

TENTH INTERNATIONAL CONFERENCE
DYNAMICAL SYSTEMS APPLIED TO BIOLOGY
AND NATURAL SCIENCES

BOOK OF ABSTRACTS

CENTRO CONGRESSI FEDERICO II, NAPOLI, ITALY

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TENTH INTERNATIONAL CONFERENCE DYNAMICAL SYSTEMS APPLIED TO BIOLOGY AND NATURAL SCIENCES (DSABNS)



The Tenth International Conference DSABNS was held at Centro Congressi Federico II, Napoli, Italy, from 3-6 February, 2019. The workshop has both theoretical methods and practical applications, covering research topics in population dynamics, epidemiology of infectious diseases, eco-epidemiology, molecular and antigenic evolution and methodical topics in the natural sciences and mathematics.

Local Organizers:

Lucia Russo, IRC-CNR; Constantinos Siettos, UniNA; Francesco Giannino, UniNA; Gerardo Toraldo, UniNA;

Administration Staff:

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International Organizers:

Maíra Aguiar, UniTN; Carlos Braumann, UE; Luís Mateus, UL; Bob W. Kooi, VU; Nico Stollenwerk, UL; Ezio Venturino, UT.

NB. UniTN: Università degli Studi di Trento, Italy; UE: Universidade de Évora, Portugal; UT: Università degli Studi di Torino, Italy; VU: Vrije Universiteit Amsterdam, The Netherlands; UL: Universidade de Lisboa, Portugal; IRC-CNR: Istituto di Ricerche sulla Combustione, Consiglio Nazionale delle Ricerche, Italy; UniNA: Università degli Studi di Napoli Federico II, Italy.

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TENTH INTERNATIONAL CONFERENCE
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SCIENTIFIC PROGRAM

CENTRO CONGRESSI FEDERICO II, NAPOLI, ITALY

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Sunday (afternoon), February 3rd, 2019	
15:00-18:30	Welcome Reception & Public Lectures
15:00-16:00	Registration
16:00-16:30	Opening and greetings
16:30-17:15	Public Lecture I. Stefano Mazzoleni. BIOLOGICAL AND ECOLOGICAL PROBLEMS SOLVED BY SYSTEM DYNAMICS MODELS OR REQUIRING HYBRID APPROACHES
17:15-18:15	Welcome Reception (Cold Appetizers, Wine and Beverages)
18:15-19:00	Public Lecture II. Piero Salatino. CIRCULAR ECONOMY AND EXPLOITATION OF BIORESOURCES CHALLENGES CHEMICAL REACTION ENGINEERING

Monday (morning), February 4th, 2019			
Aula Magna			
Cartwright. WARM LITTLE PONDS OR WARM LITTLE PORES?			
09:00-09:45	Gerardo Giorda. ENHANCING PREDICTIVITY OF MATHEMATICAL MODELS IN SPATIAL ECOLOGY: ACCURATE LANDSCAPE DESCRIPTION AND UNCERTAINTY QUANTIFICATION		
10:30-11:00	Coffee break 30 min		
	Parallell Room 1	Parallel Room 2	Parallel Room 3
11:00-12:50	Session M1: Mathematical Epidemiology	Session M2: Population and Ecology Dynamics	Session M3: Analytical & Numerical Methods
11:00-11:30	Invited Talk, Pinto. A QUANTITATIVE CHARACTERIZATION OF THE REINFECTION THRESHOLD	Invited Talk, Banerjee. TWO-PATCH PREY-PREDATOR MODEL REVISITED	Invited Talk, Kyrychko. AGING TRANSITION AND THE ROLE OF NOISE IN SYSTEMS WITH DISTRIBUTED DELAYS
11:30-11:50	Omori. HETEROGENEITY IN SUSCEPTIBILITY INDUCES UNPREDICTABLE OUTBREAK	Postnikov. A WAVELET-BASED METHOD FOR REVEALING TAYLOR'S LAW IN SPECIES ABUNDANCE	Lopez-Herrero. THE DETERMINISTIC SIS EPIDEMIC MODEL IN A MARKOVIAN RANDOM ENVIRONMENT
11:50-12:10	Aldila. MATHEMATICAL ANALYSIS ON THE BIAS OF DENGUE INFECTION PROCESS CAUSED BY HOSPITALIZATION	Mukherjee. EFFECTS OF NONLOCAL AND GLOBAL CONSUMPTION OF RESOURCES IN POPULATION MODELS	Dènes. GLOBAL STABILITY OF MULTISTRAIN SIS MODELS WITH SUPERINFECTION AND PATCH STRUCTURE
12:10-12:30	Rashkov. ON THE ROLE OF NONINFECTIOUS VIRIONS IN AN IN-HOST DENGUE INFECTION	Gandarias. SOME EXACT SOLUTIONS FOR A GENERALIZED FISHER EQUATION	Sensi. A GSPT APPROACH TO PERTURBED SIR AND SIRMS MODELS
12:30-12:50	Rafikov. CONTROLLING THE TRANSMISSION DYNAMICS OF DENGUE BY WOLBACHIA-BASED STRATEGIES	Georgescu. MUTUALISTIC INTERACTIONS: DYNAMICS IN TERMS OF REPRODUCTIVE RATIOS	Continillo. APPLICATIONS OF POD BASED MODEL REDUCTION OF NONLINEAR DYNAMICAL SYSTEMS
Lunch (from 12:50 to 14:30)			

Monday (afternoon), February 4th, 2019		
Aula Magna		
Vollmer. DOMAIN DRIFT AND DIFFUSION IN CELL-POLARIZATION PROCESSES		
14:30-15:15		
15:15-16:00	Blyuss. EFFECTS OF POPULATION AWARENESS AND DELAYED RESPONSE ON THE SPREAD OF EPIDEMICS	
16:00-16:30	Coffee break 30 min	
	Parallel Room 1	Parallel Room 2
16:30-18:00	Session M4: Population and Ecology Dynamics	Session M5: Analytical & Numerical Methods
16:30-17:00		Invited Talk. Vermiglio. PC-BASED SENSITIVITY ANALYSIS OF THE BASIC REPRODUCTION NUMBER OF POPULATION AND EPIDEMIC MODELS
17:00-17:20	Russo L. BIFURCATIONS OF TURING PATTERNS AND TRAVELLING WAVES IN REACTION/ DIFFUSION VEGETATION MODELS	Breda. HOW FAST IS THE LINEAR CHAIN TRICK?
17:20-17:40	Iuorio. INTERPLAY OF WATER AND TOXICITY IN VEGETATION PATTERNS	Invited Talk. Valenti. FINANCIAL MARKETS AS COMPLEX SYSTEMS: STABILIZING ROLE OF NOISE
17:40-18:00	Zaffaroni. A GENERAL ECO PHYSIOLOGICAL FRAMEWORK TO MODEL THE INTERACTIONS BETWEEN PHLOEM FEEDER PESTS AND PLANTS	Filatrella. JOSEPHSON JUNCTIONS FOR SIGNAL DETECTION
	Aula Magna	
18:05-18:50	Venturino. THE ROLE OF PREDATION IN EPIDEMICS PROPAGATION: THE CASE OF LADYBIRDS AND APHIDS	

Tuesday (morning), February 5th, 2019			
Aula Magna			
09:00-09:45	Pugliese. MODELLING IMMUNE MEMORY AFTER REPEATED INFECTIONS		
09:45-10:30	Maffettone. MICROFLUIDIC MEASUREMENT OF THE ELASTIC MODULUS OF DEFORMABLE PARTICLES		
10:30-11:00	Coffee break 30 min		
	Parallell Room 1	Parallel Room 2	Parallel Room 3
11:00-13:10	Session T1: Mathematical Models in Epidemiology and Ecology	Session T2: Bioprocesses & Bioengineering	Session T3: BioSystems and Dynamics
11:00-11:30	Invited Talk. Morozov. LONG TRANSIENTS AS A BUGBEAR OF ECOLOGICAL FORECASTING: CONCEPTS, MODELS AND DATA	Invited Talk. Marzocchella. DYNAMIC PHENOMENA IN BIOTECHNOLOGICAL PROCESSES	Invited Talk. Patricio. A MODEL FOR HIV INFECTION AT INDIVIDUAL AND POPULATION LEVEL
11:30-11:50	Handari. MEASLES CONTROL IN JAKARTA, INDONESIA : A VACCINATION STRATEGY	Khattabi. LONG TERM BIOGAZ POTENTIAL BASED ON GREY MODEL FORECASTING: AN APPLICATION TO RABAT REGION, MOROCCO	Iannelli. A BASIC MODEL FOR THE DESCRIPTION OF EPIDERMIS
11:50-12:10	Mateus. MODELLING VACCINE TRIALS	Russo ME. ENZYMATIC HYDROLYSIS OF LIGNOCELLULOSIC BIOMASS: MODEL DEVELOPMENT FOR REACTOR DESIGN PURPOSES	Martins F. FITTING OF A IMMUNE RESPONSE MODEL TO CD4 ⁺ T CELL DATA IN LYMPHOCTIC CHORIOMENINGITIS VIRUS LCMV INFECTION
12:10:12:30	Martins J. EVOLUTIONARY DYNAMICS OF VACCINATION STRATEGIES AND MORBIDITY RISKS IN THE REINFECTION SIRI MODEL	Martalo. A TIME OPTIMAL CONTROL PROBLEM FOR BIODEGRADATION PROCESSES IN COMPOSTING BIOCELL	Bretti. MODELING AND SIMULATION OF INDIVIDUALS BEHAVIOUR ON BIOLOGICAL NETWORKS
12:30-12:50	Manfredi. ENSURING THE LONG-TERM RESILIENCE OF VACCINATION PROGRAMS. INSIGHT FROM GENERAL BEHAVIOUR-DISEASE MODELS FOR THE CONFLICT BETWEEN PUBLIC AND PRIVATE INTEREST	Ainouz. HOMOGENIZATION OF A HEAT TRANSFER PROBLEM IN CELLULAR BIOLOGICAL MEDIA	Oliveira. RELATION BETWEEN THE CONCENTRATION OF T CELLS AND TREGS AND THEIR ANTIGENIC STIMULATION
Lunch (from 12:50 to 14:30)			

	Tuesday (afternoon), February 5th, 2019	
	Aula Magna	
14:30-15:15	Soewono. DENGUE MODELING WITH HUMAN MOBILITY BETWEEN BANDUNG AND JAKARTA	
15:15-16:00	Aguiar. THE IMPACT OF MODELING EMPIRICAL DATA ANALYSIS ON PUBLIC HEALTH PRACTICAL INTERVENTION	
16:00-18:00	POSTER SESSION + COFFE BREAK/REFRESHMENTS	
20:00	CONFERENCE DINNER	

Wednesday (morning), February 6th, 2019	
Aula Magna	
09:00-09:45	Gyllenberg. ON MODELS OF PHYSIOLOGICALLY STRUCTURED POPULATIONS AND THEIR REDUCTION TO ODES
09:45-10:30	Kooi. ON THE ROLE OF THE VECTOR IN EPIDEMIC MODELLING
10:30-11:00	Coffee break 30 min
	Parallel Room 1
11:00-12:50	Session W1: Mathematical Models in Population Biology
11:00-11:30	Invited Talk. Braumann. INDIVIDUAL GROWTH MODELLING WITH STOCHASTIC DIFFERENTIAL EQUATIONS
11:30-11:50	Lavrova. A SIMPLE MODEL OF M. TUBERCULOSIS POPULATION DYNAMICS IN HOST LUNGS
11:50-12:10	Doroshkov. WHEAT LEAF EPIDERMAL PATTERN AS A MODEL FOR STUDYING THE INFLUENCE OF STRESS CONDITIONS ON MORPHOGENESIS
12:10-12:30	Tasman. A DISCRETE-AGE STRUCTURED TB MODELS WITH FAST AND SLOW INFECTIONS
	Parallel Room 2
11:00-12:50	Session W2: Population and Ecology Dynamics
11:00-11:30	Invited Talk. Fregougia. ABOUT THE ECOLOGICAL NICHE AND EMERGENT NEUTRALITY: TOWARDS A PROPOSAL OF MODELING
11:30-11:50	Zubairova. DYNAMICAL SYSTEMS FOR MODELLING OF UNIDIRECTIONAL SYMPLASTIC GROWTH OF PLANT TISSUES
11:50-12:10	Doroshkov. WHEAT LEAF EPIDERMAL PATTERN AS A MODEL FOR STUDYING THE INFLUENCE OF STRESS CONDITIONS ON MORPHOGENESIS
12:10-12:30	Conte. RECENT ADVANCES ON NUMERICAL METHODS FOR EVOLUTIONARY PROBLEMS
	Parallel Room 3
11:00-12:50	Session W3: BioSystems and Dynamics
11:00-11:30	Fiore. ANALYSIS AND CONTROL OF GENETIC TOGGLE SWITCHES SUBJECT TO PERIODIC MULTI-INPUT STIMULATION
11:30-11:50	Kahramanoğullari. QUANTIFYING MECHANISMS OF BACTERIAL PHOSPHATE ECONOMY FOR SYNTHETIC APPS
11:50-12:10	Guseva. ENTROPY APPROACH TO IDENTIFY TISSUE SPECIFICITY IN TOTAL TRANSCRIPTOME
Lunch (from 12:30 to 14:00)	

Wednesday, February 6th, 2019			
Aula Magna			
14:00-14:45	Starke. STABLE AND UNSTABLE PEDESTRIAN FLOW SITUATIONS IN PARTICLE SIMULATIONS AND EVACUATION EXPERIMENTS		
14:45-15:30	Buonomo. MODELLING INFORMATION-DEPENDENT IMPERFECT VACCINATION		
15:30-16:00	Coffee break 30 min		
	Parallel Room 1	Parallel Room 2	Parallel Room 3
	Session W4: BioSystems & Dynamics	Session W5: Mathematical Models in Population Biology	Session W6: Analytical & Numerical Methods
16:00-16:30	Invited Talk. Capasso. TUMOUR DRIVEN ANGIOGENESIS; FROM A STOCHASTIC MODEL TO ITS MEAN FIELD APPROXIMATION	Invited Talk. Tridane. GLOBAL STABILITY ANALYSIS OF A GENERALIZED EPIDEMIOLOGICAL MODEL WITH LATENT CLASSES	Invited Talk. Cuomo. MRI DENOISING AND ENHANCEMENT BY MEANS THE HISTOGRAM MATCHING
16:30-16:50	Pauli. COMPUTECELL3D SIMULATIONS OF NEPHRON PROGENITOR CELLS REVEAL DIFFERENT SPEED POPULATIONS AROUND EXPERIMENTAL URETERIC TIP	Galdi. MODELLING AND CONTROL OF THE YEAST CELL CYCLE	Cardone. PROBLEM-BASED NUMERICAL METHODS FOR SOME LOCAL AND NON-LOCAL MODELS
16:50-17:10	Ruolo. QUANTITATIVE MODELLING OF TFEB NUCLEAR TRANSLOCATION DYNAMICS	Kebir. A GENERAL DYNAMICAL GAME MODEL FOR STRUCTURED POPULATION: HAWK-DOVE GAME APPLICATION	Skwara. ANALYTICAL AND NUMERICAL METHODS IN EPIDEMIOLOGICAL MODELS
17:10-17:30	Ben Miled. OPTIMAL CONTROL MODEL OF TUMOR TREATMENT IN THE CONTEXT OF CANCER STEM CELL		Roh. AUTOMATED DATA-DRIVEN ESTIMATION OF RARE EVENT PROBABILITIES
17:30-17:50	Boukabcha. COMPARATIVE STUDY ON THE ANALYSIS EPIDEMIOLOGICAL OF SOME CANCERS IN ALGERIA: CASE OF CHLEF REGION		Siettos. ON THE CONSTRUCTION OF EMBEDDED FUNCTIONAL CONNECTIVITY NETWORKS FROM FMRI DATA
17:55-18:40	Aula Magna		
Stollenwerk. STOCHASTIC PROCESSES WITH COMPLEX BEHAVIOUR IN POPULATION BIOLOGY			
18:40-19:15	CLOSING & POSTER AWARDS		

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PUBLIC LECTURES

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BIOLOGICAL AND ECOLOGICAL PROBLEMS SOLVED BY SYSTEM DYNAMICS MODELS OR REQUIRING HYBRID APPROACHES

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The general aim of modeling is a simplified representation of the structure and behavior of complex real-life systems, with components interacting with one another at different scales. The System Dynamics approach based on ODE/PDE applications has been largely used in ecological and biological contexts. On the other hand, the so-called Individual-Based or Agent-based models have emerged as other powerful tools to support such task. So far, these different modelling approaches have been considered as exclusive alternatives techniques instead of synergistic tools. The explicit mechanistic modelling of complex dynamic systems may benefit by the combination of different simulatory approaches. However, the design and use of hybrid models should not be seen as a limited technical solution, but rather being a philosophical solution in a broader scientific context. The study of heterogeneous, highly dynamical, often non-linear, complex systems made of numerous different entities interacting in a changing environment through feedback loops, requires an explicit recognition of the inherent existing integration of both discrete and continuous events. Coupling both aspects requires a hybrid view of the system with both reductionist agents (e.g. cells) and aggregated flows (e.g. intercellular signaling processes or environmental diffusion processes).

