



Book of Abstracts of the
Thirty-first National Conference on

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Kościełisko (Zakopane), 15–19 September 2026

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Part I

Invited speakers



Kościelisko (Zakopane), 15th–19th September 2026

WHEN TIME MATTERS: DELAY DIFFERENTIAL EQUATIONS IN MATHEMATICAL BIOLOGY

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ABSTRACT

Biological processes take time, and this time lag can have a profound impact on the dynamics of the system. When the duration of a biological process is comparable to the time scale of the population or biochemical dynamics, neglecting it may lead to qualitatively incorrect conclusions. A natural way to incorporate such effects into mathematical models is through time delays.

In this presentation, I will discuss delay differential equations and their applications in mathematical biology. I will briefly introduce the mathematical foundations of the theory and explain how the presence of a delay changes the phase space from the finite-dimensional space $\mathbb{R}^n$ to an infinite-dimensional Banach space. This fundamental difference means that some familiar intuition from ordinary differential equations no longer applies.

The main focus of the presentation will be the impact of time delays on the stability and dynamics of stationary solutions. A delay can destabilize an otherwise stable equilibrium and lead to the emergence of persistent oscillations. On the other hand, delays may also have a stabilizing effect, and multiple stability switches can occur as the delay varies. I will present mathematical techniques for determining the stability of equilibria, locating critical delay values, and identifying transitions between stable and unstable regimes.

I will also discuss the possibility of periodic solutions and the role of delay-induced oscillations in biological models. The theoretical ideas will be illustrated with examples motivated by biological processes, showing how incorporating delays can lead to qualitatively new dynamical behavior.

REFERENCES

- [1] A. Bartłomiejczyk and M. Bodnar: *Hopf bifurcation in time-delayed gene expression model with dimers*, Mathematical Methods in the Applied Sciences **46** (2023), 12087–12111.
- [2] N. Bielczyk, M. Bodnar, and U. Foryś: *Delay can stabilize: Love affairs dynamics*, Applied Mathematics and Computation **219** (2012), 3923–3937.
- [3] M. Bodnar: *General model of a cascade of reactions with time delays: global stability analysis*, Journal of Differential Equations **259** (2015), 777–795.
- [4] ———: *On the differences and similarities of the first order delay and ordinary differential equations*, Journal of Mathematical Analysis and Applications **300** (2004), 172–188.
- [5] M. Bodnar, U. Foryś, and J. Poleszczuk: *Analysis of biochemical reactions models with delays*, Journal of Mathematical Analysis and Applications **376** (2011), 74–83.
- [6] M. Bodnar and M. J. Piotrowska: *O równaniach różniczkowych z opóźnieniem — teoria i zastosowania*, Matematyka Stosowana **11** (2010).

- [7] T. Erneux: *Applied Delay Differential Equations*, Springer, 2009.
- [8] U. Foryś, M. Bodnar, and J. Poleszczuk: *Negativity of delayed induced oscillations in a simple linear DDE*, Applied Mathematics Letters **24** (2011), 982–986.
- [9] J. K. Hale and S. M. Verduyn Lunel: *Introduction to Functional Differential Equations*, Springer, 1993.
- [10] H. Smith: *An Introduction to Delay Differential Equations with Applications to the Life Sciences*, Springer New York, NY, 2011.
- [11] M. Szafrńska-Łęczycka, M. Bodnar, M. J. Piotrowska, M. Krukowski, J. Belmonte-Beitia, and U. Foryś: *Influence of time delay on the dynamics of a mathematical model of CAR-T cell therapy with logistic tumor growth*, Discrete and Continuous Dynamical Systems - B **30** (2025), 4498–4515.



Kościelisko (Zakopane), 15th–19th September 2026

NUMERICAL METHODS FOR DELAY DIFFERENTIAL EQUATIONS WITH APPLICATIONS TO EPIDEMIC MODELS

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ABSTRACT

In the present talk, we introduce a numerical method based on operator splitting techniques and Magnus integrators for solving delay differential equations. To perform a rigorous error analysis, we employ tools from functional analysis, such as operator semigroups and evolution families.

Our motivating example is the classical SIR epidemic model with a latent period $\delta > 0$, supplemented by vaccination and random movement of individuals over a domain $\Omega \subset \mathbb{R}^2$. Writing the proportions of the susceptible, infected, and recovered populations at time $t > 0$ and position $\mathbf{x} = (x, y) \in \Omega$ as $S(t, \mathbf{x})$, $I(t, \mathbf{x})$, and $R(t, \mathbf{x})$, respectively, the model has the form

$$\begin{cases} \partial_t S(t, \mathbf{x}) = \partial_x(\kappa(\mathbf{x})\partial_x S(t, \mathbf{x})) + \partial_y(\kappa(\mathbf{x})\partial_y S(t, \mathbf{x})) - \beta S(t, \mathbf{x})I(t - \delta, \mathbf{x}) - \nu S(t, \mathbf{x}), \\ \partial_t I(t, \mathbf{x}) = \partial_x(\kappa(\mathbf{x})\partial_x I(t, \mathbf{x})) + \partial_y(\kappa(\mathbf{x})\partial_y I(t, \mathbf{x})) + \beta S(t, \mathbf{x})I(t - \delta, \mathbf{x}) - \gamma I(t, \mathbf{x}), \\ \partial_t R(t, \mathbf{x}) = \partial_x(\kappa(\mathbf{x})\partial_x R(t, \mathbf{x})) + \partial_y(\kappa(\mathbf{x})\partial_y R(t, \mathbf{x})) + \nu S(t, \mathbf{x}) + \gamma I(t, \mathbf{x}), \end{cases} \quad (1)$$

with $\beta, \gamma, \nu > 0$ representing the infection, recovery, and vaccination rates, respectively, and $\kappa(\mathbf{x}) > 0$ denoting the diffusion coefficient. We impose homogeneous Neumann boundary condition, that is, the normal derivatives of S , I , and R vanish on the boundary of Ω , meaning that individuals cannot leave the domain.

