Thematic section

MBM

Mathematics in Biology and Medicine

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SCHEDULE OF THE SECTION
Mathematics in Biology and Medicine

- Tuesday – September 5th

  14:30–15:00 Urszula Ledzewicz, *Optimal Control for a Model of the Synergy of Chemo- and Radiotherapy with Immunotherapy*

  15:00–15:30 Jesús J. Bosque, *Mathematical modelling of the hotspot of metabolic activity in cancer patients*

  15:30–16:00 Agnieszka Bartłomiejczyk, *Analysis of a mathematical model of glioma growth*

  coffee break

  16:30–17:00 Marek Bodnar, *4D model of CAR-T therapy*

  17:00–17:30 Magdalena Szafrańska, *On the analysis of a mathematical model of car-t cell therapy for glioblastoma with logistic cancer growth*

  17:30–18:00 Beatriz Ocaña Tienda, *A mathematical perspective on brain metastases*

- Wednesday – September 6th

  12:00–12:30 Piotr Bartłomiejczyk, *One-dimensional dynamics in neuron models*

  12:30–13:00 Jacek Miękisz, *Time delays in evolutionary games*

  13:00–13:30 Radosław Wieczorek, *Multiscale stochastic individual based models*

- Thursday – September 7th

  14:30–15:00 Andrzej Nowakowski, *Optimization of HAP administration in cancer therapy*

  15:00–15:30 Zuzanna Szymańska, *Bayesian inference of a non-local proliferation model*

  15:30–16:00 Ryszard Rudnicki, *Some aspects of mathematical modelling of cell cycle*

  coffee break

  16:30–17:00 Katarzyna Pichór, *A general model of immune status*

  17:00–17:30 Marcin Choiński, *A discrete SIS model built on the strictly positive scheme*

  17:30–18:00 Jan Poleszczuk, *Non-invasive estimation of patient-specific cardiovascular system properties using mathematical modeling coupled with tonometry data*

Analysis of a mathematical model of glioma growth

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joint work with Marek Bodnar, Magdalena U. Bogdańska and Monika J. Piotrowska

Abstract

Low-grade gliomas (LGGs) are primary brain tumours which evolve very slowly in time, however, inevitably cause patient death. In [1], we consider a PDE version of the previously proposed ODE model that describes the changes in the densities of functionally alive LGGs cells and cells that are irreversibly damaged by chemotherapy treatment. Based on the Fenichel invariant manifold theory we show that the tumour spreads like a travelling wave, meaning that the solutions of a corresponding mathematical model move with a constant speed without changing their shape. We have also calculated analytically the minimum speed of the travelling wave which is very close to the numerically calculated speed.

[1] Bartłomiejczyk A., Bodnar M., Bogdańska M.U., Piotrowska M.J., *Travelling waves for low-grade glioma growth and response to chemotherapy model*, submitted.

One-dimensional dynamics in neuron models

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Abstract

Map-based neuron models are useful tools in modelling neural dynamics. They provide an alternative to usually computationally more expensive models based on continuous or hybrid dynamical systems. We study two discrete models of neuronal dynamics. The first model was introduced by Chialvo in 1995 ([1]) and the second one by Courbage, Nekorkin and Vdovin in 2007 ([2]). We show that their reduced one-dimensional versions can be treated as independent simple models of neural activity, which still display very rich and varied dynamics. We carry out a detailed analysis of both periodic and chaotic behaviour of the models.

[1] Bartłomiejczyk P., Llovera Trujillo F., Signerska-Rynkowska J., *Periodic and chaotic dynamics in a map-based neuron model*, Mathematical Methods in the Applied Sciences (2023), 1–26.

[2] Bartłomiejczyk P., Llovera Trujillo F., Signerska-Rynkowska J., *Spike patterns and chaos in a map-based neuron model*, to appear in International Journal of Applied Mathematics and Computer Science.