CIRCULAR ECONOMY AND EXPLOITATION OF BIORESOURCES CHALLENGE CHEMICAL REACTION ENGINEERING

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The full realization of the principles of “circularity” of the economy that are the foundation for the sustainable use of natural resources lays the path to the development of a “regenerative” chemistry, aiming at bringing back into circulation and exploiting “end products” of natural or anthropogenic transformations. Regenerative chemistry requires, by its very nature, external energy supply that, in order to be sustainable, must be generated from renewable sources. Nature offers countless examples of regenerative chemistry through the variety of metabolic biosynthetic processes, and in particular those of photosynthetic nature activated by solar radiation.

Exploitation of bioresources discloses several paths to nature-aided regenerative chemistry which pose challenging multi-scale dynamical problems to the chemical reaction engineer. Selected case studies are presented and discussed: 1) engineering of algal growth is based on optimal design and operation of photobioreactors by effective coupling of inherent algal metabolic pathways with reactor hydrodynamics and solar irradiation; 2) exploitation of organic wastes into biobutanol by ABE fermentation requires optimal framing of the metabolic pathway of clostridia into chemical reaction engineering criteria.

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PLENARY TALKS

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THE IMPACT OF MODELING EMPIRICAL DATA ANALYSIS ON PUBLIC HEALTH PRACTICAL INTERVENTION

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In this talk, we present a set of models motivated by dengue fever epidemiology and compare different dynamical behaviors originated when increasing complexity into the model framework, anticipating that temporary cross-immunity and difference between primary and secondary infections appear to be the key factors determining disease transmission, outcome of infection and epidemics. The extended models show complex dynamics and qualitatively a very good result when comparing empirical data and model simulations. The models are parametrized on the official notification dengue data from Thailand. Three real scenarios will be evaluated and the impact of empirical data analysis on public health practical intervention will be discussed.

Acknowledgements

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EFFECTS OF POPULATION AWARENESS AND DELAYED RESPONSE ON THE SPREAD OF EPIDEMICS

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When modelling the dynamics of infectious diseases, it is important to correctly account for the behavioural changes of individuals in response to their disease status, as well as to the available information about the disease. In this talk I will discuss how population awareness affects the spread of infectious diseases, making particular emphasis on the interactions between local awareness due to contacts with aware individuals, and global awareness due to reported cases of infection and awareness campaigns (1). I will show how the interplay between different types of awareness affects the stability of the system's steady states and thus determines the type of behaviour to be observed in the model. I will also discuss the effects of time delay associated with response of individuals to available information (2), which can lead to some unexpected results. For instance, due to the presence of this delay in individuals' response to infection, increasing the rates of global or local awareness actually results in stabilising the endemic equilibrium. The talk will conclude with the analysis of a vaccination program (3).

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MODELLING INFORMATION-DEPENDENT IMPERFECT VACCINATION

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In this talk we present some recent results concerning the interplay between imperfect vaccination and human behavioral change. The investigation is performed in the framework of behavioral epidemiology (1; 2). The vaccination is assumed to be information-dependent, in the sense that the vaccination rate of susceptibles depends on the current and the past information available of the disease prevalence in the population. The weight given to the past history is described by an exponential kernel. We show that the model present some new dynamical features when compared with previous literature on the subject (3; 4; 5).

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WARM LITTLE PONDS OR WARM LITTLE PORES?

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Where did life begin? Darwin famously speculated about a “warm little pond”. Indeed that is one theory today. A rival theory holds that the oceans, rather than ponds, were the cradle of life. Of course, Darwin knew nothing of hydrothermal vents on the ocean floors, discovered only in the late 1970s. A particular class of vent emitting warm, rather than hot, mineral-laden water at alkaline pH has been highlighted as of particular significance in terms of a possible birthplace of life. We shall discuss these two theories, including recent work (2) demonstrating that hydrothermal vents can function just as well as, or better than warm little ponds in terms of providing an environment in which complex chemistry can occur via cycles of condensation reactions. In this view, life began from intrinsic cycles of concentration in chemical nanoreactors in the pores within membranes of hydrothermal vents; we call them warm little pores.

References

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ENHANCING PREDICTIVITY OF MATHEMATICAL MODELS IN SPATIAL ECOLOGY: ACCURATE LANDSCAPE DESCRIPTION AND UNCERTAINTY QUANTIFICATION

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One of the aims of spatial ecology is to help public health authorities and environmental conservation agencies to take more informed decisions at the time of identifying, monitoring and countering invasive dynamics, be it an infectious disease in wildlife, or the spread of an exogenous species. In particular, invasive species (be it animal or plants) can be a major threat for an ecosystem, and contrasting exogenous agents can take a serious toll to the annual budget of Departments of Environmental Protection. Accurate mathematical models can be efficient predictive tools on which building a proper intervention strategy, but their development faces some nontrivial difficulties. One of the main difficulties in simulating the spread of an invasive species (animal or plant) in wildlife resides in properly taking into account the heterogeneities of the landscape. Forests, plains and mountains present different levels of hospitality, while large interstates, lakes and major waterways can provide strong natural barriers to the epidemic spread. Another major difficulty resides in the poor knowledge of the characterizing parameters of the population dynamics itself, such as reproductive rate, carrying capacity of the environment, and dispersal speed. In this talk I will introduce a PDE model for the diffusion of an invasive species coupled with an accurate landscape description, and discuss the coupling of Monte Carlo Method (MCM)

with meta-models (a family of methods relying on a limited number of deterministic simulations and suitable interpolation techniques) to cope with the model parameter uncertainties. I will present a case study on the dispersal of a generic exogenous agent in the region of the Basque Country to show the effectiveness of the method.

This a joint work with F. Montomoli and N. Pepper from Imperial College, London.

ON MODELS OF PHYSIOLOGICALLY STRUCTURED POPULATIONS AND THEIR REDUCTION TO ORDINARY DIFFERENTIAL EQUATIONS

Mats Gyllenberg

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Considering the environmental condition as a given function of time, we formulate a physiologically structured population model as a linear non-autonomous integral equation for the, in general distributed, population level birth rate.

We take this renewal equation as the starting point for addressing the following question: When does a physiologically structured population model allow reduction to an ODE without loss of relevant information? We formulate a precise condition for models in which the state of individuals changes deterministically, that is, according to an ODE.

Specialising to a one-dimensional individual state, like size, we present various sufficient conditions in terms of individual growth-, death-, and reproduction rates, giving special attention to cell fission into two equal parts and to the catalogue derived in an other paper of ours (submitted). We also show how to derive an ODE system describing the asymptotic large time behaviour of the population when growth, death and reproduction all depend on the environmental condition through a common factor (so for a very strict form of physiological age).

The talk is based on joint work with Odo Diekmann and Hans Metz.

ON THE ROLE OF THE VECTOR IN EPIDEMIC MODELLING

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The motivation for this research comes from modelling the spread of a vector-borne virus disease. With the modelling of the vector population both ecological processes and disease transmission are important. In order to study the role of the host versus vector dynamics and their interaction we combine simple host and vector models where the host model is a SIR model and the vector model an SIS model (3). When the rates of the processes involved in the vector dynamics are much larger than those in the host model we can use a time-scale argument to reduce the model. Then one ordinary differential equation (ODE) is replaced by an algebraic equation. This is often implemented as a quasi-steady-state assumption (QSSA) where the slow varying variable is set in equilibrium. Singular perturbation theory is a useful tool to do this derivation. An asymptotic expansion in the small parameter being the ratio of the two time scales for the dynamics of the host and vector, together with an invariant manifold equation gives the algebraic equation using a symbolic analysis. In the case of a simplified SIS model for the host this algebraic equation in its simplest form, equal to the QSSA result, is just a hyperbolic relationship. This result is very similar to that of the Holling type

II functional response in the case of a predator-prey system. In the case of a SIR model for the host, the situation is more complicated and will be discussed.

Besides time scale separation an other important subject is the effect of seasonality. In (2) seasonality was implemented where the density of the vector was modelled with an ODE. Here we will study the effect of a sinusoidal temporal change. Using the QSSA approach with the SIS model for host and vector of (3) gives that in the reduced model with sinusoidal temporal change of the vector implies a sinusoidal infection rate in the reduced model. This is in accordance with the multi-strain dengue model multi-strain dengue model in (1).

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MICROFLUIDIC MEASUREMENT OF THE ELASTIC MODULUS OF DEFORMABLE PARTICLES

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Suspensions carrying soft inclusions are frequent in nature and applications, e.g., biological cell suspensions. Their behavior is strongly influenced by the mechanical properties of the suspended particles, thus being able to measure these properties could be crucial to understand and control suspension flow. Moreover, biological cells can modify their deformability and functionality depending on their health state (1), so the measurement of their mechanical properties can be a powerful tool to discriminate whether they are healthy or not. In the last twenty years, several methods have appeared in the literature for the measurement of the mechanical properties of deformable particles, like atomic force microscopy-based techniques (see, e.g., (2) and the references therein), micropipette aspiration (3), compression between parallel plates (4), osmotic compression (5), and capillary micromechanics (6). However, all the aforementioned techniques are quite time-consuming. Some of them are also ‘invasive’ for the investigated samples and the measured values of the mechanical properties can be influenced by the contact with the probe of the measuring instrument. In the very recent years, microfluidics is turning out to be suitable tool for the measurement of the mechanical properties of biological cells (7). About a decade ago, Hudson and co-workers have developed a continuous-flow non-invasive microfluidic technique providing almost real-time measurement of the interfacial tension between a liquid droplet

and an immiscible suspending liquid (8). Their method offers considerable advantages in terms of device fabrication and operation ease, low costs, and high throughput. We propose an adaptation of such a technique to the measurement of the elastic modulus of deformable particles and we validate it through numerical simulations and experiments on homogeneous synthetic particles with sizes and elasticities in the range of interest for biological cells (1).

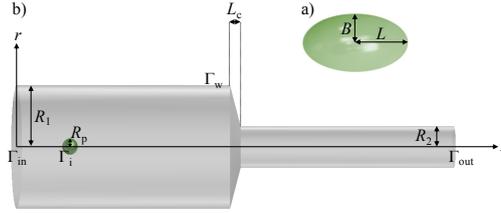


Figure 1: a) Schematic drawing of an elastic particle deformed into a prolate spheroid. b) Geometry of an initially spherical elastic bead suspended in a Newtonian liquid flowing through a device consisting of two coaxial cylindrical tubes.

In Fig. 1, the geometry of the device is depicted: an initially spherical elastic bead with radius R_p is suspended in a Newtonian liquid flowing through a cylindrical pipe with radius R_1 . This channel undergoes an abrupt radial contraction to a narrow cylinder of radius R_2 . While going through the constriction, the particle feels a time-dependent uniaxial extensional flow with extensional rate $\dot{\epsilon}(t)$ that makes it deform into a prolate spheroid. If one monitors the transient response of the elastic bead to such flow and measures the deformation parameter $D(t) = (L(t) - B(t))/(L(t) + B(t))$ (see Fig. 1a) and its time derivative dD/dt , a plot of $\eta(15/8\dot{\epsilon} - dD/dt)$ versus D (with η the suspending liquid viscosity) should show a linear trend with a slope corresponding to the particle's elastic modulus G (9). Therefore, such a flow measurement provides a means for measuring G in a continuous-flow process. This argument is conceptually analogous to that proposed by Hudson et al. for liquid droplets (8).

In order to validate our approach numerically, we have run simulations with beads having shear moduli of different orders of magnitude and verified that the aforementioned relation holds. Indeed, the data sets from numerical simulations appearing in Fig. 2a can be suitably fitted through linear functions with null intercept and a slope less than 1% different from the actual simulation input. In Fig. 2b, the sets of numerical results appearing in Fig. 2a are plotted each one scaled by the corresponding estimated value of the elastic modulus \hat{G} . As expected, the three series of data all collapse on the bisector of the first quadrant of the Cartesian plane. Experiments on PEG-DA microgel particles provide a further proof of the validity of the proposed device.

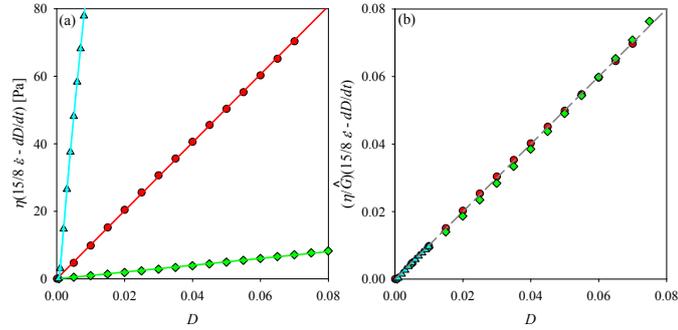


Figure 2: (a) Green diamonds, red circles, cyan triangles: Taylor plot of $\eta(15/8\dot{\epsilon} - dD/dt)$ versus D for three different G -values. Green, red, cyan lines: linear fits of the three series of symbols (the slopes are equal to 100.71, 1009.5, 9998 Pa, respectively). (b) Taylor plot of $(\eta/\hat{G})(15/8\dot{\epsilon} - dD/dt)$ versus D , with \hat{G} the estimated value of the particle shear modulus, for the same data sets as in panel (a).

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MODELLING IMMUNE MEMORY AFTER REPEATED INFECTIONS

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It is well known that memory cells can help to build a quick immune response in case of a new infection with the same (or similar) pathogen. This is indeed the principle at the basis of vaccination. It is also known that for certain pathogens a single vaccine dose can be insufficient to achieve a complete control of an infection, and that a second dose may be necessary. On the other hand, in several simple models of virus-immune interactions (e.g. (1)), the lower is the immune level before an infection, the higher it will be afterwards. Recently, Zarnitsyna *et al.* (2) have proposed a realistic model for immune response to infection by influenza virus that results in a progressive build-up of immune memory. In the talk, I will discuss several simplifications of the model by Zarnitsyna *et al.* (2) in order to assess which components of the model are essential for its qualitative behaviour. I will conclude with discussing how to incorporate these ideas in multi-scale epidemic models.

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DENGUE MODELING WITH HUMAN MOBILITY BETWEEN BANDUNG AND JAKARTA

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Dengue fever has been identified by WHO as the most rapidly spreading mosquito-borne disease in the world with an estimated fifty million dengue infections occurring annually. Although intervention and prevention programs have been conducted continuously, the spread of the dengue virus is still increasing in many regions, especially in tropical and sub-tropical countries. One of the main source of the difficulty in predicting the dengue cases is due to the unavailability of mosquito data which is highly affected by the changing of rainfall, humidity and temperature. The infection process is even more complicated. Human mobility is playing dominant role in the severity of the incidences. We construct here a mobility model arising from the dengue cases in Bandung (approx. 3 millions population) and in Jakarta (approx. 10 millions population), 150 km in distance, with more than 2 million people (weekly) commuting between the two cities. With the use of incidence data, the infection rates are estimated and the basic reproductive ratio is obtained as the (global) endemic indicator for identifying and predicting the level of dengue endemicity. Further for intervention strategy, a type reproductive number is constructed to analyze the effect of mobility to the level of endemicity in each city.

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STABLE AND UNSTABLE PEDESTRIAN FLOW SITUATIONS IN PARTICLE SIMULATIONS AND EVACUATION EXPERIMENTS

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A simplified evacuation scenario is considered where pedestrians have to leave a room passing a triangular obstacle either left or right (1). Their decision is influenced by the shortest route to the exit and the route choice of nearby pedestrians. The route choice is investigated by changing the position of the obstacle and by this the length of each route. The macroscopic measure defined as difference of the pedestrian flux left and right from the obstacle shows bistability and a hysteresis behaviour. A particle model is presented which reproduces the findings of pedestrian experiments. A control based continuation (2; 3; 4) allows to detect the branch of unstable flow situations separating the two stable branches where all pedestrians pass the obstacle either left or right.