The system (1) can be written as an abstract quasilinear delay differential equation on the space $X = C(\Omega)^3$ for the function $u(t) = (S(t, \cdot), I(t, \cdot), R(t, \cdot))$ in the form

$$\begin{cases} u'(t) = (A + Q(u(t - \delta)))u(t), & t \in [0, \infty), \\ u(\sigma) = \varphi(\sigma), & \sigma \in [-\delta, 0] \end{cases} \quad (2)$$

with a given initial history function $\varphi: [-\delta, 0] \rightarrow X$, an appropriate unbounded operator $A: D(A) \subset X \rightarrow X$, and a sufficiently smooth function Q taking values in the space of bounded linear operators on X .

In our presentation, we consider a wide class of semilinear or quasilinear delay differential equations of the general form (2) and present a fully discrete time-and-space numerical method in an abstract way. To this end, we apply an operator splitting technique to decompose the problem into simpler subproblems such as

$$\begin{aligned} u_1'(t) &= Au_1(t), \\ u_2'(t) &= B(t)u_2(t) \quad \text{with} \quad B(t) := Q(u_2(t - \delta)). \end{aligned}$$

The solution of the first subproblem is given in terms of an operator semigroup, which can be regarded as the exponential of the (unbounded) operator A in an appropriate sense. Since the second subproblem is nonautonomous, its solution is given by an evolution family, which can also be approximated by a semigroup using Magnus's idea. With a timestep $\tau > 0$, this results in the time discretization

$$u((n+1)\tau) \approx e^{\frac{\tau}{2}B((n+1/2)\tau)} e^{\tau A} e^{\frac{\tau}{2}B((n+1/2)\tau)}, \quad n \in \mathbb{N},$$

where the operator semigroup operators (denoted by the exponentials) need to be further approximated by a dimension reduction—typically a spatial discretization (finite differences or finite element method), but also allowing for a Fourier or Galerkin approach.

The aim of the talk is to show that operator semigroups provide an efficient tool for designing and analysing numerical methods even for nonlinear problems such as abstract semilinear or quasilinear delay equations, with a particularly relevant application to epidemic modeling. To this end, we will briefly introduce the necessary notions from operator theory and numerical analysis. We then outline the main ideas of the error analysis, which show that the method preserves the orders of the time and space discretization errors. This, in turn, means that the total error separates into a second-order time discretization error (arising from the Strang splitting and the Magnus method) and an independent space discretization error. Consequently, matching the space discretization to the timestep in order to obtain an optimal convergence rate becomes straightforward. We illustrate our results on the delay SIR epidemic model (1) and present numerical simulations as well.

The talk is based on our previous works. In [1], the Magnus method was introduced for ordinary delay differential equations. We showed its second-order convergence in time and its positivity preserving property. The work [2] considered the same time discretization method for partial delay differential equations, that is, for infinite dimensional spaces. We showed the existence of an exact solution, the second-order convergence of the method, and the preservation of invariant sets. As an application, we considered the model (1) and showed that the method preserves the positivity of the populations S, I, R and the size $S + I + R$ of the total population. In our most recent study [3], we generalize our results to allow for (almost) arbitrary space discretizations, which leads to a method that also preserves the order of the space discretization error. All of our papers include numerical experiments illustrating our theoretical results.

REFERENCES

- [1] P. Csomós: *Magnus-type integrator for semilinear delay equations with an application to epidemic models*, Journal of Computational and Applied Mathematics **363** (2020), 92–105.
- [2] P. Csomós and D. Kunszenti-Kovács: *A second-order Magnus-type integrator for evolution equations with delay*, IMA Journal of Numerical Analysis **43** (2023), 2965–2997.
- [3] ———: *A total discretization scheme for evolution equations with delay*, preprint.



Kościelisko (Zakopane), 15th–19th September 2026

MODELING OF FLUID AND SOLUTE TRANSPORT IN HETEROGENEOUS POROUS MEDIUM: THE ROLE OF EXTRACELLULAR MATRIX PROPERTIES IN PERITONEAL THERAPIES

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ABSTRACT

In peritoneal therapies, application of high hydrostatic and/or osmotic pressure gradients, together with concentration differences, drive the transport of fluid and solutes between the peritoneal cavity and blood through the adjacent tissue. The interstitial matrix of the peritoneal tissue can be regarded as a porous medium through which fluid and solutes are transported, enabling the delivery of drugs and the removal of toxins and excess water from the body. Therapy-induced fluid transport alters local tissue hydration and interstitial pressure, which in turn modify the local transport properties of the extracellular matrix. These properties therefore vary both spatially and temporally and depend on the local hydration state affecting fluid and solute transport and, consequently, the effectiveness of the therapy.

A mathematical model with spatially distributed transport parameters can be formulated based on experimental and clinical observations. The model combines fluid-volume and solute-mass balances across the peritoneal tissue with the local transport properties described as functions of tissue hydration. This formulation leads to a system of highly nonlinear partial differential equations describing fluid and solute transport within the interstitium. In addition, the temporal evolution of volume and solute concentrations at the boundary are described by a system of ordinary differential equations. The ODEs define the boundary conditions for the tissue transport problem, while simultaneously depending on the fluid and solute fluxes through the peritoneal tissue.

The mathematical framework provides a tool for investigating how spatial and temporal heterogeneity induced by changes in tissue hydration influences transport dynamics and treatment efficiency. The role of hydration-dependent extracellular matrix properties and their spatiotemporal heterogeneity will be illustrated by numerical simulations based on two applications: peritoneal dialysis and intraperitoneal chemotherapy.