Mathematical modelling of the hotspot of metabolic activity in cancer patients

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Abstract

The collective signature emerging from the transition of cancers to increasingly aggressive behaviors is macroscopically displayed by positron emission tomography (PET). In fact, the most readily PET measure, the maximum standardized uptake value (SUV_{max}), has been found to have prognostic value in different cancers. However, few works have linked the properties of this metabolic hotspot to cancer evolutionary dynamics. By analysing diagnostic PET images from cancer patients, we found that SUV_{max} scales superlinearly with the mean metabolic activity (SUV_{mean}) and sublinearly with the metabolic tumor volume (MTV) following power laws. This preferential accumulation of activity on the hotspot was accurately captured by a mechanistic model of tumor growth accounting for phenotypic transitions, what suggests that non-genetic changes may suffice to fuel the observed sustained increases in tumor metabolic activity. The model also revealed that the location of increasingly active proliferative cellular spots progressively drifts from the center of the tumor to the periphery, as a result of the competition between gradually more aggressive phenotypes. This last finding led to the development of a metric, NHOC (normalised distance from hotspot to centroid), based on the separation from the location of the activity hotspot to the tumor centroid. We computed the NHOC on the 3D diagnostic PET images from patients with lung cancer and patients with breast cancer by measuring the volume normalised distance from the SUV_{max} to the tumour centroid. In both cohorts, we carried out survival analyses for the NHOC and for other classical PET biomarkers, finding that the former had a high prognostic value, outperforming the latter.

[1] Bosque J.J., Calvo G.F., Molina-García D., Pérez-Beteta J., García Vicente A.M., Pérez-García V.M., *Metabolic activity grows in human cancers pushed by phenotypic variability*, iScience 26 (2023), no. 3, 106–118.

[2] Jiménez-Sánchez J., Bosque J.J., Jiménez Londoño G.A., Molina-García D., Martínez A., Pérez-Beteta J., Ortega-Sabater C., Honguero Martínez A.F., García Vicente A.M., Calvo G.F., Pérez-García V.M., *Evolutionary dynamics at the tumor edge reveal metabolic imaging biomarkers*, PNAS 118 (2021), no. 6.

A discrete SIS model built on the strictly positive scheme

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Abstract

I will present a model which is a discretization of its continuous counterpart. As a discretization method, the strictly positive scheme was chosen. I will present the basic properties of the system, including the value of the basic reproduction number $\mathcal{R}_0$ and the existence of stationary states appearing in the system. Local stability of the stationary states will be discussed. I will also focus on global stability of the state for which there is no infection in the population. Moreover, the behavior of the system for $\mathcal{R}_0 = 1$ will be discussed. Theoretical results will be complemented with numerical simulations. They constitute a continuation of the work presented in [1] and [2].

[1] Bodzioch M., Choiński M., Foryś U., *Simple Discrete SIS Criss-Cross Model of Tuberculosis in Heterogeneous Population of Homeless and Non-Homeless People*, Mathematica Applicanda 47 (2019), no. 1, 103–115.

[2] Bodzioch M., Choiński M., Foryś U., *A Non-standard Discretized SIS Model of Epidemics*, Mathematical Biosciences and Engineering 19 (2022), no. 1, 115–133.

Optimal Control for a Model of the Synergy of Chemo- and Radiotherapy with Immunotherapy

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Abstract

The release of tumor antigens during traditional cancer treatments (such as chemo- or radiotherapy) leads to a stimulation of the immune response which provides synergistic effects these treatments have when combined with immunotherapies (e.g., based on check-point blockade). Based on a classical model for tumor-immune system interactions [2], a low-dimensional mathematical model is formulated that incorporates such synergistic features [3]. The resulting dynamics exhibits the wide range of behaviors that encompass the variety of medically realistic scenarios often termed the three E's (elimination, equilibrium and tumor escape) of immunoediting [1].

Optimal control problems for the scheduling of combinations of chemo- and immunotherapy are formulated and analyzed (both analytically and numerically) [4]. Side effects of the drugs are measured indirectly by including the total doses of the respective drugs with weights as penalty terms in the objective. The formulation allows us to judge the amounts of the agents required to achieve tumor eradication as well as the time it will take to do so. Various medical scenarios reflected through different

weights in the penalty terms are considered and solutions are computed numerically and their local optimality is verified [5].

