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Zakopane-Kościelisko, 3–7 September 2018

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Table of Contents

Part I

Invited speakers

Krajowa Konferencja Zastosowań Matematyki w Biologii i Medycynie

Zakopane-Kościelisko, 3rd–7th September 2018

JAN CZEKANOWSKI – ANTROPOLOG I STATYSTYK

Mirosław Krzyśko

Adam Mickiewicz University Poznań

ABSTRACT

Jan Czekanowski was born into a landowing family, on 6 October 1882 in Głuchów, near Grójec. In spring 1902 he was accepted into the mathematics and natural science section of the Philosophy Faculty at the Cantonal University of Zurich.

While still a student in Zurich he wrote a paper, which appeared in 1904 as introduction to Rudolf Martin's anthropology texbook Lerbuch der Anthropologie, which still widely known among anthropologist today, and in 1907 was published in Czekanowski's doctoral dissertation. In it he gives a short description of the statistical methods which had been introduced to anthropology by English biometricians.

He completed his studies in July 1906, obtaining the degree of doctor of philosophy. As a fresh graduate from Zurich, starting from 1 November 1906 he took up the position of assistant at the Royal Anthropological Museum in Berlin.

In 1913 the Warsaw Scientific Society has published a book by Jan Czekanowski titled Zarys metod statystycznych w zastosowaniu do antropologii (Outline of statistical methods in application to anthropology). This was the first statistical texbook written in Polish.

From 1 October 1913, he was appointed assistant professor of anthropology and ethnology in the Philosophy Faculty of Lvov University. In the years 1934–1936 Czekanowski held the post of rector of University in Lvov.

Krajowa Konferencja Zastosowań Matematyki w Biologii i Medycynie

Zakopane-Kościelisko, 3rd–7th September 2018

OPTIMAL CONTROL IN BIOMEDICAL PROBLEMS

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ABSTRACT

We discuss a variety of optimal control problems that arise from biomedical problems with a focus on mathematical models for cancer treatments. We consider the optimization of drug administration schedules (dosage, frequency and sequencing of therapeutic agents) with the aim to minimize an objective that makes a compromise between minimizing the tumor burden and pharmacologically relevant quantities which measure side effects of the drugs. Using the Pontryagin maximum principle and tools of geometric optimal control theory insights can be gained into the optimality of bang-bang controls (representing medically maximum tolerated doses, MTD) and singular controls (corresponding to biologically optimal doses, BOD). Simple answers are not always the best ones as there is mounting medical evidence that "more is not necessarily better" and a properly calibrated dose can lead to a better outcome (metronomic therapies). In this talk, several models will be discussed that model tumor heterogeneity and various aspects of the tumor microenvironment (anti-angiogenic treatment and immunotherapies) with emphasis on combination therapies. A continuing thread in all models is the role of pharmacometrics, i.e., how the structure of optimal controls depends on whether a pharmacokinetic model (PK) for the drug action is included in the dynamics or not and how the effects of the drugs are modelled through a pharmacodynamic (PD) relation, e.g., log-kill assumption or Michaelis-Menten type kinetics. For a specific example, the treatment of chronic myeloid leukemia (CML) through a combination of tyrosine kinase inhibitors and immuno-modulatory therapies, we compare optimal solutions with best-in class solutions that only allow the use of a limited range of dosages and a priori specified timing changes. On a separate topic, a mathematical model for the selective spiking of integrate-and-fire neurons is considered from an optimal control point of view. Its analysis reveals fundamental limits on the spiking sequences that can be achieved time-optimally.

Part II

Abstracts of the talks

Zakopane-Kościelisko, 3rd–7th September 2018

MATHEMATICAL MODEL OF ENDOTHELIAL CELL PROLIFERATION AND MATURATION

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ABSTRACT

Blood vessel sprouting (angiogenesis) is one of the hallmarks of cancer. Better quantitative understanding of this process would allow more effective antiangiogenic therapies to be developed. It has been hypothesised that not only the number of endothelial cells, but also the quality of the vasculature play an important role in how chemo- and radiotherapies are delivered to tumour site. Hence in this study a minimally-parametrised mathematical model of endothelial cell proliferation and maturation is developed. Endothelial cells are subdivided into two compartments – mature and immature (or proliferating). The cells are assumed to undergo a self-mediated maturation, while loss of blood vessel quality is mediated by an external growth factor (here VEGF). The model is fitted to experimental data. The model shows how inhibition of VEGF results in better quality vasculature and slower proliferation.