Part II

Contributed talks



Kościelisko (Zakopane), 15th–19th September 2026

KRONECKER-STRUCTURE COVARIANCE ESTIMATION IN THE PHYLOGENETIC SMALL-SAMPLE-HIGH-DIMENSION CASE

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ABSTRACT

Phylogenetic comparative methods (PCMs) are concerned with modeling the evolution of traits on a between-species level. This implies that they need to take into account the phylogeny describing the evolutionary history of the species. Mathematically speaking, the considered models are Branching Markov Processes (BMPs), i.e., a Markov process evolves as a “normal one” until it reaches a branching event and there it splits into independent copies with starting points equaling the value of the ancestral process at the split. For Gaussian models of evolution, this phylogeny translates into a non-diagonal between observations covariance matrix. If the considered traits are “typical” morphological ones, like body weight, length, width, e.t.c., then direct analytical or numerical optimization of the likelihood function can be employed. However, if the traits are gene expression or coordinate-based morphological characters, then we can very easily have more unknowns (corresponding to different trait dimensions), than observations (species).

For the small-sample-high-dimension case Statistics offer alternative techniques, e.g., based on regularization. We explore here one such approach in the phylogenetic setting. We assume that the multivariate traits evolve as a Brownian motion and then the between-species-between-traits variance-covariance matrix has a Kronecker structure. In such a setting newly developed regularized structured approximations based on improved entropy loss [3] can provide more stable and comparable covariance representations.

By simulations we explore these techniques in the phylogenetic setting finding that their performance is influenced by sample size, the strength of regularization, and the degree of separation among candidate structures [5]. We illustrate the approach with a lung cancer gene expression dataset [1] and phylogenetically structured [2] canid morphological measurements [4]. For the lung cancer clone-expression data, both global gene-set and the GO-module analyses favour a diagonal diffusion matrix, indicating that gene expression variation, after taking into account between clone dependencies is domination by gene-specific variation.

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REFERENCES

- [1] A. Felberg, M. Bieńkowski, T. Stokowy, K. Myszczyński, Z. Polakiewicz, K. Kitowska, R. Sądej, F. Mohlin, A. Kuźniewska, D. Kowalska, G. Stasiłóć, I. Jongerius, R. Spaapen, M. Mesa-Guzman, L. M. Montuenga, A. M. Blom, R. Pio, and M. Okrój: *Elevated expression of complement factor I in lung cancer cells associates with shorter survival—potentially via non-canonical mechanism*, Translational Research **269** (2024), 1–13.
- [2] J. Fuentes-González and J. Muñon-Duran: *Comportamiento social y preferencias alimentarias en la evolución de los cánidos actuales*, Revista Mexicana de Biodiversidad **88** (2017), 192–206.
- [3] M. Mokrzycka, J. Pielaszkiewicz, J. Alenlöv, and A. Tillander: *Covariance structures approximation in doubly multivariate models under high-dimensionality via improved Kullback-Leibler divergence*, under review.
- [4] J. Muñon-Duran and J. Fuentes-González: *Evolución de la socialidad, estrategias alimentarias y anatomía craneo-dental en la subfamilia Caninae*, Acta Biológica Colombiana **17** (2012), 173–200.
- [5] W. Liao: *Kronecker-structure covariance estimation in the small-sample-high-dimension case with phylogenetic applications*, 2026, Master thesis in Statistics, Division of Statistics and Machine Learning, Department of Computer Science, Linköping University.
- [6] M. Ziółko and Organizing Committee: *Article title*, Journal name **13** (2000), 91–95.



Kościelisko (Zakopane), 15th–19th September 2026

MATHEMATICAL MODELING OF LOW-GRADE GLIOMA GROWTH: LINEAR VS NONLINEAR DIFFUSION

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ABSTRACT

The talk is devoted to a comparative analysis of mathematical models describing the growth dynamics of low-grade gliomas (LGG). We compare classical models based on linear diffusion with more advanced approaches incorporating nonlinear diffusion, which enables a more accurate representation of brain tissue heterogeneity and complex mechanisms of tumor cell migration. Particular attention is paid to the analysis of travelling wave solutions, which make it possible to describe the propagation of the tumor front and determine its spreading speed. The aim of the study is to assess the influence of the diffusion type on tumor growth dynamics and to compare the qualitative properties of the considered models.

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

REFERENCES

- [1] A. Bartłomiejczyk, M. Bodnar, M.U. Bogdańska, and M.J. Piotrowska: *Travelling waves for low-grade glioma growth and response to chemotherapy model*, Int. J. Appl. Math. Comput. Sci. **33**(4) (2023), 569–581.
- [2] A. Bartłomiejczyk, M. Bodnar, M.J. Piotrowska, and J. Belmonte Beitia: *Existence of wave solutions of a glioma model in a porous medium*, in preparation.



Kościelisko (Zakopane), 15th–19th September 2026

ON A NEURON MODEL WITH DYNAMICAL THRESHOLD

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ABSTRACT

We study the dynamics of a class of two-dimensional hybrid non-autonomous neuron models known as the *Meng–Huguet–Rinzel neuron model* [1, 2]. The model combines continuous subthreshold evolution with a spike-triggered reset mechanism and features a dynamical firing threshold. Its continuous dynamics consist of a linear voltage equation coupled to a threshold variable whose evolution depends nonlinearly on the membrane potential. We consider periodically driven systems, with external input given by either pulse forcing or a rectified sinusoidal current.

Our main goal is to characterize periodic responses and to understand how the reset mechanism changes the long-term dynamics. We establish existence and uniqueness results for periodic solutions and show that, when resets are absent, the periodically forced system admits a unique globally attracting periodic orbit. In the hybrid setting, we prove that there can be at most one reset-free periodic orbit that remains entirely in the subthreshold regime. At the same time, numerical simulations reveal a richer dynamical picture, including coexistence between such a reset-free periodic response and periodically spiking attractors. These results highlight the role of the dynamical threshold and reset mechanism in generating transitions between subthreshold oscillations and repetitive firing under time-dependent stimulation. This is joint work with Juan Belmonte-Beitia and Justyna Signerska-Rynkowska.