[1] Dunn G.P., Old L.J., Schreiber R.D., *The three E's of cancer immunoediting*, Annual Review of Immunology 22 (2004), 329–360.

[2] Kuznetsov V.A., Makalkin I.A., Perelson A.S., Taylor M.A., *Nonlinear dynamics of immunogenic tumors: parameter estimation and global bifurcation analysis*, Bulletin of Mathematical Biology 56 (1994), 295–321.

[3] Ledzewicz U., Schättler H., *On modeling the synergy of Cancer immunotherapy with radiotherapy*, Communications in Nonlinear Science and Numerical Simulation 118 (2023).

[4] Ledzewicz U., Schättler H., *On the optimal control problem for a model of the synergy of chemo- and immunotherapy*, Optimal Control Applications and Methods, in revision.

[5] Ledzewicz U., Maurer H., Schättler H., *Bang-bang optimal controls for a mathematical model of chemo- and immunotherapy in cancer*, Discrete and Continuous Dynamical Systems – Series B, submitted.

Time delays in evolutionary games

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Abstract

It is well known that time delays can cause oscillations in dynamical systems. Usually, the internal equilibria of evolving populations, describing the coexistence of strategies, are expected to be asymptotically stable for small time delays, while above the critical time delay at which the Hopf bifurcation occurs, they become unstable, cycles appear. Here we present a new behavior of systems with time delays, not present in any previous models of evolutionary games [1]. We show that in differential replicator equations with strategy-dependent time delays, interior stationary states, describing the level of cooperation in evolutionary games of social dilemmas, depend continuously on time delays. We also show that they may disappear or additional states can emerge. We develop small time-delay approximation to replicator dynamics [1]. One particular example of our results is that in the Prisoner's Dilemma game, for time delays of cooperation smaller than ones of defection, an unstable interior state appears, so for some initial conditions, the population converges to a homogeneous state with just cooperators. We will also discuss some results for finite populations [2].

Acknowledgments This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 955708.

[1] Bodnar M., Miękisz J., *Evolution of populations with strategy-dependent time delays*, Physical Review E 103 (2021).

[2] Miękisz J., Mohamadichamgavi J., *Small time delay approximation in replicator dynamics*, preprint, doi:2303.08200.

[3] Łopuszański K., Miękisz J., *Random walks with asymmetric time delays*, Physical Review E 105 (2022).

Optimization of HAP administration in cancer therapy

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Abstract

Solid tumors are often characterized by areas with reduced oxygen levels called hypoxia. Such regions arise when tumor vascular perfusion is limited or the interstitial diffusion is perturbed, or the rapidly expanding tumors increase the overall oxygen absorption [1]. Hypoxia is one of the causes of tumor resistance to anti-cancer treatments, including chemo-, immuno-, and radiation therapies. Therefore, new treatments are being developed that can be chemically activated only in the areas of low oxygen contents – the hypoxia-activated pro-drugs (HAPs) [2]. Such a drug is usually supplied in an inactive form (a pro-drug) that requires chemical activation to generate its lethal form (an effector drug). While several HAPs have been tested in clinical trials, they were not as successful as expected [3]. Thus, more studies are needed to investigate the methods of HAP administration in order to optimize their effectiveness.

To design optimal strategies for HAP administration, we will use the following mathematical model. Let us define a rectangular domain $\Omega = \{\mathbf{x} = (x, y) : 0 \leqslant a \leqslant x \leqslant b,\ 0 \leqslant c \leqslant y \leqslant d\}$ and boundary of Ω denoted as $\partial\Omega = O_l \cup O_r$ where $O_l = \{(a, y) : y \in [c, d]\}$, $O_r = \partial\Omega \backslash O_l$. Inside the domain Ω, we consider N tumor cells Γ_l, $l = 1, ...N$, each with N_l boundary points $\mathbf{X}_i^l$, $l = 1, ...N_l$. The domain Ω is interpenetrated by the interstitial fluid flow of velocity $\mathbf{u}(\mathbf{x})$. The flow is stationary, since over the time of this project (3 hours), the cells are assumed to be non-motile and non-proliferating.