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STOCHASTIC PROCESSES WITH COMPLEX BEHAVIOUR IN POPULATION BIOLOGY

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We review some predator-prey systems with complex bifurcation structures, where stochastic versions can be given easily. Namely, the Rosenzweig-MacArthur model with seasonal forcing shows Hopf and torus bifurcations, and then also bifurcations into chaotic attractors with positive Lyapunov exponents. Stochastic versions can be obtained by disentangling the time scale separation leading to the classical Rosenzweig-MacArthur model, where searching and handling predators as well as resource limitations for the prey via birth-death processes are considered. Markov processes and Fokker-Planck equations leading to stochastic differential equations are given and compared in their numerical performance.

Then we show some recently investigated mutator-replicator dynamics, with global or local trait specific resource limitation, in a similar way as done in the predator-prey systems mentioned above. Dynamics for local expectation values and Fokker-Planck equations can be derived in a similar way as above, and in limiting cases of continuous trait space, functional Fokker-Planck equations show up. These mutator-replicator systems are closely related to well known processes in evolutionary contexts.

Finally we will give some implications for the investigation of dynamic multi-strain epidemiological systems, i.e. where no explicit static fitness functions have to be given, with discrete or continuous trait space. Further implications will be given for data analysis of empirical systems, since we have readily the stochastic formulations obtained.

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THE ROLE OF PREDATION IN EPIDEMICS PROPAGATION: THE CASE OF LADYBIRDS AND APHIDS

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Mathematical models can be seen as a tool for testing hypotheses on the functioning of real life phenomena, with a viewpoint similar to theoretical physics, that suggests possible experiments to test the behavior of these systems.

Here we consider biological ecosystems. In particular, aphids have become the paradigm for studying the effect of bacterial endosymbionts in insects. Aphids are an important agricultural pest, and recent evolution in pesticide resistance in aphid populations leads to the need to find more sustainable control methods, e.g. by using natural enemies (parasitoid wasps, entomopathogenic fungi, generalist predators). A number of aphid bacterial endosymbionts have been shown to confer protection against parasitism by specialised parasitoid wasps, that lay eggs within the aphid. Their larvae grow inside the aphid, slowly killing the host before it emerges. The protective symbiont reduces the chance that the parasitoid egg will hatch, reducing biological control success rates. However, if the per capita risk of parasitism is low then not all aphids in a population will host these symbionts since there is also an associated fitness cost (reduced fecundity and longevity). We explored the benefits and costs of hosting these symbionts in (2).

Via a mathematical system and its simulated behavior, we hypothetize and investigate another possible way in which aphids become parasitized, as in fact the actual mechanism is so far not fully understood. Namely, we suppose that the aphids pick up the bacteria from the environment, where they also release them when they are killed by their natural predators such as ladybirds.

Acknowledgements

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DOMAIN DRIFT AND DIFFUSION IN CELL-POLARIZATION PROCESSES

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Cell polarization can be driven by the formation of signaling patterns on cell membranes. They can be modeled by two species of diffusing signaling molecules, that we call A^- and B^- . Moreover, there are also chemical compounds A^+ and B^+ on the cell surface that arise when molecules A^- and B^- attract and bind cytosolic enzymes. The enzymes drive the conversion of A^- to B^- and vice-versa. A molecule A^- switches to B^- with a rate that is proportional to the number of nearest-neighbor compounds B^+ . Conversely, B^- switches to A^- with a rate that is proportional to the number of neighboring A^+ . These chemical reactions drive the coarsening A and B -rich domains on the cell surface. Polarization amounts to the situation where the cell surface is covered by only two domains, an A -domain on one side and a B -domain on the opposing side of the cell.

Certain aspects of this domain coarsening are reminiscent to ripening of spin-up and spin-down domains in ferromagnets. In this analogy the $A^- \rightleftharpoons B^-$ conversion takes the role of spin flips of the magnetic system. However, there are also distinct differences in the dynamics. The $A^- \rightleftharpoons B^-$ conversion is driven by a dissipative chemical reaction, while spin-flips arise due to thermal fluctuations. Based on the analytical solutions for domain drift and diffusion in the two models we will discuss differences and communalities of the processes.

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TWO-PATCH PREY-PREDATOR MODEL REVISITED

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Dynamical complexity exhibited by prey-predator models with minimal models is an active area of research due to its long lasting importance. Autonomous models of prey-predator interaction can predict only three types of stationary solutions - stable coexisting steady-state, oscillatory coexistence and stable axial steady-states (partial or total extinction). However, bifurcation from one type of stable steady-state to another type of steady-state due to various types of local and global bifurcations can explain complex dynamics of interacting populations. We observe a variety of dynamical behaviors when we consider the coupled models of two interacting populations distributed over two-patches. Most of the models of this kind considered so far are based upon the fact that individuals can move between two patches, however they have no influence to the interactions between two trophic levels. Main objective of this talk is to explain how the dynamical behavior changes; if we assume that the individuals present in the second patch, who are migrated from the first patch, can influence the interaction between two trophic levels in the first patch and vice-versa. Significant outcomes will be explained with the help of a simple two-patch model of prey-predator interaction.

INDIVIDUAL GROWTH MODELLING WITH STOCHASTIC DIFFERENTIAL EQUATIONS

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A class of stochastic differential equations (SDEs) models was applied to describe the evolution of the weight of cattle. Most commonly, the weight $X(t)$ of an animal at age t can be described by a differential equation of the form $dY(t) = \beta(\alpha - Y(t))dt$, where $Y(t) = h(X(t))$ and h is an appropriate strictly increasing C^1 function. Here, $\alpha = h(A)$, where A is the asymptotic or maturity weight of the animal, and β is a rate of approach to maturity. We denote by x_0 the weight at age t_0 (initial age of observation) and let $y_0 = h(x_0)$. Using this type of models, the adjustment to data is usually done through non-linear regression methods in which independence among observed deviations from the regression curve at different times is assumed. This would be suitable if the deviations were due to measurement errors, but it is inappropriate if deviations are due to random changes on growth rates induced by environmental random fluctuations, as is the case.

So, we use stochastic differential equation models that incorporate the dynamics of the growth process and the effect of random fluctuations on the growth

dynamics. To describe individual growth in a random environment we use SDEs of the form $dY(t) = \beta(\alpha - Y(t))dt + \sigma dW(t)$, $Y(t_0) = y_0$, where α is now an average value, $W(t)$ is a standard Wiener process and $\sigma > 0$ measures the intensity of the effect on growth of the environmental random fluctuations.

In early work ((1; 2; 3)) we have studied estimation, prediction and optimization issues using cattle weight data from several females of Mertolengo cattle breed. In the present work, we have adjusted and applied the methodologies to the weight data of males of Mertolengo cattle breed and Alentejana cattle breed. In particular, since for males we have few weight data values for large ages, the classical maximum likelihood approach would estimate the parameter α with a large bias and so corrective procedures had to be introduced. Finally, we introduce the extension of the study to SDE mixed models by incorporating individual genetic values.

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TUMOUR DRIVEN ANGIOGENESIS: FROM A STOCHASTIC MODEL TO ITS MEAN FIELD APPROXIMATION

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In the field of Life Sciences it is very common to deal with extremely complex systems, from both analytical and computational points of view, due to the unavoidable coupling of different interacting structures. As an example, angiogenesis has revealed to be an highly complex, and extremely interesting biomedical problem, due to the strong coupling between the kinetic parameters of the relevant branching - growth - anastomosis stochastic processes of the capillary network, at the microscale, and the family of interacting underlying biochemical fields, at the macroscale. Here an original conceptual stochastic model of tumor driven angiogenesis will be presented, for which it has been shown that it is possible to reduce complexity by taking advantage of the intrinsic multiscale structure of the system; one may keep the stochasticity of the dynamics of the vessel tips at their natural microscale, whereas the dynamics of the underlying fields is given by a deterministic mean field approximation obtained by an averaging at a suitable mesoscale. A rigorous proof is given of the so called “propagation of chaos”, which leads to a mean field approximation of the stochastic relevant measures associated with the vessel dynamics, and consequently of the underlying TAF field.

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MRI DENOISING AND ENHANCEMENT BY MEANS THE HISTOGRAM MATCHING

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In this work we have investigated how to denoise MRI images using priors that come from the application domain. The process has lead to study and test total variation based image restoration models together with histogram matching techniques. The propose of this research is twofold: propose a model for image entrenchment and image restoration, within a unique two-stage process, and leave insights for other models. This results can lead to study more complex approaches, by using different histogram as references and by blending techniques together.

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ABOUT THE ECOLOGICAL NICHE AND EMERGENT NEUTRALITY: TOWARDS A PROPOSAL OF MODELING

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The possibility of modeling the ecological notion niche has been discussed by various authors(1). In this talk we propose a model that trues to unify the ecological concept of niche with the interactions among different species in a ecological system. We remind that an *ecological system* (or *ecosystem*) D is composed by different interacting communities. Every community is a set of species which live together and fit under specific *environmental conditions*. A community surrounded by its environment, constitutes a *niche*(2). Each niche can be represented by a *core* and a *periphery*. An *ecological transformation* is a migration of populations inside the niche as effect of the environment action (i.e. in virtue of the wind or the water or the insects etc.). We will model these transformation by suitable dynamics of populations. A mutual influence exists between the environment E and the organisms or individuals of different species living in the niche. E in its turn evolves, independently of the reproductive processes. In synthesis, an ecological niche is represented by a semi-closed complex system. We introduce the ecological interaction among the different niches of an ecosystem in the framework of Lotka-Volterra equations. To study the distribution of the populations we associate a master equation to model stochastic effects and we show as the detailed balance condition corresponds to an emergent neutrality(3) inside a niche and a

ago-antagonist equilibrium for competitive niches. Lastly we will show biological data validation.

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AGING TRANSITION AND THE ROLE OF NOISE IN SYSTEMS WITH DISTRIBUTED DELAYS

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In this talk I will discuss the influence of time delays on systems in the case when the time delay is non-constant but is taken from a particular distribution. In particular, two phenomena will be investigated. The first is concerned with the aging transition of a globally coupled network of active and inactive oscillators, and how coupling with distributed delays may lead to the suppression of oscillation in the network. The results for two particular cases of the delay distribution, namely, uniform and gamma distributions, will be discussed (1).

In the second part of the talk, the problem of calculating the noise-induced switching in systems with delay distributed kernels and Gaussian noise will be addressed. I will show how to derive a general variational formulation for the switching rate in the case of a general distribution kernel. Resulting equations of motion and boundary conditions represent an optimal path, which maximises the probability of escape. Furthermore, it is possible to obtain explicit analytical results for switching rates for small mean time delays and uniform and bi-modal distribution kernels. Analytical calculations are compared to the direct numerical simulations, and the agreement is perfect (2).

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DYNAMIC PHENOMENA IN BIOTECHNOLOGICAL PROCESSES

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The detailed characterization of performances (product yield, quality, throughput, ..) of operation units (fermenters included) adopted in biotechnological processes are often described by quite complex mathematical models. Indeed, modelling of biological systems - stand-alone or coupled with multi-phase systems may be very challenging from biological and mathematical point of view.

Models of fermenters should take into account the life evolution and mixing. On one hand, life is segregated into structural and functionally discrete entities: i) heterogeneous populations of unicellular organisms; ii) large number of molecules - interconnected in networks - within the cells. On the other hand, the mixing plays a key role as the unit scale increases and phenomena include: iii) homogeneity of the nutrients; iv) distribution of the cells, and of gaseous species (e.g. O₂ and CO₂); v) shear in the various section of the reactor; vi) distribution of the liquid, gas, and solid phases. The two classes of issues are known to impact product yield, productivity, product concentration, etc..

This contribution reports an overview of dynamic phenomena in biotechnological processes. Case studies will be presented for fermentations and operation units. In particular, the attention will be focused on: a) the performance of photobioreactor dedicated to the culture of autotrophic species; b) the application of biochemical networks simulators to investigate the kinetic dynamics of anaerobic bacteria.

LONG TRANSIENTS AS A BUGBEAR OF ECOLOGICAL FORECASTING: CONCEPTS, MODELS AND DATA

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Traditionally, ecological theory and understanding of ecological systems have been based on the idea that the observed states and ecosystem dynamics can be represented by some asymptotic behavior of models describing these systems. However, many models and empirical observations demonstrate transient behavior that may persist over very long time periods, followed by rapid changes in dynamics. Obviously, in this situation focusing solely on the long-term behavior of systems would be misleading. Correspondingly, a big new challenge for computational and empirical ecology is to understand the implications of transient dynamics, especially of long transients. For example, transients can provide an alternative explanation for observed regime shifts and population collapse that does not depend on underlying environmental changes. Although the importance of transients is now being gradually recognized, the current area of research seems to be in its infancy both in terms of lack of systematic studies and developing appropriate research techniques. Here, by using both empirical examples and model systems (both deterministic and stochastic), we comprehensively review the current knowledge of transient dynamics, showing that hitherto idiosyncratic and individual patterns can be classified into a coherent framework, with important general lessons and directions for future study. Finally, we argue that we need to include the possibility of long transient scenarios in ecosystems management and experimental design (1).

The talk is based on a series of meetings of the working group ‘Long Transients and Ecological Forecasting’ at the National Institute for Mathematical and Biological Synthesis (University of Tennessee, USA).

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A MODEL FOR HIV INFECTION AT INDIVIDUAL AND POPULATION LEVEL

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We present a methodology to connect an ordinary differential equation (ODE) model, for the coupled evolution of the HIV viral load and the CD4 leukocytes count, to an open Markov chain (OMC) model – with a finite number of states – via a stochastic differential equation (SDE) intermediate model. The ODE model here presented is formulated as a dynamic change between two regimes; one regime is of mean reverting type and the other is of inverse logistic type. For the general purpose of defining an OMC model for a human population, we associate Ito processes, in the form of SDE to the ordinary differential equations, by means of the addition of Gaussian noise terms which may be thought to model non essential characteristics of the phenomena with small and undifferentiated influences. The next step consists on associating a Markov chain transition matrix to the SDE model, by simulating trajectories of the solution process of the the SDE and counting the transitions between Infection Classes. The state space is partitioned into six Infection Classes that represent the evolution of the individuals infection without treatment.

We then exploit the open Markov chain model by considering data from the Portuguese yearly HIV newly infected population. We also include the transition matrix obtained into a population model for HIV with heterogeneous transmission and compare to the homogeneous one.

A QUANTITATIVE CHARACTERIZATION OF THE REINFECTION THRESHOLD

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The reinfection SIRI model describes the spreading of an epidemics in a population of susceptible (S), infected (I), and recovered (R) individuals, where after an initial infection the recovered individuals only have partial immunity against a possible reinfection. Grassberger, Chat and Rousseau (1) considered similar models with partial immunization, and observed transitions between phases of no-growth, annular growth and compact growth. The transition between annular growth and compact growth corresponds to the reinfection threshold in epidemiology, introduced by Gomes et al. in 2004 (2).

In this work, we propose a new concept of reinfection threshold based on the global maximum of the positive curvature of the endemic stationary state. This new maximum curvature reinfection threshold forms a smooth curve with respect to the temporary immunity transition rate, and has the property of coinciding with the previous notion of the reinfection threshold at the limit of vanishing the temporary immunity transition rate.

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GLOBAL STABILITY ANALYSIS OF A GENERALIZED EPIDEMIOLOGICAL MODEL WITH LATENT CLASSES

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This paper aims to investigate the global stability analysis, via the theory of cooperative systems, of a general epidemic model with latent classes. The model studied cover different types of epidemic model with latent classes, where cooperative system approach show that \mathcal{R}_0 is a sharp threshold with the disease dying out when $\mathcal{R}_0 < 1$ and becomes endemic when $\mathcal{R}_0 > 1$. We apply our findings to a tuberculosis epidemic model (1; 1; 2).

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FINANCIAL MARKETS AS COMPLEX SYSTEMS: STABILIZING ROLE OF NOISE

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Financial practitioners usually look at greater volatility, i.e. price fluctuations, as a source of greater market instability. However, large negative and positive price variations, i.e. crashes and rallies, respectively, follow often long periods characterized by small fluctuations of prices and returns.

Here the mean first hitting time (MFHT), i.e. the average time a stock return takes to undergo for the first time a crash or a rally, is introduced as an indicator of price stability (1; 2; 3; 4). An empirical analysis of daily returns for 1071

stocks traded in the New York Stock Exchange (NYSE) shows that the MFHT has a nonmonotonic behavior, with a maximum, as a function of volatility (5). This phenomenon is known as noise enhanced stability (NES) (6; 7; 8; 9; 10; 11; 12). Interpreting the MFHT as a stability proxy allows to conclude that an optimal volatility value exists, for which the system is far from critical events, namely downturns or upturns. In addition, we present a theoretical investigation, based on a nonlinear Heston model (2; 13), which allows to reproduce the statistical properties of the empirical analysis (5).