REFERENCES

[1] P. Bajger and M. Bodzioch: *Mathematical model of endothelial cell proliferation and maturation*, Mathematica Applicanda 46(1) (2018), 3–12, DOI 10.14708/ma.v46i1.6383.

Zakopane-Kościelisko, 3rd–7th September 2018

DYNAMICS OF A SIMPLIFIED HPT MODEL

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ABSTRACT

We propose a simplified mathematical model of the hypothalamus-pituitarythyroid (HPT) axis in an endocrine system. The considered model is a modification of the model proposed by Mukhopadhyay and Bhattacharyya in [2]. Our system of delay differential equations reconstructs the HPT axis in relation to 24h profiles of human in physiological conditions. Homeostatic control of the thyroid-pituitary axis is considered by using feedback and delay in our model. The influence of delayed feedback on the stability behaviour of the system is discussed.

REFERENCES

[1] A. Bartłomiejczyk and B. Jackowska-Zduniak: *Dynamics of a simplified HPT model in relation to 24h TSH profiles*, Mathematica Applicanda 46(1) (2018), 13–24, DOI 10.14708/ma.v46i1.6389.

[2] B. Mukhopadhyay and R. Bhattacharyya: *A mathematical model describing the thyroid-pituitary axis with time delays in hormone transplantation*, Appl. Math. 51(6) (2006), 549–564.

Zakopane-Kościelisko, 3rd–7th September 2018

THE PHYLOGENETIC EFFECTIVE SAMPLE SIZE AND JUMPS

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ABSTRACT

The phylogenetic effective sample size is a parameter that has as its goal the quantification of the amount of independent signal in a phylogenetically correlated sample. It was studied for Brownian motion and Ornstein–Uhlenbeck models of trait evolution. Here, we study this composite parameter when the trait is allowed to jump at speciation points of the phylogeny. Our numerical study indicates that there is a non–trivial limit as the effect of jumps grows. The limit depends on the value of the drift parameter of the Ornstein–Uhlenbeck process.

REFERENCES

[1] K. Bartoszek: *The phylogenetic effective sample size and jumps*, Mathematica Applicanda 46(1) (2018), 25–33, DOI 10.14708/ma.v46i1.6368.

Krajowa Konferencja Zastosowań Matematyki w Biologii i Medycynie

Zakopane-Kościelisko, 3rd–7th September 2018

PREDICTING PATHOGENICITY BEHAVIOR IN *ESCHERICHIA COLI* POPULATION THROUGH A STATE DEPENDENT MODEL AND TRS PROFILING

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ABSTRACT

An important challenge in computational biology is the analysis of genetic molecular data through sophisticated computer science and mathematical methods that are implemented by interdisciplinary research groups. In this study we propose a comprehensive approach for predicting pathogenicity in a population based on a state dependent model and TRS-PCR profiling [1]. This method is based on the Binary State Speciation and Extinction (BiSSE) model that allows the diversification rates to be controlled by a binary trait. Additionally, we have evaluated the possibility of using the BiSSE model for estimating parameters from genetic data. We analyzed a real dataset (from 251 *E. coli* strains) and confirmed previous biological observations demonstrating a prevalence of some virulence traits in specific bacterial sub-groups. Noteworthy, this is a comprehensive approach and it may be used to predict pathogenicity of other bacterial taxa. We believe that our developed software should be useful for biologists that want to use BiSSE models.

ACKNOWLEDGEMENTS

We would like to thank Military Teaching Hospital No. 2, Medical University of Lodz, Poland. KB is supported by the Swedish Research Council's grant no. 2017–04951 and SVeFUM.

REFERENCES

[1] K. Bartoszek, M. Majchrzak, S. Sakowski, A.B. Kubiak-Szeligowska, I. Kaj, and P. Parniewski: *Predicting pathogenicity behavior in Escherichia coli population through a state dependent model and TRS profiling*, PLoS Computational Biology 14 (1/2018), e1005931.