The spatial distribution of an inactive prodrug η_i is described by the following diffusion-advection-reaction equation with a constant diffusion coefficient D_{η_i}, for $(\mathbf{x}, t) \in \Omega \times [0, T]$

$$\frac{\partial \eta_i(\mathbf{x}, t)}{\partial t} = D_{\eta_i} \Delta \eta_i(\mathbf{x}, t) + \mathbf{u}(\mathbf{x}) \cdot \nabla \eta_i(\mathbf{x}, t) - \varphi(\gamma(\mathbf{x}, t)) \eta_i(\mathbf{x}, t),$$

where φ is the drug activation function that is non-zero ($\varphi_0 > 0$) only in the hypoxic areas, given by

$$\varphi(\gamma(\mathbf{x},t)) = \begin{cases} \varphi_0 & \text{if } \gamma(\mathbf{x},t) \leqslant \gamma_{hypo} \\ 0 & \text{otherwise} \end{cases}$$

the initial condition is given by

$$\eta_i(\mathbf{x},0) = 0,\ \mathbf{x} \in \Omega$$

and boundary conditions describe the pro-drug bolus injection (over time $[0,t_0]$) that defines influx from the boundary ($y \in [c,d]$) representing the tumor vessel, are defined as follows

$$\eta_i(a,y,t) = \begin{cases} w_2(y,t), & \text{if } y \in [c,d],\ t \in [0,t_0],\ t_0 < T, \\ 0 & \text{if } y \in [c,d],\ t \in (t_0,T], \end{cases}$$

$$\frac{\partial \eta_i(x,y,t)}{\partial \nu} = 0,\ (x,y) \in O_r,\ t \in [0,T],$$

The spatial distribution of oxygen γ is described by the following diffusion-advection-reaction equation with a constant diffusion coefficient D_γ and an oxygen uptake rate β, for $(\mathbf{x},t) \in \Omega \times [0,T]$

$$\frac{\partial \gamma(\mathbf{x},t)}{\partial t} = D_\gamma \Delta\gamma(\mathbf{x},t) + \mathbf{u}(\mathbf{x}) \cdot \nabla\gamma(\mathbf{x},t) - \beta\gamma(\mathbf{x},t) \sum_{l=1}^{N} \sum_{i=1}^{N_l} \chi_\varepsilon(\mathbf{x}, \mathbf{X}_i^l),$$

here, the indicator function χ_ε defines the neighborhood of radius ε for information transfer between cells and the domain where the metabolite distributions are defined

$$\chi_\varepsilon(\mathbf{x}, \mathbf{X}_i^l) = \begin{cases} 1 & \text{if } \|\mathbf{x} - \mathbf{X}_i^l\| \leqslant \varepsilon \\ 0 & \text{otherwise} \end{cases}$$

the initial condition for oxygen concentration represents a non-uniform oxygen gradient and is given by

$$\gamma(\mathbf{x},0) = \gamma_0(\mathbf{x}),\ \text{for } \mathbf{x} \in \Omega$$

and the boundary conditions are given by

$$\gamma(a,y,t) = w_1(y,t), \text{for } y \in [c,d],\ t \in [0,T],$$

$$\frac{\partial \gamma(\mathbf{x},t)}{\partial \nu} = 0,\ \text{for } \mathbf{x} \in O_r,\ t \in [0,T],$$

The spatial distribution of an active drug η_a is described by the following diffusion-advection-reaction equation with a constant diffusion coefficient D_{η_a}, the drug activation function φ, the drug uptake rate α, and a drug decay rate ω_a,

$$\begin{aligned} \frac{\partial \eta_a(\mathbf{x},t)}{\partial t} &= D_{\eta_a} \Delta\eta_a(\mathbf{x},t) + \mathbf{u}(\mathbf{x}) \cdot \nabla\eta_a(\mathbf{x},t) + \varphi(\gamma(\mathbf{x},t))\eta_i(\mathbf{x},t) \\ &\quad - \alpha\eta_a(\mathbf{x},t) \sum_{l=1}^{N} \sum_{i=1}^{N_l} \chi_\varepsilon(\mathbf{x}, \mathbf{X}_i^l) - \omega_a \eta_a(\mathbf{x},t), \\ &\qquad\qquad \text{for } (\mathbf{x},t) \in \Omega \times [0,T] \end{aligned}$$