This work offers a new perspective indicating that, contrary to conventional wisdom, higher market instability is related not only to high, but also to low volatilities. This result could bear important implications both for practitioners and policy-makers responsible for market stability. Indeed the MFHT can strongly contribute to monitor the health state of financial markets, providing a standard measurement of market stability as a possible tool for a more accurate assessment of financial risk.

These findings can be extended to biology and natural sciences, where the concurrence of nonlinearity and environmental random fluctuations can be responsible for the enhancement of stability of an ecosystem (14).

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PC-BASED SENSITIVITY ANALYSIS OF THE BASIC REPRODUCTION NUMBER OF POPULATION AND EPIDEMIC MODELS

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The basic reproduction number, simply denoted by R_0 , plays a fundamental role in the analysis of population and epidemic models (1; 2; 3; 4; 5). However in mathematical modelling the specification of the input parameters can be crucial since, due to some limitations in experimental data available, they can be uncertain and often represented as random quantities in a suitable probabilistic framework. In this context the Polynomial Chaos Expansions (PCEs), coupled with suitable numerical methods, furnish important tools for the sensitivity analysis and the uncertainty quantification of the random model response (7; 9). The aim of this paper is to describe how the variability of R_0 is affected by the variability of the input parameters, through the evaluation of Sobol indices by PC-based methods. The use of a suitable and new computational model of R_0 allows also to consider more complex epidemic models, where R_0 is defined as the spectral radius of the infinite-dimensional next generation operator. The efficiency and versatility of the numerical approach are confirmed by the experimental analysis of two examples of increasing complexity. (6; 8)

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HOMOGENIZATION OF A HEAT TRANSFER PROBLEM IN CELLULAR BIOLOGICAL MEDIA

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We present a micro-model for heat transfer in biological tissues. The model considered as a poroelastic material includes thermal diffusion on the cells and thermal exchange barrier on the interfaces between these cells. Using the two-scale convergence technique, a homogenized model is rigorously derived.

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MATHEMATICAL ANALYSIS ON THE BIAS OF DENGUE INFECTION PROCESS CAUSED BY HOSPITALIZATION

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Dengue has become a major disease in many tropical and sub-tropical countries since it is first time found in China, 256–420 AD. This disease spread by *Aedes* mosquitoes and caused by 4 different serotype of DEN viruses. Since no special medical treatment to cure infected human, the only thing that can be done to treat them is to providing hospital care which will isolate them from a possibility to infect susceptible mosquito. Many mathematical models have been developed by many authors to understand how dengue might spread among the human population. Most of the model introduced the infection process as a mass interaction between susceptible human with infected mosquito and between susceptible mosquito with an infected human. Whereas, the infection might appear mostly only between un-hospitalized infected human with susceptible mosquito, which brings us into a bias interpretation of incidence data when this data is available from hospital record.

Here in this talk, we construct an SIR-UV model of dengue spreads with an intervention of hospitalization. Quasi-Steady-State-Approximation (QSSA) method then applied to the model which reduced the model into a simple IR model. A comprehensive analysis of the existence of the equilibrium points and their stability will be analyzed together with the basic reproduction number (\mathcal{R}_0). The parameters on the model then parameterized using data from the 2017-2018 dengue outbreak in Jakarta and used to estimate the \mathcal{R}_0 when no intervention for dengue control implemented.

The parameter estimation problem is constructed an optimal control problem in a purpose to minimize the Euclidian distance between simulation and the incidence data using an optimal parameter(s). Once the parameters found, a second optimal control problem then applied to investigate the optimal strategy of hospitalization intervention which treated as a time-dependent variable to minimize the number of infected humans as small as possible. Some numerical results of the optimal control problem will be discussed in this talk.

COMPARATIVE STUDY ON THE ANALYSIS EPIDEMIOLOGICAL OF SOME CANCERS IN ALGERIA: CASE OF CHLEF REGION

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Algeria is a regional and middle power, the largest country in North Africa. The cause of cancer is multifactorial according the type. Age, radiations, tobacco and environmental are among the different risk factors. To reduce this cancers, prevention and early diagnosis are needed.

In this work, we are studying medical files of three type of cancers: breast cancer, lung cancer and skin cancer patients, either for estimate the incidence and some statistical parameters and to discover the different risk factors for each type of cancer. The region of Chlef is a sample of Algeria, either for these studied patients or the general population.

From January 2014 until the end of December 2017, we have collected more than 845 breast cancer cases, 102 lung cancer cases and 21 skin cancer cases. The number of population in the study area at the end of the study period is about about 1221951 poeple, but the total number of Algerian population is about 42,2 million inhabitants. Breast cancer incidence rate of the Algerian population is 28,45 cases per 100000 female population, but the incidence rate of Chlef region is 17,29 cases of breast cancer, about 2,09 cases of lung cancer and about 0,43 cases of skin cancer per 100000 population.

HOW FAST IS THE LINEAR CHAIN TRICK?

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The *linear chain trick* is a celebrated tool (2; 3; 5) to reduce delay differential equations with certain classes of distributed delay to systems of ordinary differential equations (ODEs). In particular, it applies when the kernel of the distributed delay is an Erlang distribution. In this case, the number of ODEs increases with the shape parameter of the latter. When this number grows unbounded, the Erlang distribution converges to the Dirac delta and the distributed delay becomes a constant delay. In this talk we present a detailed study of this convergence in the case of an SIR model including the role that information on the disease play on vaccinating behaviors (1). We prove that the convergence is linear, so that a large number of ODEs is required in general to mimic the case of information concentrated in a fixed time instant in the past. The presented results are part of the MSc thesis in Mathematics of Giulia Gava (4).

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MODELING AND SIMULATION OF INDIVIDUALS BEHAVIOUR ON BIOLOGICAL NETWORKS

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Here we present some studies on the behavior of individuals in a biological networks. The first study is about *Physarum polycephalum* slime mold and its ability to find the shortest path in a maze. Here we present a PDE chemotaxis model that reproduce its behavior in a network, schematized as a planar graph, (1). In particular, suitable transmission and boundary conditions at each node of the graph are considered to mimic the choice of such an organism to move from an arc to another arc of the network, motivated by the search for food. Several numerical tests are presented for special network geometries to show the qualitative agreement between our model and the laboratory observed behavior of the mold. The second study is about tumor associated macrophages and the mathematical modeling of the behavior of cell populations in a microfluidic chip, an environment constructed in laboratory to mimic complex biological systems. In particular, the developed model consists of reaction-diffusion-transport equations with chemotaxis: birth/death processes, interaction with chemoattractant, interaction and competition between species. Suitable transmission conditions are included in the algorithm and numerical tests are presented.

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PROBLEM-BASED NUMERICAL METHODS FOR SOME LOCAL AND NON-LOCAL MODELS

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The numerical solution of real-life models cannot disregard the behavior of the analytical solution and/or the preservation of its special properties, such as for example the periodicity, the stiffness, the (lack of) smoothness in some intervals. In this talk it will be illustrated how this approach led to effective numerical methods, both for differential and integral models.

Many practical problems in science and engineering are modeled by large systems of ordinary differential equations which arise from discretization in space of partial differential equations. For such systems there are often natural splittings of the right hand sides of the differential systems into two parts, one of which is non-stiff or mildly stiff, and suitable for explicit time integration, and the other part is stiff, and suitable for implicit time integration. Thus, here it is proposed an implicit-explicit (IMEX) scheme based on GLM methods, which has the advantage of preserving the order of the composing methods and to have enough free parameters to optimize the stability properties.

On the side of non local models, it will be illustrated the numerical discretization of Volterra integral equations (VIEs) with periodic solution and of fractional differential equations (FDEs), both suitable to model problems with memory. VIEs with periodic solution can represent periodic phenomena with memory, like the spread of seasonal diseases. Classical methods are able to follow the oscillations of the solution at a high computational cost, while the exponentially-fitted methods that we propose can considerably reduce this cost by exploiting the knowledge of an estimation of the frequency. FDEs can model the anomalous kinetics of some processes in physics, chemistry, pharmacokinetics. It will be illustrated a

spectral collocation method, which takes into account the non-local nature of the equation, with a function basis suitably chosen to reproduce the behavior of the analytical solution.

This presentation is based on the research work carried out with M. Bras (AGH Univ., Poland), K. Burrage (Oxford Univ.), D. Conte (Univ. of Salerno), R. D'Ambrosio (Univ. of L'Aquila), L.Gr. Ixaru ("Horia Hulubei" Nat.Inst. Physics & Nuclear Eng., Romania), Z. Jackiewicz (Arizona State Univ.), B. Paternoster (Univ. of Salerno), A. Sandu (Virginia Polytechnic Inst. & State Univ.), G.Santomauro (ENEA) and H. Zhang (Argonne Nat. Lab.).

RECENT ADVANCES ON NUMERICAL METHODS FOR EVOLUTIONARY PROBLEMS

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This contribution regards the numerical solution of evolutionary problems related to natural phenomena and physical processes modelled by functional equations of various type, with specific characteristics such as: oscillations, singularities, presence of stochastic terms, by focusing especially on stability properties of the methods. We will describe the construction of 'adapted' numerical methods, that is, strongly oriented to the problem and the stability will be also interpreted as preservation of the intrinsic qualitative characteristics of the problem itself.

We will consider systems of ordinary differential equations with oscillating solution, deriving for example from the spatial semi-discretization of partial differential equations of advection-diffusion in hydrodynamic problems (2). In this case, the use of non-polynomial bases reveals a powerful tool for adapting numerical methods to the known behavior of the solution. We will also discuss stochastic Volterra integral equations, deriving, for example, from the modelling of economic problems (3). The focus will be on the construction of numerical methods that can inherit the stability properties of the methods for stochastic differential equations. Finally, we will consider multi-value methods for fractional differential equations, which model, for example, the behaviour of viscoelastic materials (1), and will analyse the relative stability properties.

Acknowledgements

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APPLICATIONS OF POD BASED MODEL REDUCTION OF NONLINEAR DYNAMICAL SYSTEMS

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In this work the efficiency of Proper orthogonal decomposition (POD) methods to construct reduce models which may approximate the asymptotic behavior of PDEs is discussed. Numerical bifurcational analysis is used as a mean to evaluate the efficiency of the method. As example of application, the distributed model of a tubular reactor with recycle is considered. The model is reduced by approximating it first with a Continuous Stirred Tank Reactor (CSTR) cascade. Then, proper orthogonal decomposition (POD) with Galerkin projection is applied with special attention to study of oscillatory regimes. The dynamics of the resulting models is studied via numerical simulation, and solutions in the form of time series and phase plot diagrams are compared to those obtained for the original CSTR cascade model. Different methods to choose the minimum number of basis functions are compared and discussed. Solution diagrams built with POD models are compared with those from CSTR cascade, as a function of the Damköhler number. Features and limitations of POD models are discussed for different snapshot sampling policies and for different values of the Péclet number. Qualitative performance increases and quantitative performance decreases as samples from

steady states are considered along with periodic solution samples. Performance becomes worse as the Péclet number increases. As second example application is one-dimensional model of a tubular reactor with external heat recycle, which exhibits periodic and also chaotic solutions. The issue of the optimal construction of the POD basis is addressed by sampling of the chaotic orbits, with the aim of constructing a global basis for a reduced-order model (ROM). To demonstrate that such orbits are the most appropriate because they incorporate the maximum amount of information about the system behavior, the entropy of the orbit is calculated. Sampling of the chaotic solutions allows for the determination of the POD basis to be employed in the POD/Galerkin method. The accuracy of the ROMs is compared by means of the Hausdorff distance, computed between the asymptotic regime of the reference solution and each of the ROM-reconstructed asymptotic attractors. A norm computed on the sampled time series is employed to compare transient solutions. The POD-based ROMs work well even for values of the parameter for which the model behavior is far from chaotic, i.e. periodic orbits or fixed points. Moreover, the POD-based ROMs successfully compare with a classic orthogonal collocation method.

GLOBAL STABILITY OF MULTISTRAIN SIS MODELS WITH SUPERINFECTION AND PATCH STRUCTURE

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We study the global stability of a multistrain SIS model with superinfection. We present an iterative procedure to calculate a sequence of reproduction numbers, and we prove that it completely determines the global dynamics of the system. We show that for any number of strains with different infectivities, the stable coexistence of any subset of the strains is possible, and we completely characterize all scenarios. As an example, we apply our method to a three strains model. We also show a generalization to a group multistrain model with patch structure.

WHEAT LEAF EPIDERMAL PATTERN AS A MODEL FOR STUDYING THE INFLUENCE OF STRESS CONDITIONS ON MORPHOGENESIS

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The leaf epidermis of a monocotyledonous plant is a widely used model system for studying the differentiation of plant cells, as it contains readily observable specialized cells. We used a growing cereal leaf to study stress-induced dynamic changes in morphogenesis. In the process of formation, the linear leaf of wheat remains in the stationary growth phase for long time period. This fact permits us to observe a series of successive morphogenetic events recorded in the cellular structure of the mature leaf. In studying the cellular architecture of the wheat leaf epidermis, we obtained and processed confocal 3D images of the wheat leaves stained with fluorescent dyes. This procedure allows an accurate morphometric description and determination of quantitative characteristics of the leaf epidermal pattern. Low temperatures are among the factors limiting the growth of crop plants in the temperate zone. In the present work, we show significant aberrations of stomatal morphogenesis in the epidermis of boot leaves of wheat in response to cold stress (1). The proposed approach can provide standardized qualitative and quantitative data on stress-induced morphogenesis aberrations in wheat leaf epidermis. Subsequently, these data were used for verification of computational models of leaf morphogenesis. The reported study was funded by Russian Foundation for Basic Research (RFBR) according to the research project No 17-29-08028.

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LONG TERM BIOGAZ POTENTIAL BASED ON GREY MODEL FORECASTING: AN APPLICATION TO RABAT REGION, MOROCCO

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Developing countries are increasingly in need of a more efficient economic management because of their lack of financial resources. To meet this need, in addition to several disposal methods such as open dumping, sanitary landfilling, incineration and composting, the transformation of waste into energy can be considered. In Africa, the energy potential of organic waste is important and can reduce the impact on the environment. The purpose of this study is to evaluate how much energy can be generated from the transformation of current waste into energy and to forecast the yield in the long term. For this, grey systems have been used to predict energy quantity from municipal solid waste in Rabat region, Morocco. The results show that over a ten-year period the economic benefits would be considerable and that the model obtained is relatively accurate.

JOSEPHSON JUNCTIONS FOR SIGNAL DETECTION

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Josephson junction electrical behavior is governed by a quantum variable, the gauge invariant phase difference between the macroscopic phases of the two superconductors forming the junction. Therefore, the dynamics, as described by the celebrated Josephson equations (1), is not directly accessible, and only indirect electrical measurements (essentially, the current and the voltage) can be actually monitored. For instance, it is possible to retrieve the current at which occurs the passage from the superconducting state to the finite voltage. Repeating the measurements in the presence of a random disturbance, or because of quantum effects (2), the junction can switch to the finite voltage at slightly different current levels, thus producing a distribution of switching currents. Conversely, the analysis of the distribution of the switching can be used to reveal the presence of noise and quantum effects (3; 4; 5; 6), or it is possible to reveal a sinusoidal drive embedded in the noise (7; 8). The detection scheme, in the framework of statistical

decision theory, shows some remarkable features, such as quasi-optimal scaling behavior and stochastic resonance. In a noisy environment, the junction can also be employed to discern the non-Gaussian, in particular Poissonian, character of the non-intrinsic noise (9). In a similar configuration we propose to use the junctions to reveal Lévy noise (10), that is non-Gaussian fluctuations characterized by the so-called Lévy flights (11; 12; 13).

There are several reasons to use Josephson junctions as detectors. From a practical point of view, it is attractive to exploit the speed and low noise features of Josephson junctions. From a general point of view, stable non-Gaussian noise sources are interesting exceptions to the general rule that noise is characterized by finite variance. It is therefore valuable to have a tool that can effectively detect the presence of fat tails disturbances in the noise background.

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ANALYSIS AND CONTROL OF GENETIC TOGGLE SWITCHES SUBJECT TO PERIODIC MULTI-INPUT STIMULATION

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In this talk, we analyze a genetic toggle switch recently studied in the literature (1) where the expression of two repressor proteins can be tuned by controlling two different inputs, namely the concentration of two inducer molecules in the growth medium of the cells. Specifically, we investigate the dynamics of this system when subject to pulse-width modulated inputs. We provide an analytical model that captures qualitatively the experimental observations reported in the literature and approximates its asymptotic behavior. We also discuss the effect that the system parameters have on the prediction accuracy of the model (2). Moreover, we propose different external control strategies to regulate the mean value of the fluorescence of the reporter proteins when the cells are subject to such periodic forcing (3).