Zakopane-Kościelisko, 3rd–7th September 2018

ROBIN-TYPE BOUNDARY CONDITIONS IN TRANSITION FROM REACTION-DIFFUSION EQUATIONS IN 3D DOMAINS TO EQUATIONS IN 2D DOMAINS

Adam Bobrowski, Tomasz Lipniacki, Markus Kunze

ABSTRACT

We consider a singular limit of reaction-diffusion equations in 3D domains of thickness converging to zero.

In the 2D limit the resulting reaction-diffusion equation has a source term resulting from the Robin-type boundary conditions imposed on boundaries of the original 3D domain. The proposed approach can be applied to constructing approximate solutions of diffusion problems in thin planar, cylindrical, or spherical layers between two membranes. As an example we refer to the problem of activation of B lymphocytes, which typically have large nuclei and a thin cytoplasmic layer which can beconsidered as a spherical shell.

Zakopane-Kościelisko, 3rd–7th September 2018

ANALYSIS OF GLOBAL DYNAMICS FOR HIV-INFECTION OF CD4$^+$T CELLS AND ITS TREATMENT

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ABSTRACT

Antiviral therapy for HIV-infected patients has greatly improved in recent years. Administration of drug combinations consisting of two or more different drugs can reduce and maintain virus load below detection level in many patients. Cyclic administration of the immune activator interleukin-2 (IL-2) in combination with highly active antiretroviral therapy (HAART) has been suggested as an effective strategy to realize long-term control of HIV replication *in vivo*. In this article, we formulate a mathematical model of the immune response for HIV-infected individual in the presence of HAART and IL-2. We look for the conditions under which the immune system recovers by applying IL-2 as an immune activator along with HAART. From the analytical point of view this means global stability of the disease-free equilibrium. Comprehensive numerical simulations are presented to illustrate the analytical results.

REFERENCES

[1] M. Bodzioch, M. Choiński, and U. Foryś: *Analysis of global dynamics for HIV-infection of CD4$^+$T cells and its treatment*, Mathematica Applicanda 46(1) (2018), 35–48, DOI 10.14708/ma.v46i1.6369.

Krajowa Konferencja Zastosowań Matematyki w Biologii i Medycynie

Zakopane-Kościelisko, 3rd–7th September 2018

DECISION MAKING IN INNATE IMMUNE RESPONSES

Maciej Czerkies, Zbigniew Korwek, Wiktor Prus, Marek Kochańczyk, Joanna Jaruszewicz-Błońska, Karolina Tudelska, Sławomir Błoński, Marek Kimmel, Allan R. Brasier and Tomasz Lipniacki

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ABSTRACT

The innate immune system processes pathogen-induced signals into cell fate decisions. How information is turned to decision remains unknown. By combining stochastic mathematical modelling and experimentation, we demonstrate that feedback interactions between the IRF3, NF-κB and STAT pathways lead to switch-like responses to a viral analogue, poly(I:C), in contrast to pulse-like responses to bacterial LPS. Poly(I:C) activates both IRF3 and NF-κB, a requirement for induction of IFNβ expression. Autocrine IFNβ initiates a JAK/STAT-mediated positive-feedback stabilising nuclear IRF3 and NF-κB in first responder cells. Paracrine IFNβ, in turn, sensitises second responder cells through a JAK/STAT-mediated positive feedforward pathway that upregulates the positive-feedback components: RIG-I, PKR and OAS1A. In these sensitised cells, the "live-or-die" decision phase following poly(I:C) exposure is shorter–they rapidly produce antiviral responses and commit to apoptosis. The interlinked positive feedback and feedforward signalling is key for coordinating cell fate decisions in cellular populations restricting pathogen spread.

REFERENCES

[1] M. Czerkies and et al.: *Cell fate in antiviral response arises in the crosstalk of IRF, NF-κB and JAK/STAT pathways*, Nature Communications 9:493 (2018).

Zakopane-Kościelisko, 3rd–7th September 2018

MATHEMATICAL MODEL OF BATS' SUBPOPULATIONS DEVELOPMENT

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ABSTRACT

The paper deals with the description of the mathematical model of bats' subpopulations and fission-fusion societies development. The model is based on the system of ordinary differential equations. Bats' behaviour and their searching strategy is presented on the basis of cavity roosting bats living in Białowieża Forest located in Poland. Theoretical results are illustrated by a computer simulation and its comparison with biological remarks.