under initial condition

$$\eta_a(\mathbf{x}, 0) = 0, \text{ for } \mathbf{x} \in \Omega$$

and boundary conditions

$$\eta_a(a, y, t) = 0, \text{ for } y \in [c, d], \ t \in [0, T]$$

$$\frac{\partial \eta_a(\mathbf{x}, t)}{\partial \nu} = 0, \text{ for } \mathbf{x} \in O_r, \ t \in [0, T],$$

[1] Brown J.M., Wilson W.R., *Exploiting tumour hypoxia in cancer treatment*, Nature Reviews Cancer 4 (2004), no. 6, 437–47.

[2] Hay M.P., Wilson W.R., *Targeting hypoxia in cancer therapy*, Nature Reviews Cancer, 11 (2011), no. 6, 393–410.

[3] Houben R., Niemans R., de Ruysscher D., Spiegelberg L., Theys J., Yaromina A. et al. *Hypoxia-activated prodrugs and (lack of) clinical progress: The need for hypoxia-based biomarker patient selection in phase III clinical trials*, Clinical and Translational Radiation Oncology 15 (2019), 62–69.

A mathematical perspective on brain metastases

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Abstract

Brain metastases (BMs) are a major clinical problem, as they represent the most common intracranial tumors in adults. These tumors are caused by single tumor cells or groups of cells that detach from the primary site and migrate to the brain, where they give rise to clusters of metastatic cells that grow and form macrometastases.
Understanding the underlying mechanisms of BM formation is crucial for the development of effective therapeutic strategies. To shed light on this process, we have used a discrete agent-based model (ABM). Our ABM is based on a fixed vasculature and cells that are characterized by a continuous phenotype variable ranging from 0 to 1. In this model, cells can proliferate, migrate, undergo cell death, or become quiescent, resulting in the emergence of complex phenomena and the formation of large metastases.
We also wanted to study the growth dynamics of BMs. To do that we have employed scaling laws, specifically a reduced form of the Von-Bertalanffy equation

$$\frac{dV}{dt} = \alpha V^{\beta},$$

to describe the growth patterns of these tumors before and after treatment [1]. Interestingly, we have found that different growth patterns are observed for radiation necrosis, an adverse event that frequently occurs after irradiation and tumor recurrence [2]. This distinction can be useful in the clinical setting to differentiate between these two conditions, which is a clinical issue at the moment since both events have the same characteristics in medical images and however, completely different actions should be taken.
To further validate these findings, mathematical models incorporating aspects of tumor biology and inflammatory response have been developed. The results obtained from these models are consistent with the observations made in the data.

[1] Jiménez-Sánchez J., Ocaña-Tienda B., Pérez-Beteta J. et al., *The Growth Laws of Brain Metastases*, medRxiv:10.1101/2022.02.03.22270146v2

[2] Molina-García D., Ocaña-Tienda B., Pérez-Beteta J. et al., *Growth dynamics of brain metastases differentiate radiation necrosis from recurrence*, Neurooncology Advances 5 (2022), no. 1.




A general model of immune status

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Abstract

The immune status is the concentration of specific antibodies, which appear after infection with a pathogen and remain in serum, providing protection against future attacks of that same pathogen. Over time the number of antibodies decreases until the next infection. During an infection, the immunity is boosted and then the immunity is gradually waning, etc. The densities of antibody concentration satisfy some partial differential equation with an integral boundary condition, which generates a stochastic semigroup. We present general results concerning asymptotic stability and sweeping of stochastic semigroups [1] and then we apply them to our model [2]. We also analyze special cases of the model, e.g. when immunity decreases exponentially; with constant increase of antibodies after infection; with a threshold concentration of antibodies at the re-infection; and with seasonal infections.

[1] Pichór K., Rudnicki R., *Asymptotic decomposition of substochastic operators and semigroups*, Journal of Mathematical Analysis and Applications 436 (2016), 305–321.