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MODELLING AND CONTROL OF THE YEAST CELL CYCLE

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The collective rhythmicity of biological oscillators has fundamental importance in the coordination of life processes. Within a yeast cell population each cell divides with the same period but asynchronously and asymmetrically, with a mother cell generating multiple daughter cells. The purpose of this work was to design and implement a feedback control strategy to synchronize the cell cycle in a yeast population, whose cells can be seen as uncoupled phase oscillators. Two engineered yeast strains were analysed to this end. In both strains, a medium lacking the amino-acid methionine enable the cell cycle to start. The main difference is that one strain is also able to cycle on its own, while the other strictly requires lack of methionine to grow.

A model made of two ordinary differential equations to represent a yeast cells growth and division was proposed by Charvin et al. (1). We adapted the model to both yeast strains and numerically simulated the time evolution of cell-cycle phase, volume and cell division of each cell. A phase resetting condition was added in order to model the effect of the input (medium with or without methionine). First, conditions for phase-locking between the cells and the stimulus were investigated by simulating individual cells. Then, the collective behaviour of a

cell population was studied with the evaluation of an order parameter that was proposed by Kuramoto (2) as a value to quantify synchronization. A simple Relay controller and a Model Predictive Control (MPC) strategy were designed and numerically implemented to achieve synchronization. Their performances were compared to periodic and random open-loop stimulation, thus demonstrating the convenience of predictive control with respect to the other tested strategies.

This work was also presented as a Poster.

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SOME EXACT SOLUTIONS FOR A GENERALIZED FISHER EQUATION

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Fisher's equation is commonly used in biology for population dynamics models and in bacterial growth problems as well as development and growth of solid tumours. Generalizations of the Fisher equation are needed to more accurately model complex diffusion and reactions effects found in many biological systems. In this talk, a generalized Fisher equation is studied from the point of view of the theory of symmetry reductions and conservation laws in partial differential equations. Some of the equations admit Lie symmetries which yield to further reductions, moreover we obtain some exact solutions of biological and medical interest. (1; 2; 3; 4; 5)

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MUTUALISTIC INTERACTIONS: DYNAMICS IN TERMS OF REPRODUCTIVE RATIOS

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Many models of mutualism have been proposed and studied on a case-by-case basis. Also, while most existing models of mutualism are bi-dimensional, ecosystems are seldom limited to groups of only two interacting species. To overcome these issues, we develop a general model of a mutualistic interaction with an arbitrary number of species which encompasses several classic two-species models, even when extended to their respective multidimensional versions.

Our model is defined in terms of consistency hypotheses introduced *ad hoc*, the focus being on obtaining conditions for the boundedness and unboundedness of solutions, respectively, in terms of threshold parameters which are similar in scope to the basic reproduction number from Mathematical Epidemiology. Our threshold parameters, however, are computed in very different conditions. That is, they are not computed in a near-extinction situation, as it is the case in Mathematical Epidemiology and, to a lesser extent, in Ecology, but at high population densities, under given species proportionality.

The reason is that, as far as the validity of the model is concerned, what is important is not the extinction of species, but their blow-up. Also, a model of mutualism has an entirely different structure, not exhibiting the asymmetry which is characteristic to disease propagation models and predator-prey models. A single threshold parameter, based on the dynamics of a single species or compartment, may consequently not be enough to describe the behavior of solutions for a model of mutualism, and we employ one reproductive ratio per species to introduce our boundedness conditions.

We also observe that for a representative class of models, the boundedness condition can be expressed in terms of eigenvalues for a certain matrix of coefficients, which represents an useful algebraic test for boundedness. We then discuss

particular cases in which there is a single threshold parameter separating boundedness from unboundedness. The situation in which the unboundedness is caused by a particular subset of species is also of concern.

For the particular case of two-species mutualisms, using mild assumptions on the growth and self-limiting functions, we prove the global stability of a unique coexistence equilibrium whenever it exists. Our results also allow each of the mutualists to be subject to a weak Allee effect. Moreover, we find that if one of the interacting species is subject to a strong Allee effect, then the mutualism can overcome it and cause a unique coexistence equilibrium to be globally stable.

Joint work with Hong Zhang (Jiangsu University, P.R. China) and Daniel Maxin (Valparaiso University, U.S.A.).

ENTROPY APPROACH TO IDENTIFY TISSUE SPECIFICITY IN TOTAL TRANSCRIPTOME

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The aim of the work is to check whether total transcriptome allows identification of tissue specific sequences in the ensemble. The total transcriptome comprises 610 954 contigs; 6654 entities longer 4 000 bp have been selected for the study. To reveal the structuredness in the contigs ensemble, they were transformed into triplet frequency dictionaries ($W_{(3,1)}$ and $W_{(3,3)}$), of two types: the former had reading window move equal to $t = 1$, and the latter had $t = 3$.

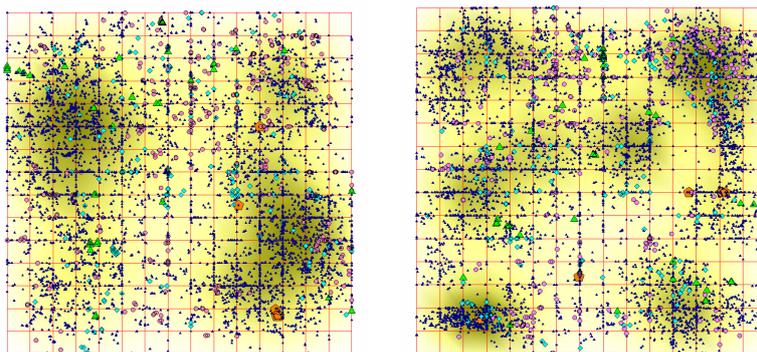


Figure 3: Distribution of contigs with increased \bar{S}_k .

All reads were labeled with tissue source. Each contig from the total transcriptome was aligned against the set of tissue specific reads, so that the part of these

latter has been determined, for each tissue. Hence, the distribution of tissue types has been determined, for each contig. To measure

$$\bar{S}_k = \sum_{j=1}^4 \varphi_j \cdot \ln \left(\frac{\varphi_j}{f_j} \right) \quad (1)$$

this distribution, specific entropy of each contig has been calculated. Here j enlists tissue types. φ_j is the frequency (part) of reads from j -th tissue observed in a contig. f_j is average frequency of all reads of j -th type observed over the entire ensemble of contigs. Fig. 4 shows the distribution of tissue specific contigs, for two types of frequency dictionary (left is $W_{(3,1)}$ and right is $W_{(3,3)}$). Reasonable performance in tissue specificity is observed, for both types of the dictionaries.

MEASLES CONTROL IN JAKARTA, INDONESIA: A VACCINATION STRATEGY

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Seasonal fluctuation is a common phenomenon in the transmission of an infectious disease, including measles. In this talk, a mathematical model of measles with vaccination intervention is used to capture seasonal measles in Jakarta. A periodic infection parameter is used to estimate weekly incidence data of measles in Jakarta, Indonesia. Once the parameter is estimated, numerical simulations to find the optimal vaccination strategy under some circumstances for future prediction are given. Mathematical analysis of the model related to equilibrium points and the basic reproduction number are also discussed in this talk.

A BASIC MODEL FOR THE DESCRIPTION OF EPIDERMIS

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The epidermis (the outermost part of the skin) is a stratified epithelium formed by multiple layers of cells that undergo a continuous renewal process. In the innermost layer - the basal cells layer - cell proliferation occurs. Progenitor cells produce quiescent differentiated cells (post-mitotic keratinocytes) that detach from the underlying basement membrane and move outward forming the suprabasal layers. Suprabasal cells undergo a progressive maturation, called keratinization and, at the end of this process, cells filled of keratin die, and the dead cells (corneous cells or corneocytes) form the stratum corneum. The inner cells of the stratum corneum adhere each other, but, when the corneocytes are pushed to the surface by newly formed cells, they lose their adhesion and eventually are shed from the surface, through a process named desquamation.

To describe the process outlined above, we propose a model (1)-(5) with age and space structure, including different types of cells that, after proliferation in the basal layer, move with the same velocity, under the constraint that the local volume fraction occupied by the cells is constant in space and time. The stationary state of the model corresponds to the spatial organization of the normal, homeostatic epidermis, or the state that may be reached after prolonged and time-invariant damaging. This state should also be the limit of the time evolution of the skin after any perturbation. Existence of a solution, both in the stationary and in the dynamic case, requires conditions that can be viewed as parameters restrictions for skin formation. A numerical scheme to compute the solution of the model is proposed and simulations are provided for realistic values of the parameters.

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INTERPLAY OF WATER AND TOXICITY IN VEGETATION PATTERNS

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Vegetation patterns are largely present in nature. The underlying mechanisms leading to their formation, however, are not yet fully understood. A prevailing view is to treat water availability as the main causal factor for the emergence of vegetation patterns, as they are mostly observed in arid and semiarid regions. While successful, this hypothesis fails to explain other ecologically relevant phenomena, such as the presence of vegetation patterns in environments where water resources are not scarce. We present here a novel toxicity-mediated model for vegetation pattern formation and investigate its rich structure. This model consists of three PDEs accounting for a dynamic balance between biomass, water, and toxic compounds. Different (ecologically feasible) regions of the models parameter space give rise to stable spatial vegetation patterns in Turing and non-Turing regimes. Strong negative feedback gives rise to dynamic spatial patterns that continuously move in space while retaining their stable topology.

QUANTIFYING MECHANISMS OF BACTERIAL PHOSPHATE ECONOMY FOR SYNTHETIC APPS

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Escherichia coli have developed one of the most efficient regulatory response mechanisms to phosphate starvation. The machinery involves a cascade with a two-component system (TCS) that relays the external signal to the genetic circuit, resulting in a feedback response. Achieving a quantitative understanding of this system has implications in synthetic biology and biotechnology, for example, in applications for wastewater treatment. We present a computational model and experimental results with a detailed description of the TCS, consisting of PhoR and PhoB, together with the mechanisms of gene expression (1). The model is parameterised within the feasible range, and fitted to the dynamic response of our experimental data on PhoB as well as PhoA, the product of this network that is used in alkaline phosphatase production. Deterministic and stochastic simulations with our model predict the regulation dynamics in higher external phosphate concentrations while reproducing the experimental observations. Flux analysis on stochastic simulations reveal the distribution of the system resources in response to starvation signal (2). In a cycle of simulations and experimental verification, our model predicts and explores phenotypes with various synthetic promoter designs that optimise the inorganic phosphate intake in *E. coli*. Our results suggest directions for investigations on engineering new sensors and regulators for living technologies.

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A GENERAL DYNAMICAL GAME MODEL FOR STRUCTURED POPULATION: HAWK-DOVE GAME APPLICATION

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In this work, we elaborated a general dynamical game model that includes a finite number of strategies and a finite number of physiological structures. We consider that population structure distribution is the result of environmental conditions and that strategies are the result of behavior plasticity. Our aim is to understand how structure-dependent fitness can affect the existence and the stability of strategies distributions. As a first result, we prove the existence of an equilibrium state that describe mixed population with pure strategies over a partition of the structure set and give a sufficient condition for its local asymptotic stability. Then, we extend the analysis in the particular case of a structured Hawk-Dove game. We prove that the form of cost, gain and initial population function by size can shift the population from the total coexistence to pure strategies at each structure.

A SIMPLE MODEL OF *M. TUBERCULOSIS* POPULATION DYNAMICS IN HOST LUNGS

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Tuberculosis (TB) has a long history as a major disease in humans and animals. A causative agent of TB *Mycobacterium tuberculosis* causes severe implications for a patient. The pathogen manipulates the host immune response and thus stimulates inflammatory processes leading to an even greater imbalance of specific enzymes/inhibitors facilitating tissue destruction (2; 4). Such positive feedback could also be conditioned by the initially damaged immune status of the host. We have developed large-scale model describing the lung lesion taking into account key metabolic pathways governed by bacteria. The model was reduced to two ODE equations to highlight main mechanisms of host-pathogen interaction. We have shown that micobacterial reproduction in lungs can be attributed to dynamical behaviour described, in particular, in Holling's model (2), where the population growth is conditioned by the searching of "convenient" substrate (lung tissue) with time delay for reproduction in the selected focus.

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STABILITY OF PERIODIC SOLUTIONS OF RENEWAL EQUATIONS

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Realistic models of structured populations are often based on delay equations. It is usually unfeasible to study their dynamics analitically, therefore one must resort to numerical approximation. In the case of delay differential equations, the study of the stability of a periodic solution can be approached by linearizing the equation around the solution and determining the spectrum of the monodromy operator of the linearized equation, thanks to the Floquet theory and the principle of linearized stability (4). A numerical method based on pseudospectral collocation to approximate this spectrum was developed in (2). Recently, we proposed in (1) a method for renewal equations based on the same ideas and numerical techniques, despite the lack of a Floquet theory and of the principle of linearized stability. In this talk we present our efforts at giving the method a solid theoretical foundation based on (3; 4), which have eventually been successful.

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THE DETERMINISTIC SIS EPIDEMIC MODEL IN A MARKOVIAN RANDOM ENVIRONMENT

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A large number of authors have developed computational and qualitative results concerning the basic deterministic SIS model and variants that take into account special characteristics, such as the inclusion of demography, latent periods, population heterogeneities, etc. The stochastic counterpart of the SIS model has also received considerable attention. Its crucial difference from the deterministic one, is that extinction of the epidemic occurs with probability one in the stochastic model, when there is no external source of infection. Thus, the interest of the investigators lies in the behavior of the epidemic till its extinction, that is usually quantified with the so-called quasi-stationary distribution.

One drawback of many studies dealing with SIS models (both deterministic and stochastic) is that they do not account for seasonality effects and environmental changes that may influence the infection and/or the recovery rates. Seasonality is a very important factor in epidemic models and encompasses the variation patterns in climate and social behavior that are repeated every year. For instance, in temperate regions, influenza outbreaks occur annually during the winter, while meningococcal and measles outbreaks occur with the beginning of the dry season in warmer regions. Apart from seasonality, random or regular events may influence the weather conditions and/or the human behavior and consequently affect the dynamics of an epidemic process (e.g. sudden changes in temperature or humidity, the passing of a typhoon, a school holiday, etc.). Seasonality has often been incorporated into epidemic models by representing the transmission/recovery rates as sinusoidal forcing functions. However, the consideration of an underlying Markov chain, that models the changes of the environment and influences these rates, can represent both regular seasonal variation and random events.

Our research builds on the earlier works of Slatkin (1) and Gray et al. (2) and aims to quantify further the deterministic SIS model in a Markovian environment. In particular, we propose computational approaches for the determination of various distributions that quantify the evolution of the number of infective individuals in the population.

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ENSURING THE LONG-TERM RESILIENCE OF VACCINATION PROGRAMS: INSIGHT FROM GENERAL BEHAVIOUR-DISEASE MODELS FOR THE CONFLICT BETWEEN PUBLIC AND PRIVATE INTEREST

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Ensuring a high degree of long-term resilience of vaccination programs with respect to the external threats that might appear in voluntary vaccination systems is a main task of modern public health systems (PHS). In this paper we study two coupled behaviour-infection models for voluntary vaccination systems (2; 3; 4; 5). The first one is a simpler model where the PHS is the only provider of information about the payoffs of infections and vaccines. We show the conditions under which the PHS can fail in reaching the objective of infection elimination even in this potentially optimal circumstance. The second one is a general model for the conflict between private and public interest (2; 4) where the information provided by the PHS considered in the previous model, competes with the private information that is spontaneously exchanged by private individuals during their daily (real or virtual) social encounters. The analysis of this model allows to offer a quite complete picture of which are the critical communication parameters, and related actions, that wise public health systems should undertake to influence individuals perceptions on payoffs of vaccination and infection, in order to mitigate

resistance to vaccination and enhance the resilience of vaccination programs.

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A TIME OPTIMAL CONTROL PROBLEM FOR BIODEGRADATION PROCESSES IN COMPOSTING BIOCELL

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A landfill is nowadays conceived as a biological active environment where the natural and spontaneous process of degradation is controlled to treat the organic fraction of solid waste. In particular, the aerobic phenomenon of digestion is strongly used to reduce the total amount of organic matter and produce compost that can be used as a fertilizer in agriculture.

In this framework we propose a model for composting processes in biocell where the organic matter is degraded by an aerobic bacterial population. Besides the digestion process, other phenomena, like hydrolysis and biomass decay, are taken into account.

