behaviour in terms of sensitivity was therefore based on comparison of those pairs.

In the tests, only 3 candidates performed in a desired way - having higher sensitivity for changes in the feedforward path. All of them had the core feedback loop built with miRNA level acting as a controller and mRNA level acting as a plant.

Discussion

The results of the sensitivity analysis required a closer look at the 6 candidates that passed the first two stages. All of the candidates follow a common structural pattern, shown schematically in Fig. 1, with two additional interactions (marked in red) modifying the feedback loop. Depending on whether

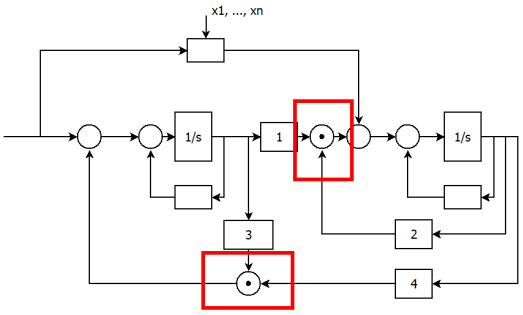

Figure 1. Structural pattern of candidates found

the role of a controller was assigned to miRNA or mRNA, either blocks 1 and 3 or blocks 2 and 4 were filled by a function that was nearly constant in the operating range of the model, while the other two were a constant equal to 1. When block 3 was equal to 1 and block 4 was a nearly constant function (as was the case for mRNA as a controller) the feedback loop was almost insensitive to changes of output, breaking the structure's fundamental assumption.

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AROUND LOTKA-VOLTERRA MODELS WITH DIFFUSION AND TAXIS

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ABSTRACT

We study a prey-predator system and a competition system, both with Lotka-Volterra reaction terms, assuming, in addition to the diffusion movement of both species, an avoidance strategy of one of them modeled as repulsive taxis.

$$N_t = D_n\Delta N + \nabla\cdot(\chi N\nabla P) + \alpha_1 N - \alpha_2 N^2 - \alpha_3 NP\,,$$
$$P_t = D_p\Delta P + \beta_1 P - \beta_2 P^2 + \beta_3 NP$$

in $\Omega\times(0\,,\infty)$ where N and P denote the densities of prey and predator or the densities of two competitors. It is assumed that the set $\Omega\subset R^n$ is a region with a smooth boundary. The system is suplemented by initial conditions and Neumann, no-flux, boundary conditions. The coefficients $D_n\,, D_p$ are diffusion constants, $\chi > 0$ is a taxis sensitivity coefficient. The taxis term describes the movement against the predator or competitor density in order to reduce the frequency of encounters.

The aforementioned model describes the mechanism of so called direct taxis. The taxis is called direct if the animals are guided by the density gradient of another population or indirect if they are guided by the density of a chemical secreted by individuals of another population. It is interesting to understand the relation between both models of taxis and in paper [3] we consider the asymptotic transition from the model with indirect taxis to the model with direct taxis as a fast reaction limit.

The prey-predator model and the competition model, can be considered from the perspective of the itraguild predation and then the sign of the parameter β_3 changes from $\beta_3 < 0$ (competition) to predation, $\beta_3 > 0$, depending on the carrying capacity of the common food resources for both species. The problem of blow-up prevention for the models turns out to be challenging for space dimension $n > 1$ and we present partial results from [2]. Mechanism of pattern formation will be described for the models and illustrated by the results of numerical simulations (c.f. [1, 2]).

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VOICE FREQUENCY ANALYSIS IN PCOS SCREENING TESTS

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ABSTRACT

Voice analysis is a convenient and easily accessible method for conducting medical screening tests. A low-pitched voice in women may be a symptom of polycystic ovary syndrome (PCOS). This symptom is frequently observed by doctors, but confirming it requires a specific method of voice frequency analysis. Traditional frequency analysis methods did not yield satisfactory results. Our database includes recordings of text read by 42 patients and 38 subjects from the control group. We used the frequency analysis of 25-second voice samples. To distinguish the voices of women with PCOS from those of the control group, we used Fourier transform and analyzed the quotients of amplitude spectra between the PCOS group and the control group. The analysis is optimized by a function that selects the appropriate frequency ranges. Our method achieved an average diagnostic accuracy of 81% in the control group and 69% for patients with PCOS.

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