REFERENCES

[1] A. L. Dawidowicz and A. Poskrobko: *Mathematical model of bats' subpopulations development*, Mathematica Applicanda 46(1) (2018), 49–57, DOI 10.14708/ma.v46i1.6371.

Zakopane-Kościelisko, 3rd–7th September 2018

ESTIMATION OF INITIAL FUNCTIONS FOR SYSTEMS WITH DELAYS FROM DISCRETE MEASUREMENTS

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ABSTRACT

The work presents a gradient-based approach to estimation of initial functions of time delay elements appearing in models of dynamical systems. It is shown how to generate the gradient of the estimation objective function in the initial function space using adjoint sensitivity analysis. It is assumed that the system is continuous-time and described by ordinary differential equations with delays but the estimation is done based on discrete-time measurements of the signals appearing in the system. Results of gradient-based estimation of initial functions for exemplary models are presented and discussed.

REFERENCES

[1] K. Fujarewicz: *Estimation of initial functions for systems with delays from discrete measurements*, Mathematical Biosciences and Engineering 14(1) (2017), 165–178, DOI 10.3934/mbe.2017011.

Krajowa Konferencja Zastosowań Matematyki w Biologii i Medycynie

Zakopane-Kościelisko, 3rd–7th September 2018

MONITORING OF MEAN FOR ASYMMETRIC DISTRIBUTIONS

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ABSTRACT

Nowadays control charts are used not only to control glass thickness, the diameter of rods etc. Have been invented many types of modern charts to control meteorological, medical, financial or telecommunications data. They often have heavy tails, skewness, and asymmetry. Approximation such data by Gaussian distribution is not the most beneficial. We need to model. Hence the need to model data with a different distribution. Controlling a process that exhibits asymmetry is a more difficult task than monitoring symmetric features (v. Figueiredo & Gomes (2013)). It was assumed to construct a chart to control the work of the heart. This is definitely an asymmetrical process. Three control charts were constructed: to monitor average and grand mean of Rayleigh distribution and grand mean for approximated distribution to Gaussian distribution.

REFERENCES

[1] M.K. Gądek and K.J. Szajowski: *Monitoring of mean for asymmetric distributions*, Mathematica Applicanda 46(1) (2018), 59–75, DOI 10.14708/ma.v46i1.6373.

Zakopane-Kościelisko, 3rd–7th September 2018

METHOD FOR MASS SPECTROMETRY SPECTRUM DEISOTOPING BASED ON FUZZY INFERENCE SYSTEMS

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ABSTRACT

Proteins are very significant molecules that can construct the fingerprint of cancer. When dealing with large molecules, such as proteins, the crucial issue is their trustful and precise identification. In the majority of cases, mass spectrometry is used to identify the protein. Processing of data gathered in mass spectrometry experiment consists of several steps, and one of them is deisotoping. It is an essen- tial part of preprocessing because some peaks in the spectrum are not the unique compound, but they are members of an isotopic envelope. There are several exist- ing methods of deisotoping, but none of them is general and can be used in any experimental settings. To manage this, we propose a new algorithm based on fuzzy inference systems. The method was tested on the data provided by Institute of On- cology in Gliwice, that has been gathered in MALDI experiment in two different settings on head and neck cancer tissue samples. The comparison study, done between the developed fuzzy-based algorithm and mMass method revealed that the proposed method was able to identify more consistent with the expert annotation isotopic envelopes

REFERENCES

[1] A. Glodek and J. Polańska: *Method for mass spectrometry spectrum deisotoping based on fuzzy inference systems*, Mathematica Applicanda 46(1) (2018), 77–86, DOI 10.14708/ma.v46i1.6384.

Zakopane-Kościelisko, 3rd–7th September 2018

A MODEL FOR RANDOM FIRE INDUCED TREE-GRASS COEXISTENCE IN SAVANNAS

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ABSTRACT

Tree-grass coexistence in savanna ecosystems depends strongly on environmental disturbances out of which crucial is fire. Most modeling attempts in the literature lack stochastic approach to fire occurrences which is essential to reflect their unpredictability. Existing models that actually include stochasticity of fire are usually analyzed only numerically. We introduce minimalistic model of tree-grass coexistence where fires occur according to stochastic process. We use the tools of linear semigroup theory to provide more careful mathematical analysis of the model. Essentially we show that there exists a unique stationary distribution of tree and grass biomasses.