We formulate a minimal time problem to reduce the amount of substrate below a given threshold by controlling the effects of oxygen on the aerobic digestion process. We can give a full characterization of the controllability set of any target and prove the existence of an optimal control strategy to reach the target configuration in a finite time from any initial state in the controllability set.

We can prove rigorously that the optimal control profile is constant assuming its maximal value or of bang-bang type with a unique switching time passing from the minimal to the maximal value.

FITTING OF A IMMUNE RESPONSE MODEL TO CD4⁺ T CELL DATA IN LYMPHOCYTIC CHORIOMENINGITIS VIRUS LCMV INFECTION

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We fit a immune response model to data reporting the immune response CD4+ T cell concentration from mice infected with lymphocytic choriomeningitis virus LCMV. We used an ODE model that considers both CD4+ T cells, regulatory T cells (Tregs) and interleukine-2 (IL-2) density. The fittings of this model were able to explain the immune activation phase following infection and the subsequent relaxation phase for both the gp61 and NP309 LCMV epitopes. Furthermore, the fittings for the gp61 epitope and the NP309 epitope differ only through the intensity of antigen stimulation and its action times.

EVOLUTIONARY DYNAMICS OF VACCINATION STRATEGIES AND MORBIDITY RISKS IN THE REINFECTION SIRI MODEL

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For diseases in which vaccination is not compulsory, individuals take into account different aspects when deciding between to vaccinate or not. Namely, the decision depends on the morbidity risks from both vaccination and infection, and also depends on the probability of being infected, which varies with the course of the disease and the decisions of other individuals.

Using some basic game theoretical concepts, we study the evolution of the individual vaccination strategies depending upon the morbidity risks and upon the parameters of the basic reinfection SIRI model. In (1), it was introduced the evolutionary vaccination dynamics for an homogeneous vaccination strategy of the population, where the individuals change their strategies along time, such that their payoffs increase. Here, we also introduce the dynamical evolution of the morbidity risks and analyze the changes provoked on the population vaccination strategy.

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MODELLING VACCINE TRIALS

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In this talk we apply a simple stochastic epidemiological process, the linear infection model, to a vaccine trial and estimate the vaccine efficacy. We do this first in a maximum likelihood framework and then improve the analysis via a Bayesian approach to explicitly obtain a probability for the vaccine efficacy based on the empirical data from the trial.

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OPTIMAL CONTROL MODEL OF TUMOR TREATMENT IN THE CONTEXT OF CANCER STEM CELL

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We consider cancer cytotoxic drugs as an optimal control problem to stabilize a heterogeneous tumor by attacking not the most abundant cancer cells, but those that are crucial in the tumor ecosystem. We propose a mathematical cancer stem cell model that translates the hierarchy and heterogeneity of cancer cell types by including highly structured tumorigenic cancer stem cells that yield low differentiated cancer cells. With respect to the optimal control problem, under a certain admissibility hypothesis, the solution of our problem is the well-known most rapid approach path to the equilibrium. In other cases, we use bang bang controls as an optimal solution. These control treatments can retain the entire tumor in the neighborhood of an equilibrium. We simulate the bang bang numerically and demonstrate that the optimal drug scheduling should be administered continuously over long periods with short rest periods. Moreover, our simulations indicate that combining multidrug therapies and monotherapies is more efficient for heterogeneous tumors than using each one separately.

EFFECTS OF NONLOCAL AND GLOBAL CONSUMPTION OF RESOURCES IN POPULATION MODELS

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Spatio-temporal pattern formation in interacting population models are studied with the help of system of reaction-diffusion equations. Some of them are unable to generate stationary patterns in presence of self-diffusion terms, for e.g., Rosenzweig-MacArthur model, competition model etc. Introduction of cross-diffusion terms and advection terms in such models, with appropriate ecological justifications, can induce stationary patterns. Recently, researchers have explored that considering integro-differential equation models can capture such patterns (3). Inclusion of nonlocal as well as global consumption and/or interaction terms facilitate the generation of such patterns along with stationary and moving pulse solutions. In this talk, I consider spatio-temporal population models with nonlocal as well as global consumption of resources. Conditions for Turing and spatial Hopf bifurcation around the coexisting homogeneous steady-state are derived from the nonlocal model and the analytical results are numerically verified (2). Conditions for the bifurcation of stationary and moving pulses in the case of global consumption of resource are also determined. Their existence is confirmed through numerical simulations.

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RELATION BETWEEN THE CONCENTRATION OF T CELLS AND TREGS AND THEIR ANTIGENIC STIMULATION

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We study an ODE system that models immune responses by CD4⁺ T cells, with the presence of Regulatory T cells (Tregs) (3). T cells trigger an immune response in the presence of their specific antigen. However, auto-immune diseases may appear when T cells are stimulated by our self-antigens. Regulatory T cells (Tregs) play a role in limiting these responses due to their immune-suppressive ability (2).

We use the model presented in Pinto *et al.* (3), that was based in the model from Burroughs *et al.* (1). We assume that the secreting T cells have a lower death rate than the non secreting T cells and that the active Tregs also have a lower death rate than the inactive Tregs, as in Pinto *et al.* (3). Furthermore, we also consider the linear tuning between the antigenic stimulation of T cells and the antigenic stimulation of Tregs presented in Pinto *et al.* (3).

We present explicit exact formulas that explain the numerical results observed by Burroughs *et al.* (4) and improve the results in Oliveira *et al.* (5). We obtained

a polynomial that gives the relation at equilibria (stable or unstable) between the concentration of T cells, the concentration of Tregs and the antigenic stimulation of T cells. Furthermore, we present the Jacobian matrix that allows us to compute its eigenvalues, and to determine the equilibria stability. For some parameter values, we found a hysteresis, characterized by a region of bistability, with two stable equilibria and one unstable equilibrium, bounded by two thresholds of antigenic stimulation of T cells. For some parameter values, we observe an unfold of the hysteresis. Furthermore, for some values of the slope parameter of the tuning, we observe the appearance of an isolated region with equilibria, an isola, and for other values of the slope parameter, we observe a transcritical bifurcation.

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HETEROGENEITY IN SUSCEPTIBILITY INDUCES UNPREDICTABLE OUTBREAK

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Reinfection is known to induce complex epidemiological dynamics (e.g. sustained oscillation) due to the time-series change in susceptibility. The simplest model describing reinfection shows three epidemiological dynamics; disease-free, epidemic and endemic. These three dynamics can be classied by two reproduction numbers, basic reproduction number and reproduction number by only reinfection. However, the simplest model takes into account only two variations of susceptibility, susceptibility at first infection and second or later infection. To relax this assumption we construct a parsimonious model describing three susceptibilities, i) susceptibility at first infection, ii) partial protection at second or later infection and iii) perfect protection at second or later infection. This model demonstrates an interesting dynamics, outbreak occurs after the temporal decrease in the number of infected individuals. We named this dynamics as "delayed outbreak". Basic reproduction number cannot capture outbreak potential of this dynamics. Our model is too simple to understand rich dynamics induced by heterogeneity in susceptibility, for example, endemic situation is not captured in this model. To understand the dynamics with heterogeneity in susceptibility, we expand our model to a model describing the transition of susceptibility by reinfection. We confirmed that "delayed outbreak" is robust if the heterogeneity in susceptibility against reinfection is existed.

TIME-DEPENDENT PROPAGATORS FOR STOCHASTIC MODELS OF GENE EXPRESSION: AN ANALYTICAL METHOD

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The inherent stochasticity of gene expression in the context of regulatory networks profoundly influences the dynamics of the involved species. Mathematically speaking, the propagators which describe the evolution of such networks in time are typically defined as solutions of the corresponding Chemical Master Equation (CME). However, it is not possible in general to obtain exact solutions to the CME in closed form, which is due largely to the high dimensionality thereof. Here, we propose an analytical method for the efficient approximation of these propagators. We illustrate our method on the basis of two categories of stochastic models for gene expression that have been discussed in the literature. The requisite procedure consists of three steps: a probability-generating function is introduced which transforms the CME into (a system of) partial differential equations (PDEs); application of the method of characteristics then yields (a system of) ordinary differential equations (ODEs) which can be solved using dynamical systems techniques, giving closed-form expressions for the generating function; finally, propagator probabilities can be reconstructed numerically from these ex-

pressions via the Cauchy integral formula. The resulting ‘library’ of propagators lends itself naturally to implementation in a Bayesian parameter inference scheme, and can be generalised systematically to related categories of stochastic models beyond the ones considered here.

A WAVELET-BASED METHOD FOR REVEALING TAYLOR'S LAW IN SPECIES ABUNDANCE

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Taylor's ecological law, which states the power-law functional dependence between the variance and the mean number of organisms sampled within their habitat area is a phenomenon indicated for a large variety of species. It can be associated with their distribution satisfying the exponential dispersion models (1). The latter fact results also in certain deviations from the exponential population growth dynamics (2). At the same time, revealing an accurate power exponents and distribution fitting under realistic conditions of the non-uniform sampling of spatially scattered data may represent a non-trivial optimization procedure.

Here a novel approach will be reported. It is based on plotting the logarithms of the Haar wavelet and averaging coefficients at the smallest scale squared that allows for an effective decomposition of samples into Taylor's law component and the rest stochastic counterpart with a robust linear regression of the former.

Applicability of the method is illustrated by both simulated samples satisfying the Poisson-gamma distribution and the real catch rates of Bocaccio rockfish (*Sebastes paucispinis*).

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CONTROLLING THE TRANSMISSION DYNAMICS OF DENGUE BY *WOLBACHIA*-BASED STRATEGIES

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Dengue is a mosquito-borne viral disease transmitted through the bite of infected female of *Aedes spp.*, with predominance of *Aedes aegypti*. These mosquitoes are also able to transmit chikungunya, yellow fever and Zika infection. Dengue infection can be caused by four distinct RNA viruses of the *Flaviviridae* family, each of them causes a different type of clinical manifestation of dengue, varying from classic form to severe dengue shock syndrome and the fatal hemorrhagic dengue form.

The deliberated infection of *A. aegypti* with *Wolbachia* bacterium has been study for many years, as an potential mosquito control technique. *Wolbachia*-infected mosquitoes can reduce dengue transmission via two mechanisms: by inhibition of the viral replication (1), and by reduction of the mosquito lifespan (2), reducing the probability to infect a susceptible human.

The aim of this work is to find a strategy of introduction of *Wolbachia*-infected mosquitoes to control the transmission dynamics of dengue. A mathematical compartmental model is considered, which quantifies the effect of introduction of the *Wolbachia* into the mosquito population on human population dengue cases (3). This model describes four human population compartments: susceptible, exposed, infected and recovered. Also a wild and *Wolbachia*-infected mosquito populations are considered of four compartments each: aquatic, susceptible, exposed and infected. This model is extended by the introduction of the control function u , that characterizes the daily releases of *Wolbachia*-infected mosquitoes. Based on the

optimal control theory (4), a strategy that cause the extinction of dengue epidemic is obtained. Numerical simulations reveal that the proposed strategy permits the suppression of the dengue disease in a population.

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ON THE ROLE OF NONINFECTIOUS VIRIONS IN AN IN-HOST DENGUE INFECTION

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Synthesis of new virions in DENV-infected cells requires cleavage of the membrane protein prM to M by the cellular enzyme furin before secretion of mature virions from the cell (1). This process, however, appears to be inefficient for DENV because of the high proportion of immature virions containing uncleaved prM in patient serum (2). The immature prM-containing DENV particles are essentially not infectious to cells because uncleaved prM renders them incompetent for membrane fusion (3). However, the immature virions regain full infectivity when they interact with anti-prM antibodies because opsonisation facilitates virion fusion into Fc receptor-expressing cells (4).

We propose a mathematical model for an in-host DENV infection which takes into account the infectivity state of the virions, and the interaction of DENV-producing cells with plasmacytoid dendritic cells (pDCs). pDCs have an important role for sensing invading pathogens and are major producer of interferon- α , which triggers the innate immune response (5). We compute the basic reproduction number R_0 as a function of the proportion of infected cells producing noninfectious DENV and use numerical simulations to compare the host's immune response in a primary and a secondary dengue infection. The results from the simulations can be placed in an evolutionary context whereby the virus strives to maximise its chance for post-infection transmission from the human host to the mosquito vector, as well as in the immunoregulatory framework with pDCs serving as a bridge between innate (NK cells) and adaptive (T cells and antibody) immune response.

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AUTOMATED DATA-DRIVEN ESTIMATION OF RARE EVENT PROBABILITIES

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Recent development and improvement of computational tools enabled researchers to create high-fidelity dynamical models in various scientific disciplines. Such detailed model may help the researcher discover insights into the system or consider multiple scenarios without costly or difficult experiments. However, use of a dynamical model may not be computationally feasible if the event of interest is rare. Presence of multiple reaction rate parameters combined with a large ensemble of simulations that are required to obtain an accurate estimate makes the rare event characterization one of the most challenging problems in stochastic simulation.

Rare event by definition does not occur often. Therefore, generating unweighted trajectories to estimate its probability requires a large ensemble, and variance reduction is slow (square root of the ensemble size (1)). Another difficulty is obtaining information on the amount of perturbation required in each reaction rate parameter to produce the rare event of interest. Randomly perturbing each parameter in a linearized manner is not computationally feasible for large systems. Doubly weighted stochastic simulation algorithm (dwSSA) by Daigle et al (2) introduces a modified version of Gillespie's stochastic simulation algorithm (3) that efficiently and automatically computes the probability of a rare event without sacrificing accuracy. In their paper authors illustrate the dwSSA performing orders of magnitude more efficiently than the SSA. However, the multilevel cross entropy method (4) in dwSSA does not always converge when system exhibits low stochasticity. In this talk, we introduce an enhanced version of the dwSSA called dwSSA⁺⁺ (5), that significantly improves the speed of convergence to the rare event of interest when the conventional multilevel cross-entropy method is either unable to converge or converges very slowly. This achievement is enabled by

a novel polynomial leaping method that uses past data to detect slow convergence as well as to find direction toward the rare event of interest. We demonstrate the performance of dwSSA⁺⁺ on a susceptible-infectious-recovered-susceptible (SIRS) disease dynamics model and compare its computational efficiency to that of dwSSA.

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QUANTITATIVE MODELLING OF TFEB NUCLEAR TRANSLOCATION DYNAMICS

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Introduction. The Transcription Factor EB (TFEB) is a key component of the transcriptional regulation of autophagy. Autophagy is a self-degradative process important for balancing sources of energy at critical times in development and in response to nutrient stress. In normal conditions, TFEB cytosolic inhibition is mediated by mTORC1 phosphorylation. Under starvation, TFEB is dephosphorylated promoting its activation and consequently its nuclear translocation. Recently, a similar behavior has been shown to occur in the nuclear compartment. The aim of this work was to develop a quantitative dynamical model of this biological system to study its behavior starting from single-cell time-series data of TFEB nuclear translocation upon periodic starvation and refeeding stimulation via an automated microfluidic device we developed in the lab.

Methods. A two-compartment model (nucleus and cytoplasm) was developed where two different species (de/phosphorylated TFEB) for each compartment are considered. The transport and (de)phosphorylation kinetics are assumed to be first order kinetics function of the input (the nutrients concentration). By introducing a conservation relation of the total TFEB amount, the model is reduced to a 3D system of differential linear equations in the states and nonlinear in the input. A feedback action on the output was also considered to model TFEB regulation of autophagy. The model parameters were fitted from the literature.

Results. The model is able to recapitulate the behaviour observed in the microfluidic experiments, without any additional parameter fitting. It also captures the different time scales of TFEB translocation and autophagic action. The model supports the hypothesis and autophagy activation counteracts the effects of starvation revealing a novel feedback loop biological mechanism.

BIFURCATIONS OF TURING PATTERNS AND TRAVELLING WAVES IN REACTION/DIFFUSION VEGETATION MODELS

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Regular vegetation patterns fascinated plant ecologist since long time and development of a comprehensive theory of their formation is still in progress. Different patterns, such as spots, labyrinths, gaps, and stripes, as well as plant rings and fungal fairy rings occur in a variety of natural environments. It has been hypothesized that their development is affected by global phenomena like climate change. In order to explain such vegetation patterns, especially for semiarid ecosystems, water limitation has been proposed as the causal mechanism in both empirical and modeling studies. Several models were formulated as systems of PDEs, or using individual-based modelling approach, representing plant biomass, soil-water and surface water ((1; 2; 3; 4; 5; 6; 7; 8)). Treating water availability as the only controlling mechanism of pattern formation fails to explain the occurrence of vegetation patterns in arid environments. An alternative explanation for the occurrence

of regular vegetation patterns has been related to the plant-soil negative feedback. In a recent study Carteni et al. (9) analyzes the important role of the plant-soil negative feedback in the occurrence of ring patches in clonal plants (10). While previous studies considered water limitation and plant-soil feedback negative as alternative explanations for the development of regular vegetation patterns, for the first time, Marasco et al. (1) and (11) explored the hypothesis that both water limitation and negative plant-soil feedback contribute in the formation of regular and irregular vegetation patterns and tree biodiversity (Mazzoleni et al. (12)).