REFERENCES

- [1] X. Meng, G. Huguet, and J. Rinzel: *Type III excitability, slope sensitivity and coincidence detection*, Discrete Contin. Dyn. Syst. **32** (2012), 2729–2757.
- [2] A. Granados and G. Huguet: *Gluing and grazing bifurcations in periodically forced 2-dimensional integrate-and-fire models*, Commun. Nonlinear Sci. Numer. **70** (2019), 48–73.



Kościelisko (Zakopane), 15th–19th September 2026

A NON-STANDARD DISCRETIZED SIS MODEL OF CO-INFECTION IN A HETEROGENEOUS POPULATION

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ABSTRACT

A discrete-time model of co-infection dynamics in a heterogeneous population is presented. In such a population we distinguish two subpopulations with different levels of individual susceptibility to any of the two diseases. As a discretization method we use a non-standard discretization scheme that preserves positivity of system's variables. The novelty of our works lies in assuming that each parameter describing a specific biological process has a different value for each subpopulation. This assumption makes the investigated population completely heterogeneous. We investigate a local stability analysis of a disease-free stationary state. Because of our system's complexity, we only give insight into local stability of equilibria that correspond to the presence of a single disease. For such states we provide conditions for their local stability, considering boundary cases. We conduct numerical simulations that suggest such postulated stability. Moreover, the simulations show that there should exist a locally stable state, which reflects the simultaneous presence of both diseases. The simulations also illustrate the concept of an infection rate, which helps compare the impact of both diseases on the dynamics of co-infection spread.

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REFERENCES

- [1] M. Choiński: *A non-standard discretized SIS model of co-infection in a heterogeneous population*, Journal of Difference Equations and Applications **32(7)** (2026), 1153–1179.



Kościelisko (Zakopane), 15th–19th September 2026

HYBRID AGENT-BASED SID MODELLING OF AFRICAN SWINE FEVER IN WILD BOAR POPULATIONS

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ABSTRACT

African Swine Fever (ASF) remains one of the most important infectious diseases affecting wild boar populations in Europe. Existing epidemiological models often simplify social structures and carcass-mediated transmission. To address these limitations, we developed a unique hybrid agent-based Susceptible-Infected-Dead (SID) model that integrates individual-based spatial mobility, fine-grained demography, and stochastically-driven environmental transmission pathways.

Heavily informed by nearly a decade of the author's empirical field observations, this computational framework realistically reflects natural wild boar ethology, including complex demographic sounder structures (divided into family groups of sows leading young, yearlings, and solitary mature boars), intergroup spatial interactions, and a potent behavioral attraction to infected carcasses as major environmental reservoirs.

Stochastic simulations executed over a 300 km² (15 × 20 km) domain reveal three distinct density-dependent epidemiological regimes: stochastic fade-out in low-density cohorts ($N \leq 25$; density ≤ 0.1 ind./km²), multi-phase outbreaks in medium-density populations ($N \approx 50$ –150; density 0.13–0.50 ind./km²), and self-sustaining epidemics in high-density environments ($N \geq 200$; density ≥ 0.61 ind./km²). Crucially, our analysis of transmission kinetics demonstrates a non-linear escalation in the significance of carcass-mediated (indirect) transmission. In high-density populations, this environmental pathway becomes dominant, accounting for 70–75% of all transmission events and generating a catastrophic population mortality plateau of 90–96%. This underscores that the rapid removal of viral reservoirs from the environment must be the absolute priority for effective ASF containment, whereas traditional population reduction via hunting remains secondary.

The current SID-ABM framework has proven to be an exceptionally viable baseline for structural extensions informed by recent literature. Consequently, initial simulation prototypes of an extended SEIRD (Susceptible-Exposed-Infectious-Recovered-Dead) model incorporating an explicit latent phase and stochastically-derived sickness behavior are currently under development.

These upcoming models will undergo collaborative calibration and empirical validation with specialized scientific units focusing on viral virology, GPS telemetric tracking, wild boar ethology, and hunting management. Ultimately, integrating this hybrid framework with GIS databases will enable

real-time spatial predictions of carcass deposition and reinforce transboundary bio-border engineering within the EU regulatory framework.



Kościelisko (Zakopane), 15th–19th September 2026

WANG'S MODEL OF DECISION-MAKING WITH ALPHA WAVE ACTIVITY

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ABSTRACT

Wang's decision-making model reproduces neuronal dynamics in a two-choice task driven by noisy inputs. It bridges single-neuron computational models and population-level dynamics while remaining biophysically grounded. The visual choice task described by the model is one in which alpha oscillations - a multifunctional pattern of brain activity - appear to play a significant role. I will briefly present the model, its biological basis, and its main features, and then review mechanisms of alpha oscillations and their proposed roles in visual perception. Next, I will outline strategies for incorporating alpha activity into this framework. I will focus on presenting preliminary results from one such implementation, discuss its advantages and limitations, and indicate directions for ongoing work.



Kościelisko (Zakopane), 15th–19th September 2026

FORECASTING MALARIA INCIDENCE IN RWANDA USING NEURAL CONTROLLED DIFFERENTIAL EQUATIONS INTEGRATED WITH OPTIMAL CONTROL TOOLS

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ABSTRACT

Malaria remains a major public-health concern in Rwanda. After an 85% reduction between 2019 and 2023, the country recorded a resurgence to about 518,000 infections in the first nine months of 2024, while Africa continues to bear roughly 95% of an estimated 282 million cases reported world-wide. Designing time-dependent intervention schedules that balance epidemiological impact and operational cost is a nonlinear, vector-mediated optimal-control problem for which classical value-function and Pontryagin-type approaches are difficult to apply, because the value function determined by the running cost cannot be expected to be smooth for nonlinear vector–host systems.