REFERENCES

[1] P. Klimasara and M. Tyran-Kamińska: *A model for random fire induced tree-grass coexistence in savannas*, Mathematica Applicanda 46(1) (2018), 87–96, DOI 10.14708/ma.v46i1.6382.

Zakopane-Kościelisko, 3rd–7th September 2018

A MATHEMATICAL MODEL OF SOME VIRAL-INDUCED AUTOIMMUNE DISEASES

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ABSTRACT

We propose a new mathematical model of viral-induced autoimmune diseases. The model is described by a bilinear system of four integro-differential equations of Boltzmann type. We present numerical results illustrating several typical outcomes of autoimmune diseases. In particular, special attention is devoted to the role of the ability of effector immune cells to destroy target cells for the development of autoimmune diseases.

REFERENCES

[1] M. Kolev and I. Nikolova: *A mathematical model of some viral-induced autoimmune diseases*, Mathematica Applicanda 46(1) (2018), 97–108, DOI 10.14708/ma.v46i1.6391.

Zakopane-Kościelisko, 3rd–7th September 2018

ON THE NONLOCAL DISCRETIZATION OF THE SIMPLIFIED ANDERSON-MAY MODEL OF VIRAL INFECTION

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ABSTRACT

We present five nonstandard finite difference methods designed for numerical simulation of the simplified Anderson-May model of viral infection. The proposed methods, based solely on the principle of nonlocal discretization, are able to preserve all of the essential qualitative features of the original model: the non-negativity of the solution and local stability of the equilibrium points, along with their stability conditions. One of the proposed methods preserves the types of the equilibrium points (i.e. the presence and absence of oscillations) as well. All of these results are independent of the chosen step-size of simulation.

REFERENCES

[1] A. Korpusik and M. Bodnar: *On the nonlocal discretization of the simplified Anderson-May model of viral infection*, Mathematica Applicanda 46(1) (2018), 109–116, DOI 10.14708/ma.v46i1.6395.

Zakopane-Kościelisko, 3rd–7th September 2018

SINGLE STRANDED-DNA DETECTION: THE ROLE OF WIP1 IN ATR-DEPENDENT PATHWAY

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ABSTRACT

Single-stranded DNA (ssDNA) areas arise in cells as a result of exposure to stress agents like UVC or during repair of DNA double-strand breaks. ATR (ataxia telangiectasia mutated and Rad3-related) is responsible for detecting ssDNA. Recently, it has been shown that one of the most important components of cellular response to the damage is Wip1 phosphatase, which inactivates main elements of DNA damage response (DDR) pathways. We developed a mathematical model of ATR detector system, connected to p53 tumor suppressor responsible for activation of genes involved in the cellular response to the damage (DNA repair/apoptosis). Moreover, we added Wip1 phosphatase, as the main agent responsible for turning off DDR. Our results show, that with an accurate dose of UVC and silenced or blocked Wip1, it may be possible to drive cancer cells to apoptotic pathway.

REFERENCES

[1] M. Kurpas, K. Jonak, and K. Puszynski: *Single stranded-DNA detection: the role of Wip1 in ATR-dependent pathway*, Mathematica Applicanda 46(1) (2018), 117–126, DOI 10.14708/ma.v46i1.6375.

Zakopane-Kościelisko, 3rd–7th September 2018

THE INTERPLAY BETWEEN STOCHASTIC GENE SWITCHING AND CERTAIN METRONOMICS THERAPIES

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ABSTRACT

In this work I present some preliminary results of the exploration of the interplay between stochastic gene switching and certain metronomics therapies. During the research a simple model of gene-mRNA-protein network subjected to the metronomic therapy was investigated. The results show that the stochastic gene switching process, especially the time expected between successive switching plays a significant role in determining the size of the responding cells fraction.

REFERENCES

[1] K. Puszyński: *The interplay between stochastic gene switching and certain metronomics therapies*, Mathematica Applicanda 46(1) (2018), 127–136, DOI 10.14708/ma.v46i1.6392.