In this work we present a numerical bifurcation analysis of a vegetation model which includes negative plant-soil feedback, based on the PDE model of Marasco et al. (1). The study has revealed the existence of variety of different spatial patterns in the space arising from Turing bifurcation of the homogeneous state, which then may manifest symmetry-breaking and symmetry-preserving bifurcations. The effect of the precipitation rate is analyzed as system parameter. Co-existence between different patterns has been observed in a wide range of precipitation rate. The effect of boundary conditions on the nonlinear dynamics is discussed and the appearance of travelling waves and different kind of periodic solution is also exterminated. Finally, we discuss the prediction of catastrophic shifts from vegetation patterns to bare soil solutions, as the precipitation rate is reduced as consequence of climate change.

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ENZYMATIC HYDROLYSIS OF LIGNOCELLULOSIC BIOMASS: MODEL DEVELOPMENT FOR REACTOR DESIGN PURPOSES

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Biorefinery processes for the production of second generation biofuels and bio-commodities are based on the use of waste lignocellulosic biomasses as a renewable feedstock. The sugar-based biorefinery platform includes biomass pretreatment and hydrolysis of structural polysaccharides as the first steps of the feedstock transformation. Hydrolysis of cellulose and hemicellulose in real biomass can be catalyzed by cellulase enzymes cocktails. The process has been developed up to industrial scale even though the scientific community is still active in investigating several critical issues in order to reduce costs of the process. The process allows obtaining a concentrated sugar aqueous solution (hydrolysate) from the heterogeneous conversion of the complex substrate (biomass) by the catalytic action of cellulases and beta-glucosidase dissolved in the liquid phase. The issues related to the reactor design include multi-scale phenomena affecting reaction kinetics, hydrodynamics as well as mass transfer of the biphasic system. The recent literature has been reviewed in order to highlight the state of the art about modelling of enzyme-catalyzed cellulose hydrolysis kinetics (1; 2) , modelling of hydrolysis reactors (3) , and optimization of process strategies (4) . Moreover, in the framework of the project Waste2Fuels (H2020-LCE-11-2015 g.a. n654623), semi-mechanistic models of agro-food waste enzymatic hydrolysis have been assessed in order to obtain quantitative tools for bioreactor modelling. The effect

of biomass pretreatment in terms of delignification degree has been quantified through the assessment of kinetic parameters of two agro-food wastes (apple pomace and coffee silverskin).

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A GSPT APPROACH TO PERTURBED SIR AND SIRWS MODELS

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In this seminar we use tools from geometric singular perturbation theory to analyse two perturbed versions of the classic SIR model, and a modified version of the SIRWS model proposed by Dafilis et al. in 2012 (1). The main tool we exploit is the entry-exit function, as presented by De Maesschalck and Schecter in 2015 (2), which gives details regarding the behaviour of the orbit near the critical manifold.

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ON THE CONSTRUCTION OF EMBEDDED FUNCTIONAL CONNECTIVITY NETWORKS FROM FMRI DATA

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Functional magnetic resonance imaging (fMRI) produces 3D images of brain activity as reflected by the hemodynamic response, i.e. the flow of blood to active neurons, usually for a period of 3-15 min every 1-4 sec. In a typical fMRI experiment (e.g. using a 3Tesla MRI) are acquired 45 slices every approximately 3 sec. This results to several thousands of images of a typical size of 64x64 pixels. Usually, the experiment may be repeated several times for the same subject and may also involve groups of subjects to facilitate and strengthen the statistical analysis. Thus, regarding the construction of functional connectivity networks between brain regions one confronts with the challenge of dimensionality reduction ((1)). Here, we employ a data-driven approach to dimensionality reduction aiming to construct embedded brain functional connectivity networks in low dimensional manifolds spanned by few independent vectors. Towards this aim, we use and compare the classification efficiency of both linear (PCA, MDS) and non-linear Isometric Feature Mapping (ISOMAP) ((2)) and Diffusion Maps ((3)) manifold learning algorithms. The experiment regards the resting-state activity of normal subjects and patients suffering from schizophrenia.

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ANALYTICAL AND NUMERICAL METHODS IN EPIDEMIOLOGICAL MODELS

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We describe the dynamics of vector-borne diseases using mathematical tools. We discuss numerical aspects of this subject (2). We concentrate on spatial epidemiological models (3) and models described by stochastic differential equations (1).

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IMPROVING THE MATHEMATICAL MODEL OF BCG IMMUNOTHERAPY IN SUPERFICIAL CANCER AND ITS ANALYSIS

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We present a theoretical study of superficial bladder cancer growth and its treatment with Bacillus Calmette-Guerin (BCG), an attenuated strain of *Mycobacterium bovis*. The purpose of this work is to improve an existing mathematical model as a result of new biological research. The model describes tumor-immune interactions in the bladder cancer as a result of BCG therapy. Here we explore the effect of recent biological developments on the model. The innovation is expressed in the changing model equations, including the addition of the Tumor-Ag-activated APCs (TAA) mechanism, the inclusion of a delay in the immune system equation and the addition of a new equation that describes the immune system inhibitors, *Tregs* cells.

We utilized a systems biology approach to describe the BCG-tumor-immune-*Tregs* rapport and translate it into a set of mathematical ordinary differential equations (ODEs). The variables in the system of equations are the bacteria cells, immune cells, tumor infected cells, tumor uninfected cells and *Tregs* cells. We performed a mathematical analysis of the new model, including an update of equilibria, analysis of their stability properties by Lyapunov function and Hurwitz matrix, analysis of numerical simulations in MATLAB and comparison of the results to the original model. (1; 2)

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A DISCRETE-AGE STRUCTURED TB MODEL WITH FAST AND SLOW INFECTIONS

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TB infection in children is unique. Children get TB infection only from adults, not from other infected children. Currently, there are fast and slow infections in TB. It is a slow infection because the latency period is long enough. It becomes fast infection because of second infection. In this paper, we derive a deterministic model to understand the dynamics of TB spread with child and adult populations and fast and slow infections. Equilibrium and stability of equilibrium depending on basic reproduction ratio are derived. Some numerical simulations are given to explore TB spread dynamics.

COMPUCELL3D SIMULATIONS OF NEPHRON PROGENITOR CELLS REVEAL DIFFERENT SPEED POPULATIONS AROUND EXPERIMENTAL URETERIC TIP

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Mouse kidney developmental phase E11.5 consists of abnormal nephron progenitor (NP) cell movements (1). The purpose of this research was to find the reasons to the very slow NP cell speeds. Accordingly, the behaviour of NP cells in different locations were studied with CompuCell3D simulations that used Cellular Potts model (2). The main driving forces in those models were chemotaxis and adhesion between two different cell types. The simulations revealed two different cell speed populations, one near ureteric bud (UB) tip, and other at the corner UB. The finding was validated by comparing simulation speeds and locations to experiments. For this comparison, python and Self-Organizing Maps were used (1; 3).

This work was also presented as a Poster.

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A GENERAL ECO-PHYSIOLOGICAL FRAMEWORK TO MODEL THE INTERACTIONS BETWEEN PHLOEM FEEDER PESTS AND PLANTS

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Phloem feeder pests alter plant development and can transmit lethal viruses, thus representing a major threat for crops. In agronomy, mathematical models describing temporal plant growth dynamics have rarely been coupled to demographic models of pest dynamics. In ecology, resource-consumer models have been often applied to plant-pest system, but they usually adopt a simplistic description of the plant, which is not suited to address agronomic issues. In the present work, we extended a classical plant growth model, describing carbon and nitrogen assimilation and allocation, by integrating *i)* the population dynamics of a phloem feeder and *ii)* the development of plant defence. We demonstrated the model by calibrating it against data of peach trees *Prunus persica* subjected to different fertilization and irrigation regimes, infested by the green aphid *Myzus persicae*. Our results suggest that aphid infestation induces the plant to produce defensive compounds that impair aphid fecundity. Moreover, both plant and pest biomass positively respond to an increase of fertilization and irrigation, thus suggesting the existence of a mechanism of bottom-up control in the plant-pest system. The proposed framework enables novel predictions on phloem-feeder control through cultural practices, along with possible effects of climate change which is expected to alter water availability in the next future.

DYNAMICAL SYSTEMS FOR MODELLING OF UNIDIRECTIONAL SYMPLASTIC GROWTH OF PLANT TISSUES

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Understanding the principles and mechanisms of cell growth in plant tissue remains an outstanding challenge for modern developmental biology. Cell-based modeling is a widely used technique for studying the geometric and topological features of plant tissue morphology during growth. We proposed a system that allows to simulate symplastic unidirectional growth of linear plant organs and thereby generate cellular patterns for plant tissues in computational experiments. To do this, we modified the formalism of differential L-systems for describing a dynamic model for symplastic growth of tissue, taking into account the biomechanical properties of cells (1). Taking into account the specificity of geometry (parallel longitudinal rows of cells) for modeling tissue from growing and dividing cells, we modified the formalism of L-systems. The dynamics of the cellular structure consisting of N parallel longitudinal rows of cells, we modeled using N one-dimensional dL-systems, each of which simulates the dynamics of the structure of a separate longitudinal row. In order to provide the coordinated work of these dL-systems, we introduced another one-dimensional dL-system, which simulates the dynamics of the structure of cell fragments. As an example, we demonstrate the results of computational experiments for epidermal cells of a linear leaf (2), and cells of a root tip. The reported study was funded by Russian Foundation for Basic Research (RFBR) according to the research project No 17-29-08028.

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MODELLING THE SPREAD OF HCV AMONGST PEOPLE WHO INJECT DRUGS

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Mathematical modelling techniques are now being used by health organizations worldwide to help understand the likely impact that intervention strategies treatment options and combinations of these have on the prevalence and incidence of hepatitis C virus (HCV) in the people who inject drugs (PWID) population. In this talk, we develop a deterministic, compartmental mathematical model to approximate the spread of the HCV in a PWID population. The model assumes that after injection needles adopt the most infectious state of their previous state or that of the PWID who last injected with them. Using analytical techniques, we find that the model behaviour is determined by the basic reproductive number R_0 , where $R_0 = 1$ is a critical threshold separating two different outcomes. If $R_0 \leq 1$ there is only the disease-free equilibrium whereas if $R_0 > 1$ there is the disease-free equilibrium and a unique endemic equilibrium. The disease-free equilibrium is globally stable if $R_0 \leq 1$ and unstable if $R_0 > 1$. Then we look at an approximate model obtained by using the fact that the timescale on which injections take place is much faster than the timescale of epidemiological change. The approximate model has the same equilibria as the full model. For the approximate model we showed that if $R_0 > 1$ the endemic equilibrium is locally stable. Simulations with realistic parameter values are used to illustrate the analytical results. A brief summary concludes the talk.

THE LOTKA-VOLTERRA COMPETITION MODEL WITH HOLLING TYPE II FUNCTIONAL REPOSE

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In this work we present a two species interference competition model with Holling type II functional response (1) that extends the classical Lotka-Volterra competition model (4).

In Nature, species coexistence is much more frequent than what the classical competition model predicts, so that scientists look for mechanisms that explain such a coexistence (2), (3), (5), (6). The incorporation of the Holling type II functional response to the classical model can be understood as the ability of one species to limit the effect of competitors provided that the number of individuals of each species is different enough. The model presented herein expands the scenarios found in the classical competition model in two different ways:

1. Displaying dynamical scenarios not allowed by the classical model in the form of *conditional coexistence*. That is, depending on the initial number of individuals there is i) bi-stable conditional coexistence when either species coexist or one of the species goes extinct or ii) tri-stable conditional coexistence, meaning that either species coexist or any of the species goes extinct.
2. Expanding the range of parameter values that enable coexistence in the classical model. In addition, new regions show up in the parameter space related to the above mentioned bi and tri-stable conditional coexistence.

In particular, we fully analyze the model with Holling type II functional response on just one species. We deal also with the full model under the assumptions of symmetrical and asymmetrical competition. In the most general case, numerical simulations illustrate the possible competition outcomes.

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COMPUTING PERIODIC SOLUTIONS FOR COMPLEX MODELS IN POPULATION DYNAMICS

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Periodic solutions of renewal equations (REs) can be approximated, within a continuation framework, using collocation methods. In this context periodic solutions are conveniently expressed as solutions of two-point BVPs. Collocation for REs has mainly been developed for IVPs so far, thus we investigate a method based on piecewise polynomials, following those introduced in (1) for delay differential equations (DDEs). The final aim is to extend it to coupled RE/DDE systems modeling, e.g., structured populations. Moreover, in view of a theoretical convergence analysis, we mention a possible alternative inspired by (2), where a general approach to numerically solve BVPs for neutral functional differential equations is proposed. Periodic solutions of non-neutral DDEs and REs, as well as coupled systems, can be expressed as solutions of a BVP in the required form. However, this standard formulation of the problem as a two-point BVP does not satisfy the necessary conditions for the convergence of the method. We suggest, therefore, a different formulation which allows us to overcome the problems above.

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COMPARTIMENTAL MODEL OF THE TRANSMISSION OF HEPATITIS A VIRUS. GLOBAL STABILITY EQUILIBRIUM

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This paper deals with the transmission and the propagation of the hepatitis A virus in the central west of Tunisia (the city of Thala). The target of this framework is to estimate the basic reproduction number to study the global stability. We model this situation by means of a SEIRD epidemiological model where the infectious compartment is divided into symptomatic and asymptomatic ones. We study the global stability of the endemic equilibrium state by using the Lyapunov function that depends on the value of basic reproduction number R_0 . Hence, we prove that when $R_0 < 1$, the disease-free equilibrium (DFE) is globally asymptotically stable, but when $R_0 > 1$ the DFE is unstable and the endemic equilibrium is globally stable.

FINES IMPOSED ON ILLEGAL AGENTS IN THE EXPLOITATION OF THE GROUNDWATER RESOURCE. A DIFFERENTIAL GAME APPROACH

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In this paper we study a model, with a differential game approach, that proposes the exploitation of a common groundwater resource, taking into account the strategic and dynamic interactions among the users of the resource. Several factors may increase the welfare gains of firms but also the overexploitation of the aquifer can be influenced by the behavior of the agents. We show as the illegal extractions can be considered as a significant stumbling block on the path towards the implementation of better management and environmental policies. The effects of the presence of legal and illegal firms and the contribution of penalties imposed by a public authority to illegal ones, are analyzed in the study of the equilibria of the model in order to analyze the problem of non compliance with resource management regimes and discuss about policy options.

BIOINFORMATICS ANALYSIS OF DNA APTAMERS AGAINST HUMAN CARDIAC TROPONIN I

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In this study, aptamers against cardiac troponin I (cTnI) — a biomarker for the early diagnosis of acute myocardial infarction, were developed using the Systematic evolution of ligands by exponential enrichment (SELEX) and selected based on the results of bioinformatics analysis. Computational analysis of SELEX data included selection of potent sequences for further analysis and molecular docking of the selected aptamers with the target molecule (cTnI). The selection was performed based on both frequencies of these oligonucleotides and results of clusterization. Clustering was performed using USEARCH software with the 97% homology criterium. This was followed by molecular docking of the first top 10 most frequent aptamers with the molecular target using NPDock server. Two previously published aptamers were also added to the analysis. Selectivity and specificity of the selected aptamers were checked with molecular docking of both the aptamer developed for another target and the aptamer with the lowest frequency. Results of bioinformatics prediction were evaluated using experimentally determined dissociation constants (Kd) of the selected aptamerscTnI complexes. Dissociation constants were measured by bioluminescent solid-phase analysis us-

ing Ca²⁺-regulated photoprotein obelin as a label. The obtained data could be applied for the development of cTnI aptasensors as biospecific elements in molecular analyses at the acute myocardial infarction diagnostics.