We formulate malaria control in Rwanda as a continuous-time optimal control problem governed by a SEIRS–SEI compartmental model with state

$$Z(t) = (S, E, I, R, I_m)^\top \in \mathbb{R}^5$$

– the susceptible, exposed, infectious and recovered human compartments together with the infectious-mosquito proportion – and two time-dependent controls

$$u(t) = (u_p(t), u_k(t)) \in U = [0, 1]^2.$$

u_p aggregates vector control (long-lasting insecticidal nets, indoor residual spraying, larval source management), modifying the biting and mosquito-mortality rates, while u_k represents treatment effort acting on the human recovery rate. Given the controlled dynamics

$$\dot{Z}(t) = F(Z(t), u(t)), \quad Z(0) = Z_0,$$

the primal optimal-control problem is

$$\min_{u(\cdot) \in U} J(u) = \int_0^T \left[A_1 I(t) + A_2 I_m(t) + \frac{1}{2} A_3 \|u(t)\|^2 \right] dt,$$

which penalises human infectious prevalence I , infectious-mosquito proportion I_m and intervention effort, with positive weights $A_1, A_2, A_3 > 0$.

To solve this problem we adopt a dual dynamic programming (DDP) framework. Rather than work with a value function – which need not be smooth for the nonlinear five-dimensional system – we work with an auxiliary pair (q, Q) defined on a dual parameter space

$$P = B(0, \rho) \subset \mathbb{R}^5$$

satisfying the dual dynamic equality

$$\frac{\partial Q}{\partial t}(t, p) + \inf_{u \in [0, 1]^2} [p^\top F(p \cdot Q, u) + L(p \cdot Q, u)] = q(t), \quad Q(0, p) = c \neq 0,$$

the Hamilton–Jacobi analogue of the framework on P . The dual arc $p(\cdot)$ is determined purely on P by a dual trajectory equation with terminal condition $p(T) = 0$, and the recovered state

$$Z(q, Q)(t; u) := p(t) \cdot Q(t, p(t))$$

is reconstructed from p ; the requirement

$$Z(q, Q) = Z(\cdot; u)$$

is a consistency condition on (q, Q) , not a defining equation for p .

On this foundation we establish two theoretical results. An Optimality Verification Theorem certifies that any candidate control satisfying the verification equality

$$\partial_t Q + p^\top F(Z(q, Q), u) + L(Z(q, Q), u) = q$$

is optimal for the primal problem, with a proof that uses neither Pontryagin’s maximum principle nor an adjoint boundary-value problem. The associated residual

$$r(t) := q(t) - \partial_t Q - p^\top F(Z(q, Q), u) - L(Z(q, Q), u)$$

supplies a computable ε -optimality certificate, and a complementary theorem provides sufficient conditions, expressed through the effective reproduction number R_{eff} , under which prevalence remains below a chosen threshold during an initial window.

These results are assembled into a three-stage procedure. Stage 0 constructs the auxiliary pair (q, Q) by solving the dual dynamic equality as a parametrised scalar ODE in p : with $q \equiv 0$ and the dual variable p ranging continuously over P , each fixed p yields an initial-value problem whose closed-form pointwise minimiser

$$u^\star(t, p) = \Pi_{[0, 1]^2}(-A_3^{-1}b)$$

with

$$b = (\beta Q_2 p_1 p_5 (p_1 - p_2), Q p_3 (p_4 - p_3))$$

delivers $Q(t, p)$ on $[0, T] \times P$ by fourth-order Runge–Kutta integration, without any prescribed (e.g. affine) shape for Q .

Stage 1 generates a candidate intervention schedule by projected back-tracking gradient descent on $U = [0, 1]^2$ from a constant initial guess

$$u^{(0)} \equiv 0.30,$$

simulating the primal state from

$$\dot{Z} = F(Z, u)$$

and updating

$$u^{(n+1)} = \Pi_U(u^{(n)} - \alpha^{(n)} \nabla_u J^{(n)}).$$

Stage 2 propagates the dual arc $p(\cdot)$ backward on P from $p(T) = 0$ via the dual trajectory equation, recovers the state through

$$Z(q, Q)(t; u) = p(t) \cdot Q(t, p(t)),$$

verifies the matching identity

$$Z(q, Q) = Z(\cdot; u)$$

and evaluates the residual $r(t)$, realised as the projected-gradient variational-inequality residual

$$r(t) = u^\star(t) - \Pi_{[0,1]^2} (u^\star(t) - \nabla_u J[u^\star](t)),$$

whose supremum norm

$$\varepsilon = \sup_{t \in [0, T]} |r(t)|$$

is the ε -optimality certificate of the verification theorem.

This procedure is applied to a Rwanda-specific parameter set drawn from the malaria-modelling literature: a planning horizon of $T = 180$ days (one transmission season), objective weights

$$(A_1, A_2, A_3) = (100, 10, 1)$$

that prioritise reduction of human infectious prevalence while still penalising intervention effort, and SEIRS–SEI parameters covering human demography

$$\mu = 4.09 \times 10^{-5},$$

incubation and recovery

$$\sigma = 0.065, \quad \gamma = 0.05,$$

loss of immunity

$$\omega = 0.00274,$$

and the vector chain

$$a = 0.30, \quad \beta = 0.12, \quad c = 0.45, \quad \mu_m = 0.0714,$$

all in day^{-1} .

The controlled dynamics are integrated by a fourth-order Runge–Kutta scheme with step 0.25 day, the control $u = (u_p, u_k)$ is represented on a mesh of 61 nodes taking continuous values in $[0, 1]^2$, and the initial state

$$Z_0 = (0.80, 0.04, 0.045, 0.115, 0.09)^\top$$

uses an infectious prevalence consistent with the malaria resurgence reported for Rwanda in 2024. The presentation will discuss the SEIRS–SEI formulation, the dual dynamic equality and verification theorem, the construction of (q, Q) on the continuous dual space P , and the three-stage ε -optimality algorithm applied to this Rwanda parameter set.