Zakopane-Kościelisko, 3rd–7th September 2018

ANALYSIS OF A PREDATOR-PREY MODEL WITH DISEASE IN THE PREDATOR SPECIES

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ABSTRACT

In the paper we analyse a diffusive predator-prey model with disease in predator species proposed by Qiao et al. [1]. In the original article there appears a mistake in the procedure of the model undimensionalisation. We make a correction in this procedure and show that some changes in the model analysis are necessary to obtain results similar to those presented by Qiao et al.
We propose corrected conditions for global stability of one of the existing equilibria – disease free steady state and endemic state in the case without diffusion as well as in the model with diffusion. On the basis of the corrected analysis we present new stability results.

REFERENCES

[1] M. Qiao, A. Liu, and U. Foryś: *Qualitative analysis for a reaction-diffusion predator-prey model with disease in the prey species*, J. Appl. Math. Art. ID 236208 (2014), DOI 10.1155/2014/236208.

[2] P. Radziński and U. Foryś: *Analysis of a predator-prey model with disease in the predator species*, Mathematica Applicanda 46(1) (2018), 137–147, DOI 10.14708/ma.v46i1.6385.

Krajowa Konferencja Zastosowań Matematyki w Biologii i Medycynie

Zakopane-Kościelisko, 3rd–7th September 2018

A KINETIC APPROACH TO SELF-PROPELLED PARTICLES DYNAMICS IN CONFINED DOMAINS

Elżbieta Ratajczyk

ABSTRACT

Active matter consists of large numbers of self-driven agents converting chemical energy, usually stored in the surrounding environment, into mechanical motion. The main motivation for our work is a potential usage of active ink (ink with active bi-metal nanoparticles) in 3D printers. It may result in smaller voxel size and increase the printing speed. Decreased viscosity allows for smaller outlet of nozzle which, in turn, results in better resolution of printing.

In this presentation I focus on a kinetic description of active matter represented by self-propelled rods swimming in a viscous fluid and in presence of confinements. It is well-known that confinements may significantly affect trajectories of active rods in contrast to unbounded or periodic containers. Among such effects are accumulation at walls and upstream motion (also known as rheotaxis). We rigorously derive boundary conditions for the active rods' probability distribution function in the limit of zero inertia. These boundary conditions are important since the active rod possesses self-propulsion thus its velocity does not vanish at the no-slip wall, as for passive particles. Moreover, this limit allows us to reduce a dimension (and so computational complexity) of the kinetic description.

The second part of the talk is devoted to investigation of vanishing translational diffusion. This case is natural, because in experimental observations, rod-like micro-swimmers, are more likely to spontaneously turn rather than jump to another position implying that translational diffusion is small. It is a singular limit, that is one cannot simply set D_{tr} to zero in the Fokker-Planck equation and no-flux condition. This is because active particles tend to accumulate at walls and in particular they form a boundary layer.

This is a joint work with Mykhailo Potomkin, Leonid Berlyand and Pierre-Emmanuel Jabin.

Zakopane-Kościelisko, 3rd–7th September 2018

ON A STOCHASTIC GENE EXPRESSION WITH PRE-MRNA, MRNA AND PROTEIN CONTRIBUTION

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ABSTRACT

During my speech I will present a model of gene expression, where stochastic effects originate from random fluctuations in gene activity status, but we precede mRNA production by the formation of pre-mRNA, which enriches classical transcription phase [1]. We obtain a stochastically regulated system of ordinary differential equations describing evolution of pre-mRNA, mRNA and protein levels. We describe mathematical analysis of a long-time behavior of this stochastic process, identified as a piece-wise deterministic Markov process. We observe that in the deterministic (adiabatic) limit state of the process, it can exhibit two specific types of behavior: bistability and the existence of the limit cycle [2]. We will also shortly mention more complex hybrid stochastic models which are under investigation [3].

REFERENCES

[1] R. Rudnicki and A. Tomski: *On a stochastic gene expression with pre-mRNA, mRNA and protein contribution*, Journal of Theoretical Biology 387 (2015), 54–67.

[2] J. Jaruszewicz, P. Żuk, and T. Lipniacki: *Type of noise defines global attractors in bistable molecular regulatory systems*, Journal of Theoretical Biology 317 (2013), 140–151.

[3] J. Hu, W. Wu, and S. Sastry: *Modeling subtilin production in Bacillus subtilis using stochastic hybrid systems*, Lecture Notes in Computer Science: 7-th International Workshop, Hybrid Systems: Computation and Control (2004), 417–431.