[2] Pichór K., Rudnicki R., *Asymptotic properties of a general model of immune status*, SIAM Journal on Applied Mathematics (SIAP) 83 (2023), 172–193.

Non-invasive estimation of patient-specific cardiovascular system properties using mathematical modeling coupled with tonometry data

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Abstract

Assessment of detailed status of cardiovascular (CV) system state in hemodialysis patients is of utmost importance as the risk of CV associated death is in that group the highest among all other comorbidities. The aim of our study was to develop a mathematical model which, after calibration with patient-specific data, would provide new personalized information about CV system state.

We model the blood transport in a bifurcating binary tree of fifty-five larger systemic arteries in which individual vessels are axisymmetric elastic cylinders tapering along their length. We describe spatiotemporal changes in the cross-sectional area of the artery (equivalently blood pressure) and blood flow using an 1D approach. Proposed model was confronted with radial pressure wave profiles recorded before, during and after two independent hemodialysis sessions in 35 anuric prevalent hemodialysis patients and once in a group of 32 healthy volunteers. Each recording was used to estimate six subject-specific parameters of pulse wave propagation model.

The model identified increased arterial stiffness of both large and small arteries in hemodialysis patients compared to their healthy counterparts. Interestingly, regular pulse wave analysis based biomarkers failed to show significant differences.

Our study shows that, after parameter estimation procedure, proposed mathematical model is able to provide new patient-specific insights into CV system state that are unattainable with existing non-invasive methods.

[1] Dabrowski W., Debowska M., Poleszczuk J. et al., *Patient-specific pulse wave propagation model identifies cardiovascular risk characteristics in hemodialysis patients*, PLOS Computational Biology 14 (2018), 1–15.

A mathematical model of the interplay of labile and glycated hemoglobin with glucose for clinical and research applications

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Abstract

Diabetes mellitus continues to be a major global burden, and innovations remain necessary in its early diagnosis and treatment [1]. Glycated hemoglobin (HbA1c) is an established indicator of the average glucose levels of a given patient during the two months prior to its measurement. In our project, we combine dimensionality reduction alongside an ordinary differential equation model to analyze the relationship of labile hemoglobin (HbA1d), an unstable molecule and an intermediary step in cell glycation, with the glucose and HbA1c levels in patients. It has historically only been studied as a source of error in HbA1c measurements but has recently gained interest as a biomarker of diabetes-related malignancies and an indicator of the glycemic state of patients [1], [2]. These methods are applied to two different sets of patients: a group of sixty pediatric patients on which a glucose tolerance test was performed alongside concurrent measurements of their HbA1d and HbA1c, and a group of forty thousand adult patients in which the fast- ing plasma glucose (FPG), HbA1c, and HbA1d were measured once. Through this study, we managed to find a close relationship between the dynamics of HbA1d and glucose in short time intervals and develop a predictive mathematical model that may serve to assist in the personalized treatment of individual diabetic patients. Furthermore, we examined labile hemoglobin as an indicator of diabetes in patients in whom both FPG and HbA1c give inconclusive results.

These results and models are both analyzed mathematically and tested for their biological validity. This is done by exploring the stability of their solutions and the biochemical mechanisms that dictate cell glycation, alongside their ability to predict and fit the clinical data used in this project [4].

[1] Delanghe J.R. et al., *Labile glycated hemoglobin: an underestimated laboratory marker of short term glycemia*, Clinical Chemistry and Laboratory Medicine 60 (2022), no. 3, 451–455.

[2] León-Triana O. et al., *Labile haemoglobin as a glycaemic biomarker for patient-specific monitoring of diabetes: mathematical modelling approach*, Journal of the Royal Society Interface 15 (2018), no. 142.

[3] Romero J. et al., *Interplay of labile and glycated hemoglobin with glucose for short-term monitoring of diabetic patients: Insights from a mathematical model*, in preparation.

[4] Sun H. et al., *Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045*, Diabetes Research and Clinical Practice 183 (2022), 109–119.