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Kościelisko (Zakopane), 15th–19th September 2026

NASH EQUILIBRIUM OF DRUGS CONTROL IN THE MATHEMATICAL MODEL OF ALZHEIMER AND MATHEMATICAL ANALYSIS OF PET

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ABSTRACT

Alzheimer is mainly an aging disease characterized by dementia, where symptoms include cognitive decline, memory loss, and impairment of daily functioning. The main hallmarks of the disease are aggregation of plaques of amyloid- β ($A\beta$) and neurofibrillary tangles of tau proteins (τ). They can be detected in PET scans of the brain. The disease can remain asymptomatic for decades, while the densities of $A\beta$ and τ continue to grow. Drugs are urgently needed for the treatment of AD and unfortunately almost all clinical trials of AD drug candidates have failed or been discontinued to date. Mathematical, computational and statistical tools were employed in the construction of clinical trial simulators to assist in the improvement of trial design and enhance the chances of success of potential new therapies. In [1] was developed a mathematical model that can produce simulated patterns of ($A\beta$ and τ) seen in PET scans of AD patients. The model is based on the assumption that early inflammations R and $\bar{R}$ drive the growth of $A\beta$ and τ , respectively. The essential point is that in these equations are not included explicitly exterior drugs. One of the objectives of this article is to include to some of these equations injection of drugs and to optimize the choice of drugs according to some rules. The rules means a kind of functional that should measure the behavior of interesting result with respect to these injections. By an interesting result, we mean loss of plaques amyloid- β and τ as well growth of the number of microglia cells and astrocytes glial cells. Next, we formulate a differential game problem. One of the aim of the paper is to formulate a sufficient conditions in a form of verification theorem for the existence of a feedback Nash equilibrium. As a result, based on the verification theorem, we state an algorithm that allows efficient calculation to find optimal treatment of drugs in the given time. Next for given treatment (calculated from the first problem), a maximum surface of reactive oxygen species (ROS) with which, during the treatment, plaques amyloid- β and τ is still losing to a healthy stage. The last study concerns the problem of the amyloid hypothesis vs the tau hypothesis. This is a continuation of the talk from the former (XXX) conference.

REFERENCES

- [1] Lee C, Friedman A (2024) Generating PET scan patterns in Alzheimer's by a mathematical model. PLoS ONE 19(4): e0299637. <https://doi.org/10.1371/journal.pone.0299637>



Kościelisko (Zakopane), 15th–19th September 2026

MODELING TWO-STRAIN DENGUE TRANSMISSION

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ABSTRACT

In this talk, we examine two-strain dengue models that capture the interactions between human and mosquito populations. The proposed models incorporate the possibility of reinfection with a different strain and vertical transmission of the virus from adult mosquitoes to their offspring. We discuss the local stability of the disease-free equilibrium, the existence and local stability of endemic equilibria in the single-strain case, as well as the existence of two-strain endemic equilibria. Remarkably, some of these results are obtained despite the non-constant size of the mosquito population. To support our findings, we present numerical simulations using realistic dengue parameters that reflect biological phenomena.



Kościelisko (Zakopane), 15th–19th September 2026

DNA COMPUTING METHOD FOR CANCER DIAGNOSIS

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ABSTRACT

Over the past three decades, beginning with the pioneering laboratory experiments of Leonard Adleman [6], DNA computing has evolved into an established interdisciplinary research field that combines theoretical computer science with molecular biology and has inspired novel models of computation. Recent experimental implementations of DNA-based computational systems have shown considerable potential for molecular diagnostics [2, 3].

The presentation will (i) review recent advances in DNA computing and (ii) present our recent research findings, with particular emphasis on molecular diagnostics. Special attention will be devoted to the interpretation of cancer in terms of information encoding in DNA, emphasising how mutations disrupt the encoding and processing of genetic information. This perspective will be developed within the formal apparatus of automata theory and formal language theory, with particular emphasis on theoretical models of DNA computation [4].

REFERENCES

- [1] L. M. Adleman: *Molecular Computation of Solutions to Combinatorial Problems*, Science **266** (1994), 1021–1024.
- [2] C. Zhang, Y. Zhao, X. Xu, R. Xu, H. Li, X. Teng, Y. Du, Y. Miao, H. Lin, and D. Han: *Cancer diagnosis with dna molecular computation*, Nature Nanotechnology **15** (2020), 709–715.
- [3] Z. F. Tang, J. Zeng, Y. Chen, D. H. Yang, J. H. Fu, Z. P. Chen, and R. Q. Yu: *A Practical DNA Molecular Computing Platform for Identifying Expression Patterns of Multiple miRNAs Related to Diseases*, Analytical Chemistry (2026).
- [4] S. Sakowski, M. Holzer, C. Rauch, T. Poplawski, M. Jain, and D. Page: *Biomolecular computers application for cancer molecular diagnosis*, DNA31: 31st International Conference on DNA Computing and Molecular Programming, Program & Abstracts Booklet, 2025, p. 67.



Kościelisko (Zakopane), 15th–19th September 2026

COMPARISON OF DIFFERENT TYPES OF DELAYS IN A MATHEMATICAL MODEL OF EMT–MET DYNAMICS

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ABSTRACT

We investigate the role of time delays in a mathematical model describing the dynamics of TGF- β in epithelial–mesenchymal transition (EMT) and mesenchymal–epithelial transition (MET) in cancer cells. The model describes the dynamics of free and receptor-bound TGF- β , with the latter representing the biologically active form of the protein. Starting from a kinetic model of TGF- β dynamics, we introduce a time delay to account for the fact that the biological effects associated with TGF- β binding may depend not only on the current state of the system, but also on its past states.

We focus on the comparison of different representations of delayed processes. In particular, we consider the classical model without delay and a model with a discrete delay, in which the influence of the past is represented by a single fixed time lag. Such a formulation leads to a system of delay differential equations in which the past value of free TGF- β directly affects the current production of the bound form. The resulting model is analysed with respect to the existence, uniqueness, non-negativity and boundedness of solutions, as well as the stability of its equilibrium states.

For the model with discrete delay, we show that the set of non-negative initial functions is positively invariant and that solutions exist globally in time. We identify the conditions under which the trivial equilibrium and the positive equilibrium exist and determine their stability properties. In particular, under appropriate parameter conditions, the stability of the equilibrium states is independent of the magnitude of the discrete delay. The analysis is supported by characteristic equations and Lyapunov functionals formulated in the appropriate phase space of continuous history functions.