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SIMULATION OF PATIENT FLOW AND PATHOGEN TRANSMISSION IN A SYSTEM OF HEALTHCARE FACILITIES

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ABSTRACT

Recently multidrug-resistant Enterobacteriaceae (MDR-E) is an important public healthcare problem in many European countries. While traditional infection control strategies primarily target the containment of intra-hospital transmission, there is a growing evidence that the inter-hospital patient traffic is an important factor for the spread of MDR-E within healthcare systems.

We propose network-based models, which reflect a patient traffic between the healthcare facilities and thus provide the framework to systematic study of transmission dynamics of MDR-E together with the effectiveness of infection control strategies to contain their spread. Although model dynamics is based on the network structure, the spread of bacteria within the healthcare system is modelled separately by different submodels, e.g. systems of ordinary differential equations.

In our study we would like to compare two different approaches. Within the first approach we treat the patients in the proposed mathematical model as a bulk and we use a deterministic model to mimic the patient flow within the network and predict the disease spread rate. Second possibility is to focus on the individual patients and to introduce some probabilistic factors into the model, like for example probability of patient transfer to another facility or probability of transfer already infected patients. Thus the results are no longer deterministic, but also the simulation may be much more costly. However, it can capture more details. We would like to discuss pros and cons of both approaches, and also explore their various properties. Examples of results of simulations with both model types will be presented and discussed.

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NONPARAMETRIC ESTIMATION OF QUANTILE VERSIONS OF THE LORENZ CURVE

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ABSTRACT

Estimators of quantile versions of the Lorenz curve are proposed. The pointwise consistency and asymptotic normality of the estimators is proved. The efficiency of the estimators is also studied in simulations.

REFERENCES

[1] A.M. Siedlaczek: *Nonparametric estimation of quantile versions of the Lorenz curve*, Mathematica Applicanda 46(1) (2018), 149–157, DOI 10.14708/ma.v46i1.6372.

Krajowa Konferencja Zastosowań Matematyki w Biologii i Medycynie

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MATHEMATICAL MODELING REVEALING CROSSTALK MECHANISMS BETWEEN HEAT SHOCK AND NF-κB SIGNALING

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ABSTRACT

Though it is known that elevated temperature, inducing the heat shock (HS) response, modulates cell proliferation, apoptosis and the immune and inflammatory responses, specific mechanisms of such regulation are not fully understood. In [1] we used integrated computational and experimental approaches to analyze several hypothetical crosstalk mechanisms between the HS-response and the NF-κB system, which is involved in regulation of crucial intracellular processes, determining cell fate. Following initial experimental results, showing inhibition of NF-κB p65 response to TNFα treatment, we postulated several mechanisms that might be responsible for this effect at different stages of NF-κB signalling cascade. They included inhibition of the processes of activation of intermediary proteins, nuclear transport, transcription and translation.

Mathematical modeling of single cells indicated that individual crosstalk mechanisms, mentioned above, lead to the same population-level responses of the NF-κB pathway but exhibit different characteristics as far as individual cell responses are concerned. Two hypothetical mechanisms lead to almost total inhibition of NF-κB system response in majority of cells, while a small number of cells exhibited responses at normal level ("all-or-nothing" response). Other hypotheses lead to simulations in which all cells responded in a similar manner, with NF-κB system response attenuated proportionally to the HS duration.

In order to discriminate between these mechanisms, we used live-cell imaging and compared main characteristics of the NF-κB response of single cells (first peak height, time of reaching the first peak, number of cells responding) with simulation results. We concluded that the most likely crosstalk mechanism involves inhibition of activation of the IKK protein. Detailed knowledge of the kinetics of the processes involved should facilitate advances in hyperthermia-based anticancer treatment strategies.

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REFERENCES

[1] M. Kardyńska, A. Paszek, J. Śmieja, D. Spiller, W. Widłak, M.R.H. White, P. Paszek, and M. Kimmel: *Quantitative analysis reveals crosstalk mechanisms of heat shock-induced attenuation of NF-κB signaling at the single cell level*, PLOS Comp Biol 14(4) (2018), e1006130.