Some aspects of mathematical modelling of cell cycle

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Abstract

Modeling of cell cycle is one of the fundamental subject of mathematical biology because it could help to solve such problems as synchronization of cell division in cancer therapy and allows to understand dynamics of growth of cellular populations (e.g. tissues). There are many different models of cell cycles. In this talk we consider an age-size structured cell population model based on the cell cycle length [1]. The model is described by a first order partial differential equation with initial-boundary conditions. Using the theory of semigroups of positive operators we establish new criteria for an asynchronous exponential growth of solutions to such equations. We discuss the question of exponential size growth of cells. We study in detail a constant size growth model and a model with target size division. We also present versions of the model when the population is heterogeneous. The discussion on model generalizations will be a good excuse to present some new challenges in the study of asymptotic behaviour of semigroups of operators.

[1] Pichór K., Rudnicki R., *Cell cycle length and long-time behaviour of an age-size model*, Mathematical Methods in the Applied Sciences 45 (2022), 5797–5820.

On the analysis of a mathematical model of CAR-T cell therapy for glioblastoma with logistic cancer growth

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Abstract

In the era of new technologies and rapidly developing medicine, scientists are trying to find better and better methods of cancer therapy. In my presentation, I will discuss the analysis of a mathematical model of CAR-T cell therapy for glioblastoma with logistic tumor growth.

The main purpose of the analysis is to determine model steady states and to study their stability. In addition, numerical simulations were performed for two cases: a single injection of CAR-T cells, which is reflected in the initial state (dose) and the case of a constant influx of CAR-T cells, which is the simplest mathematical approximation of treatment. Mathematical analysis with simulations allows us to better understand the dynamics of glioblastoma development under the influence of CAR-T cell therapy, what can help in the development of more effective therapeutic strategies.

[1] León-Triana O., Perez-Martinez A., Perez-Garcia V., *Dual-target carts with on- and off-tumour activity may override immune suppression in solid cancers: A mathematical proof of concept*, Cancers 13 (2021), no. 4.

[2] Li J.J., Lu P.H., Zhang X., *Advances in the development of chimeric antigen receptor-T-cell therapy in B-cell acute lymphoblastic leukemia*, Chinese Medical Journal 133 (2020), no. 4, 474-482.

Bayesian inference of a non-local proliferation model

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Abstract

We present a new proliferation model of cells living within a colony that is a non-local equation with a discontinuous interaction kernel. We discuss the range of applicability of the model, select suitable data and apply the Bayesian method to perform parameter estimation. We discuss proof of the well-posedness of the problem and we investigate the convergence of the EBT algorithm applied to solve the equation. The main difficulty lies in the low regularity of the kernel which is not Lipschitz continuous, thus preventing the application of standard arguments. Therefore, we use the radial symmetry of the problem instead and transform it using spherical coordinates. The resulting equation has a Lipschitz kernel with only one singularity at zero. We introduce a new weighted flat norm and prove that the particle method converges in this norm. We prove the well-posedness of the problem and we investigate the convergence of the EBT algorithm applied to solve the equation. Finally, we prove the stability of posterior distributions in the total variation norm which exploits the theory of spaces of measures equipped with the weighted flat norm.

[1] Gwiazda P., Miasojedow B., Skrzeczkowski J., Szymańska Z., *Convergence of the EBT method for a non-local model of cell proliferation with discontinuous interaction kernel*, IMA Journal of Numerical Analysis 43 (2023), no. 1, 590–626.

[2] Gwiazda P., Miasojedow B., Skrzeczkowski J., Szymańska Z., *Bayesian inference of a non-local proliferation model*, Royal Society Open Science 8 (2021), no. 11, 211–279.

Multiscale stochastic individual based models

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Abstract

Individual-based models or stochastic particle models are very common in modern mathematical modelling, especially in biology and chemistry. Behavior of such systems when the number of particles is big is interesting both from mathematical and application point of view.

In the talk we will consider a situation when one of the population is abundant enough to use macroscopic approximation, while the other consist of a few particles and is described by a stochastic particle system. Such a scale separation leads to the so called hybrid models, where a stochastic particle system is coupled to partial differential equation. Some examples of such models and related limit theorems will be presented.

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