The influence of the delay representation on the model dynamics is further investigated numerically. Solutions of the delayed and non-delayed models are compared for biologically motivated parameter values and consistent history functions. The simulations demonstrate that the introduction of a discrete delay may generate transient oscillations while preserving the asymptotic stability of the positive equilibrium. At the same time, the effect of the delay is particularly visible in the variable directly affected by the delayed term, highlighting the importance of an appropriate representation of biological memory.

As a further step, we consider the extension of the model towards distributed delays, in which the past states of the system influence the present dynamics over a whole interval of time rather than at a single prescribed time point. This formulation allows different distributions of biological response times to be incorporated through a delay kernel and provides a more flexible description of

intracellular signalling processes. We compare the mathematical properties and dynamical behaviour associated with discrete and distributed delays, with particular emphasis on their influence on stability, transient dynamics and the biological interpretation of the model.

The comparison highlights the limitations of representing a biologically heterogeneous response time by a single discrete delay and motivates the use of distributed-delay models as a potentially more realistic framework for describing delayed TGF- β signalling during EMT/MET. The results provide a mathematical basis for selecting an appropriate delay formulation in models of cancer-cell plasticity and for further investigation of how different types of biological memory affect the long-term dynamics of the system.

REFERENCES

- [1] T. Celià-Terrassa et al.: *Hysteresis control of epithelial-mesenchymal transition dynamics conveys a distinct program with enhanced metastatic ability*, Nat. Commun. **9** (2018).



Kościelisko (Zakopane), 15th–19th September 2026

INTEGRATING EMT DYNAMICS IN MODEL-BASED METASTASIS PREDICTION

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ABSTRACT

Introduction

Cancers are a group of diseases characterized by uncontrolled cell proliferation, leading to the disruption of tissue homeostasis and the destruction of adjacent structures. In the global population, lung cancer - specifically Non-Small Cell Lung Cancer (NSCLC) - remains the leading cause of cancer-related mortality. The vast majority of these deaths result from the presence of metastases, a complex process where cancer cells lose intercellular connections and spread to secondary sites. A key mechanism facilitating this transition is the epithelial-to-mesenchymal transition (EMT), which promotes cellular motility and the generation of circulating tumor cells (CTCs) [1].

While Transforming Growth Factor beta (TGF- β) is recognized as a primary regulator of EMT, its effectiveness as a static prognostic biomarker remains a subject of clinical debate [2]. This study aims to demonstrate that the temporal dynamics of TGF- β , rather than its absolute concentration at a single time point, is the crucial factor in predicting metastasis-free survival (MFS).

Methods

The proposed computational framework integrates intracellular signaling with population-level dynamics through a two-stage simulation pipeline.

The core of the approach is an EMT signaling network model adapted from [3], refitted to human lung A549 cells. We extended this model by introducing extracellular TGF- β production stimulated by the tumor micro-environment. By simulating a heterogeneous population of cells, a cumulative density function (CDF) for the probability of metastasis was derived based on the count of cells achieving a full mesenchymal or mesenchymal-like hybrid phenotype.

Population-level dynamics was modeled as a two-compartmental ODE system, incorporating the effects of chemotherapy and radiotherapy with parameters derived from [4]. A cohort of 1000 virtual patients was generated to match the T and M stage distribution of a real clinical dataset of 657 from the National Institute of Oncology in Gliwice.

Simulation outcomes in terms of Overall Survival (OS) and MFS were validated against clinical survival data using the Kaplan-Meier estimator and log-rank statistical test. Additionally, the EMT-based approach was compared to a simple arbitrary metastasis threshold approach.

Results

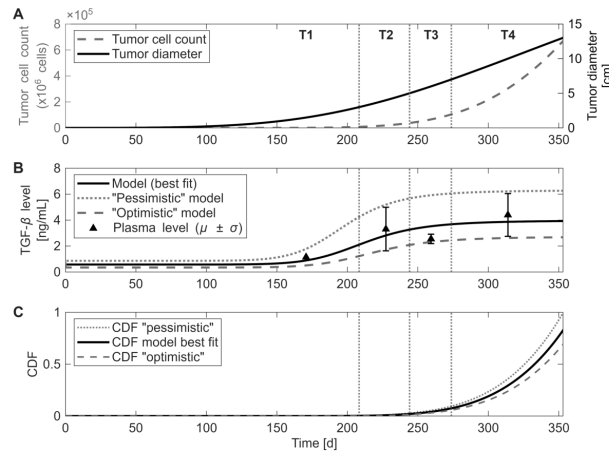


Figure 1. Example simulation results of a model combining tumor growth and intra-cellular processes **A)** the tumor growth dynamics (expressed as number of cells and tumor diameter), **B)** TGF- β dynamics for different simulation protocols (scenarios) and their comparison with experimental data, and **C)** CDF curves corresponding to different simulation protocols.

The integration of EMT dynamics allowed the model to reproduce OS and MFS curves that were consistent with clinical observations. Analysis of different simulation scenarios revealed that the rate of TGF- β increase significantly influences the metastasis probability (Fig. 1).

In "pessimistic" scenarios, characterized by a rapid rise in TGF- β during early stages (T1-T2), the CDF curves reached critical thresholds much earlier than in "optimistic" scenarios. Furthermore, the EMT-based metastatic switch provided more accurate long-term MFS predictions compared to models using an arbitrary tumor-size threshold.

Conclusions

The findings suggest that the clinical ambiguity regarding TGF- β as a biomarker stems from ignoring its dynamic nature. To improve prognostic accuracy, the study recommends replacing single "snapshot" measurements with time-series monitoring of TGF- β levels. From a modeling perspective, this approach demonstrates how linking intracellular processes to population dynamics can provide results of similar quality but with much better biological grounding. This idea serves as a "proof of concept" for personalized treatment, potentially allowing for the use of treatment protocols based on individual biomarker trajectories.