Zakopane-Kościelisko, 3rd–7th September 2018

THE ROLE OF INTERVENTIONS IN THE CANCER EVOLUTION – AN EVOLUTIONARY GAMES APPROACH

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ABSTRACT

We propose to endow evolutionary game models with changes of the phenotypes adjustment during the transient generations performed by the parameters in the payoff matrix which determine the fitness resulting from different interactions between players. These changes represent an alteration of access to external resources which, in turn, may reflect anticancer treatment. In the case of spatial games, these functions are represented by an additional lattice where another and parallel game based on cellular automata is performed. The main assumption of the spatial games is that each cell on the lattice is represented by a player following only one strategy. We propose to consider cells on the spatial lattice as heterogeneous (instead of homogeneous), so that each particular player may contain mixed phenotypes. Spatial games of the type, proposed by us, are called multidimensional spatial evolutionary games (MSEG). It may happen that within the population, all of the players have diverse phenotypes (which probably better describes biological phenomena). The additional lattice representing the evolution of resources increases only the dimension of the lattice in the MSEG. The paper has been accepted for publication in Mathematical Bioscience and Engineering in 2018.

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THEORY OF TAILOR AUTOMATA

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ABSTRACT

The new theory of tailor automata makes it possible to define deterministic and nondeterministic finite tailor automata which correspond to informally characterized biomolecular automata of DNA in the spirit of the works [1, 2], but make use of only one restriction enzyme [3]. The theory presents elements of biomolecular automata of DNA on four levels: words, dual words, bi-words, and indiscernible bi-words. The first level enables to represent single-stranded DNA, the second one allows a 'planar' representation of selected double-stranded DNA, the third makes it possible to 'spatially' represent selected double-stranded DNA, whereas the fourth level – indiscernibility, from the point of view of the functioning of a biomolecular automaton of DNA, of certain bi-words determined on the third level. In this sense, the elements of words make representations of nucleotides, while bi-words are sets to which all indiscernible dual words belong and which can be represented by each of the dual words belonging to these sets (are abstract classes).

In this way elements of biomolecular DNA such as: input molecule, transition molecules, detection molecules and output molecule, are represented in the theory of tailor automata by bi-words which we call, respectively: input component, transition components, detection components and finish component. In order to theoretically represent the working of the restriction enzyme and ligase enzyme, the notion of cutting function (bi-words) and that of sticking function (two bi-words) are introduced. They are defined on bi-words, but "act" on dual words being their representations. Hence, on the levels of words and dual words, the following relations are introduced, among others: inclusion of words, concatenation of words, prefix and suffix of a word, inclusion of dual words, concatenation of selected dual words, stickability of dual words.

The constructs introduced in the theory of tailor automata allow defining a deterministic and nondeterministic finite tailor automaton (including the transition function for the automaton), extending the transition function, acceptability of words built from symbols of the alphabet of the tailor automaton, as well as language acceptability by the tailor automaton.

REFERENCES

[1] P.W.K. Rothemund: *DNA and restriction enzyme implementation of Turing machines*, in: R.J. Lipton, E.B. Baum (Eds.), DNA Based Computetrs, Vol.27 of DIMACS Series in Discrete Mathematics and Theoretical Computer Science, American Mathematical Society, (1995), 75–120.

[2] Y. Benenson, T. Paz-Elizur, R. Adar, E. Keinan, Z Livneh, and E. Shapiro: *Programmable and autonomous computing machine made of biomolecules*, Nature 414 (6862) (2001), 430–434.

[3] J. Waldmajer, Z. Bonikowski, and S. Sakowski: *Theory of Tailor automata*, in review (2018).

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COMPOSITION OF WAVELET AND FOURIER TRANSFORMS

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ABSTRACT

The paper presents are the basic properties of the serial composition of two transformations: wavelet and Fourier. Two types of transformations were obtained because wavelet and Fourier transformations do not commute. The consequences of a phenomenon known as a "wavelet crime" are presented. Using of wavelets with compact supports in the frequency domain (e.g. Meyer wavelets) leads to the representation of signals as sparse matrices. Speech signals were used to tests the presented transforms.

REFERENCES

[1] M. Ziółko, M. Witkowski, and J. Gałka: *Composition of wavelet and Fourier transforms*, Mathematica Applicanda 46(1) (2018), 159–168, DOI 10.14708/ma.v46i1.6376.

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