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REFERENCES

- [1] Xiao-Xiang and Zhang Jie Xiao-Yan and Xu: *Epithelial-to-mesenchymal transition, circulating tumor cells and cancer metastasis: Mechanisms and clinical applications*, *Oncotarget* **8** (2017), DOI 10.18632/oncotarget.18277, 81558–81571.
- [2] Zhen and Fan Deng Tao and Xiao: *TGF- β signaling in health, disease and therapeutics*, *Signal Transduction and Targeted Therapy* **9** (2024), DOI 10.1038/s41392-024-01764-w, 61.

- [3] J. and Tian Zhang X. J. and Zhang: *TGF- β -induced epithelial-to-mesenchymal transition proceeds through stepwise activation of multiple feedback loops*, Science Signaling **7** (2014), DOI 10.1126/scisignal.2005304, ra91.
- [4] Chen and Paganetti Geng Harald and Grassberger: *Prediction of Treatment Response for Combined Chemo- and Radiation Therapy for Non-Small Cell Lung Cancer Patients Using a Bio-Mathematical Model*, Scientific Reports **7** (2017), DOI 10.1038/s41598-017-13646-z, 13542.



Kościelisko (Zakopane), 15th–19th September 2026

WHEN MATHEMATICAL MODELLING MEETS CLINICAL REALITY: CHALLENGES REVEALED BY LONGITUDINAL ONCOLOGY DATA

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ABSTRACT

Longitudinal clinical data promise a more complete description of disease evolution and treatment response than static baseline characteristics and have therefore become an attractive target for mathematical modelling. Two broad philosophies naturally emerge: employing general statistical methodology capable of handling repeated measurements, or constructing specialised models that explicitly describe the underlying biological process. Regardless of the chosen approach, the ultimate objective remains the same — to support medical decisions by producing information that is robust, interpretable, and actionable for an individual patient. However, the clinical reality often challenges assumptions of existing modelling frameworks.

This perspective emerged while working on two oncology studies conducted at the Maria Skłodowska-Curie National Research Institute of Oncology Gliwice Branch. Despite addressing very different clinical questions, they converged on the same methodological dilemmas. The first study investigated longitudinal complete blood count (CBC)-derived inflammatory biomarkers in advanced non-small cell lung cancer, asking whether post-baseline laboratory trajectories improve prognostic assessment during immunotherapy. The second examined therapeutic monitoring of mitotane concentrations in adrenocortical carcinoma, an ultra-rare malignancy, evaluating whether achieving therapeutic drug levels translates into improved clinical outcomes. Although one biomarker primarily observed the disease while the other actively influenced treatment, both projects gradually revealed remarkably similar modelling challenges.

The first obstacle, particularly relevant for the mechanistic approach, proved to be the process itself. For inflammatory, and more generally, CBC-related biomarkers, the biological mechanisms underlying longitudinal changes are too numerous and interconnected to model explicitly. Mitotane concentrations initially appear to offer a simpler pharmacokinetic problem, yet in practice their trajectories reflect not only drug metabolism but also physician-guided dose modifications, treatment tolerance, patient adherence, and other incompletely recorded clinical factors, such as the drug accumulation in adipose tissue, itself a dynamic component.

A second challenge concerns the definition of clinically meaningful outcomes. The processes of genuine interest — tumour progression, treatment efficacy or biological response — are rarely observed directly or continuously. They must instead be approximated by surrogate endpoints such as progression-free, recurrence-free, or overall survival. Choosing an endpoint therefore becomes part of the modelling process rather than a purely clinical decision. In the mitotane study, for example, analysing recurrence only during the treatment period proved more informative than considering the entire disease course, as post-recurrence or post-discontinuation management introduced additional sources of heterogeneity unrelated to the original clinical question. Additionally, time-to-event analyses are defined not only by the endpoint but also by the choice of time zero. As longitudinal biomarker measurements frequently occur after this point, immortal time bias becomes a common pitfall.

The third challenge arose from the observations themselves. Neither study generated regularly sampled longitudinal trajectories. Laboratory measurements were obtained according to routine clinical practice rather than a predefined schedule, patients differed in follow-up duration, and clinically important events frequently altered the observation process itself. These characteristics naturally reflect retrospectively collected real-world clinical data, where biomarker measurements follow the realities of everyday oncology care rather than the regular schedules of prospective study protocols. These limitations were particularly evident in the mitotane cohort. Although concentration measurements were available approximately monthly (denser than in most published studies) they still contained substantial gaps and irregular sampling intervals. Moreover, the extreme rarity of adrenocortical carcinoma — approximately 30–80 new cases nationally each year — combined with the evolving landscape of diagnostics, imaging and treatment guidelines, makes cohort construction a delicate balance between maximizing sample size and preserving cohort comparability. Consequently, methodological choices begin long before model fitting, as inclusion criteria and cohort definition become parts of the analytical strategy rather than merely preparatory steps.

Instead of converging on a single analytical solution, these observations encouraged an iterative process in which the problem was repeatedly reformulated and examined from several methodological perspectives. Landmark analyses with trajectory summaries, time-dependent models, clinically motivated endpoint redefinition, and carefully selected analysis populations each captured different aspects of the same process. These seemingly competing approaches may prove complementary, provided that their interpretation remains anchored in the clinical question they were designed to answer. Looking at the same longitudinal data through several well-understood methodological lenses may ultimately provide more meaningful clinical insight than searching for a universally optimal model.

Rather than presenting these case studies as methodological success stories, this contribution uses them as examples of recurring challenges encountered when mathematical modelling meets routine clinical practice. The aim is to encourage dialogue between clinicians, biostatisticians and mathematicians on how future methods can better accommodate the realities of longitudinal clinical data. Ultimately, meaningful clinical translation depends not on choosing between clinical intuition and mathematical rigour, but on allowing each to shape the other.

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