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MODELING OF ANTIOXIDANT SYSTEM OF A PLANT CELL IN CONTROL AND STRESS CONDITIONS

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Reactive oxygen species (ROS) is one of the key factors that damage living systems. Plants have an antioxidant system (AOS) that effectively fights against the ROS. We present our model for AOS of a plant cell. The model was developed in COPASI environment [1]. Our study includes a complex description of the dynamics of the plant's AOS in response to stress, taking into account the separation between compartments. Our assumptions about the kinetic mechanisms and kinetic parameters of enzymes of the AOS, concentration of enzymes in different cell compartments, and generation rates of free radicals are based on the literature data and databases. In addition to chloroplasts, models of peroxisome and mitochondrial components of the AOS were created. Based on these data, stationary states in normal and stressed conditions (salt stress, water-deficient) were calculated. The research was supported by RSF (project No. 17-74-10198).

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A FRACTIONAL-ORDER RULKOV-TYPE NEURONAL MODEL

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Necessary and sufficient conditions for the asymptotic stability and instability of two-dimensional linear autonomous incommensurate systems of fractional-order Caputo difference equations are presented, similar to the continuous-time counterparts from (1; 2) and using definitions and properties of the fractional-order difference operators from (3). Moreover, the occurrence of discrete Flip and Hopf bifurcations is also discussed, choosing the fractional orders as bifurcation parameters. The theoretical results are later applied to the investigation of the stability and instability properties of a fractional-order version of the Rulkov neuronal model, as the integer-order version has been introduced in (4). Numerical simulations are further presented to illustrate the theoretical findings, revealing complex bursting behavior in the fractional-order Rulkov model.

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MATHEMATICAL MODEL FOR AUTOIMMUNE DIABETES IN HIV INFECTED PATIENTS

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Diabetes Mellitus (DM) is a disease that affects the levels of glucose in our body. It is a common condition with noteworthy related morbidity and mortality. DM diagnosis and management among patients infected with the human immunodeficiency virus (HIV) is extremely important. These patients live longer lives due to the anti-retroviral therapy (ART) and have significant chronic medical comorbidities. DM has higher prevalence among pre-ART HIV-infected patients. Moreover, more educated, hypertensive and obese HIV-infected adults are also more prone to have DM as comorbidity (1).

In this paper, we propose a within-host model for the dynamics of HIV in an infected person who has developed type 1 diabetes (T1D) (2). The model also includes macrophages, and cytokines. T1D is an autoimmune disease characterized by the destruction of β -cells, which are responsible for the production of insulin. T1D develops from an abnormal immune response, where specific clones of cytotoxic T-cells invade the pancreatic islets of Langerhans. We compute the reproduction number of the model and the disease-free equilibrium. Numerical simulations reveal interesting dynamics and help understand the role of macrophages.

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OPTIMAL PUBLIC HEALTH INTERVENTION IN A BEHAVIOURAL VACCINATION MODEL UNDER SEASONALLY VARYING TRANSMISSION

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Hesitancy and refusal of vaccines preventing childhood diseases are spreading due to ‘pseudo-rational’ behaviours: parents overweigh real and imaginary side effects of vaccines. Nonetheless, the ‘Public Health System’ (PHS) may enact public campaigns to favour vaccine uptake. To determine the optimal time profiles for such campaigns, we apply the optimal control theory to an extension of the susceptible–infectious–removed–based behavioural vaccination model by d’Onofrio *et al.* (2). The new model is of susceptible–exposed–infectious–removed type under seasonal fluctuations of the transmission rate (1). Our objective is to minimize the total costs of the disease: the disease burden, the vaccination costs and a less usual cost: the economic burden to enact the PHS campaigns. We apply the Pontryagin minimum principle and numerically explore the impact of seasonality and human behaviour on the control and spread of the target dis-

ease. We focus on two noteworthy case studies: the low (resp. intermediate) relative perceived risk of vaccine side effects and relatively low (resp. very low) speed of imitation. One general result is that seasonality may produce a remarkable impact on PHS campaigns aimed at controlling, via an increase of the vaccination uptake, the spread of a target infectious disease.

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CONSTRUCTING A VERTEX MODEL FOR CELLS OF THE WHEAT LEAF EPIDERMIS BASED ON 3D IMAGE ANALYSIS

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We consider a method for acquisition and processing images of the wheat leaf epidermis in the growth and mature zones. The aim was to classify cells according to their morphology that may predict their specialization and function. Samples of leaf fragments were stained and scanned with laser scanning microscope which was used to obtain two-channel 3D images. The virtual cut was processed with an ImageJ-plugin LSM-W² (1). The plugin has a function for obtaining a 2D image of a virtual cut reflecting the cellular structure of the epidermal layer from the 3D image. By this 2D image containing information on the position of the cell walls and nuclei, segmentation of the cells and a vertex model construction were performed using a program CellSeT (2). As a result, the vertex model of the epidermal cell structure was constructed. According to this model, the following parameters were measured: cell length and width, number of neighbors, area and other cell shape parameters. The dependence of these parameters on the spatial position of the cell in the tissue was estimated. K-means clustered cells for five clusters based on morphological properties of its shapes. Based on this clustering, the leaf fragment was marked for three zones: (i) a zone composed of round cells, (ii) a transition zone, and (iii) a zone of cell files determination. These data are useful for verifying cell-oriented models of leaf growth. The reported study was funded by Russian Foundation for Basic Research according to the research project No 17-29-08028.

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MODEL OF RODENT POPULATION DYNAMICS: CHANGES IN DYNAMIC MODES AMPLIFIED BY WEATHER FLUCTUATIONS

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The paper studies the influence of both density-dependent regulation and modifying (climatic) factors on the dynamics of a mouse-like rodent population using a mathematical model that describes the dynamics of populations with a short life cycle. The model takes into account the population age structure and density-dependent regulation of birth rate and can be expressed as follows:

$$\begin{cases} X_{n+1} = (A_1 \cdot X_n + A_2 \cdot Y_n) \cdot \exp(-\beta_1 \cdot X_n - \beta_2 \cdot Y_n) \\ Y_{n+1} = s \cdot X_n + v \cdot Y_n \end{cases}, \quad (2)$$

where n denotes the number of reproductive season; X is the number of first-time participants in the reproductive process, Y is the number of last years participants in reproduction that have survived the winter, A_1 and A_2 are reproductive potentials, s and v are survival rates and β_1 and β_2 are the limitation coefficients that characterize the influence of competition between mature individuals on the birth rate. In accordance with the biological meaning of the problem, the coefficients A_1 and A_2 are not negative, and $s \in [0, 1)$, $v \in [0, 1)$.

A substitution of the variables $s\beta_2 \cdot X \rightarrow x$, $\beta_2 \cdot Y \rightarrow y$ and coefficients $A_1 \rightarrow a_1$, $s \cdot A_2 \rightarrow a_2$, $\rho = \beta_1 / (s\beta_2)$ transforms the model (2) into a system with four parameters:

$$\begin{cases} x_{n+1} = (a_1 \cdot x_n + a_2 \cdot y_n) \cdot \exp(-\rho \cdot x_n - y_n) \\ y_{n+1} = x_n + v \cdot y_n \end{cases} \quad (3)$$

Model (3) describes relative (dimensionless) population size. x is the number of underyearlings, and y is the number of adults. The survival rate of group X is included in the birth rate a_2 , and the contribution of underyearlings to the birth rate limitation is determined by the relative intensity of its participation in the process of density-dependent regulation ρ .

It is revealed multimodality in the model proposed. This phenomenon consists in the existence of various dynamic modes under the same values of parameters, a transition to these modes determined by the initial conditions. In particular, the alternative appearance of three modes, for example, 1-, 3- and 4-cycles, as well as their bifurcation results was shown. The appearance of these modes is noteworthy, since both three-year and four-year cycles, as well as fluctuation disappearance, are noted for real populations of rodents.

We proposed an approach that reveals the multimodality in real populations. The approach is based on observation data of population dynamics and the model parameter estimates corresponding of the survey. The application of the proposed model to the description of dynamics of the bank vole population size (*Myodes glareolus*) showed that the model trajectory describes well enough the dynamics tendency, but weakly captures the real values of the population size peaks. To improve the approximation quality, a climatic factor, indirectly characterizing the food supply, was included in the model. The study of the model showed that the climatic factor influence leads to a change in the attraction basins form of the dynamic modes or the model parameter values. Both can give a trajectory shift from one mode to another. As a result, the population size is shifting from some mode attraction basin to the attraction basin of another one. Only in certain years the population can remain in an area of parameter values with similar modes (the same period cycles). In other words, population dynamics can be described by the following scheme. In the current year with certain climatic conditions, the population develops and tends to a stable mode. Next year, with different climatic conditions, this mode cannot be achieved or does not exist, and the population, adapting to new conditions, tends to another stable mode. In particular, the real dynamics of the bank vole can be represented by a sequence of alternating transients that would lead to fluctuations with 3-, 6-, 7- or 14- year period under constant climatic conditions.

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FUNCTION OVERCOMES TAXONOMY: CASE OF *atp* GENES OF FUNGI MITOCHONDRIA

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We studied the interplay between triplet composition of genes and taxonomy of the bearers. ATP synthase genes of fungal mitochondria has been studied. Each gene sequence was transformed into triplet frequency dictionary, where the reading frame shift was equal either to $t = 1$, or to $t = 3$. All gene sequences were extracted from a genome in two versions: the former contains introns, and the latter corresponds to mRNA. The distribution of the relevant points in 64-dimensional space was studied.

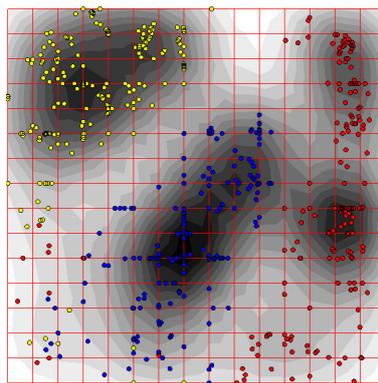


Figure 4: Clustering of genes.

We studied clustering of genes in 64-dimensional metric space; Fig. 4 shows

this distribution, *atp6* are shown in red, *atp8* are shown in green and *atp9* are shown in yellow. Obviously, the genes from the same family occupy the same cluster.

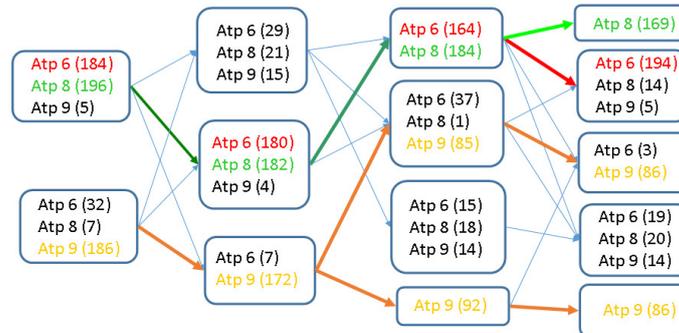


Figure 5: Distribution of genes in a series of K -means classifications.

Also, we separated the set of dictionaries by K -means into the classes, for $2 \leq K \leq 5$. For each classification we traced the composition of classes in terms of the transfer of the elements of “elder” classification into a given one. Fig. 5 shows this pattern of genes transfer. Besides, we checked a similar pattern for species distribution; that latter yielded no regularity. This difference proves the prevalence of function over taxonomy.

THE EFFECT OF WEATHER CHANGES AND SEXUAL TRANSMISSION ON THE SPREAD OF ZIKA FEVER

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In this talk, we present a compartmental model to study the transmission of Zika virus disease including spread through sexual contacts and asymptomatic carriers. To incorporate the impact of the periodicity of weather on the spread of Zika, we apply a nonautonomous model with time-dependent mosquito birth rate and biting rate, which allows us to explain the differing outcome of the epidemic in different countries of South America: using Latin Hypercube Sampling for fitting, we were able to reproduce the different outcomes of the disease in various countries. Sensitivity analysis shows that, although the most important factors in Zika transmission are the birth rate of mosquitoes and the transmission rate from mosquitoes to humans, spread through sexual contacts is also shown to be an important factor in the transmission of Zika virus: our study suggests that the practice of safe sex among those who have possibly contracted the disease, can significantly reduce the number of Zika cases.

WILSON-COWAN NEURONAL INTERACTION MODELS WITH DISTRIBUTED DELAYS

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We generalize the original Wilson-Cowan model of excitatory and inhibitory interactions in localized neuronal populations that has been derived in 1972 (1), by considering distributed time delays. We present a stability and bifurcation analysis of the generalized model with respect to two characteristic parameters of the system and we plot the stability region in the characteristic parameter plane using several types of delay kernels, highlighting the importance of a careful choice of delay kernels in the mathematical model. To substantiate the theoretical results obtained so far, we also present some numerical simulations in which we consider a Dirac kernel and a strong Gamma kernel.(2; 3; 2; 6)

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ANALYSIS OF VECTOR DISEASES WITH VERTICAL TRANSMISSION AND SPATIAL MOVEMENT

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A reaction-diffusion model of vector-borne infectious diseases is presented, which takes into account the vector's ability to keep the virus within their own population through vertical transmission, in addition to local interactions between reservoirs and vectors (1). The existence and the stability of disease free and endemic equilibria, together with the existence of backward bifurcation, are discussed. Then, we investigate analytically and numerically the traveling wave solutions of our model (3). Finally, disease threshold dynamics is studied by comparing the basic reproduction number in spatial homogeneous and heterogeneous case, through both asymptotic and numerical analysis (2).

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ADAPTED NUMERICAL METHODS FOR ADVECTION DIFFUSION PROBLEMS

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We present exponentially fitted two step peer methods for the numerical solution of systems of ordinary differential equations having oscillatory solutions (2; 3). Such equations arise for example in the semi-discretization in space of advection-diffusion problems whose solution exhibits an oscillatory behaviour, such as the Boussinesq equation (1). Exponentially fitted methods are able to exploit a-priori known information about the qualitative behaviour of the solution in order to efficiently furnish an accurate solution. Moreover peer methods are very suitable for a parallel implementation, which may be necessary when the number of spatial points increases. The effectiveness of this problem-oriented approach is shown through numerical tests on well-known problems.

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STABILITY OF THE EQUILIBRIA OF A DYNAMIC SYSTEM MODELING STEM CELL TRANSPLANTATION

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In this work we perform a complete analysis of the stability of the steady-states for a three-dimensional system modeling cell dynamics after bone marrow transplantation in chronic myeloid leukemia (CML). The basis for our approach is a two-dimensional system modeling the evolution of normal and abnormal stem cell populations, owed to Dingli and Michor (1), and its three-dimensional extension considered by Precup et al. (5) as a model for cell dynamics after bone marrow transplantation. Noticing that both mentioned systems can only deal with the acute phase of the disease, in the paper Parajdi et al. (3; 4), inspired by an idea of Neiman (2), the Dingli-Michor model has been refined in order to describe the transition from the normal state to the chronic and accelerated-acute phases in CML. The three-dimensional version of this system is considered in the present work. Its analysis involves more steady-states and is much more complex than in the case of the simplified model from (5). In addition to the theoretical results, numerical simulations are performed in order to visualize the equilibrium points, one and two-dimensional stable manifolds, and the separation surface between the basins of attraction of the asymptotically stable equilibria. Our results could serve as a basis for further research concerning personalized treatment protocols.

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FOCUSING ON LACTATE SHUTTLE: A MODEL OF BRAIN METABOLISM ANALYZED WITH CSP

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The mammalian brain utilizes glucose as its main source of energy. However, it has been recently discovered that lactate can also be considered important as a fuel and a signaling molecule in neuronal activity, especially during neuronal activation. The shuttling of lactate between the highly energy-demanding neurons and the astrocytes and during brain activation is of great importance. This lactate shuttling is currently described by two conflicting hypotheses, each one supported by experimental data: the Astrocyte to Neuron Lactate Shuttle (ANLS, according to which astrocytes provide lactate to neurons) and the Neuron to Astrocyte Lactate Shuttle (NALS, according to which neurons provide lactate to astrocytes). The mathematical models governing the brain metabolism processes are multi-scale in character, due to the wide range of time scales characterizing the various sub-processes. In such multi-scale models, it is often challenging to identify the driving processes and time-scales characterizing the dynamics of the

system. Here, a modified version of the Simpson et al. (1) model that complies with both the ANLS and NALS hypotheses is analyzed using Computational Singular Perturbation (CSP) algorithm (2), in order to acquire the underlying physical understanding of the various features exhibited by this model (e.g, metabolic profiles of astrocytes and neurons). CSP is an algorithmic method for asymptotic analysis, which was introduced in the late 1980s and has been used extensively in systems of reactive flows and biological systems. Among others, CSP can lead to the identification of (i) the processes generating the fast and slow time scales, (ii) the processes contributing to the establishing equilibrium states, (iii) the processes that control the evolution of the chemical species. The comparison of the two contradicting ANLS and NALS hypotheses is carried out via CSP, by identifying the physical features of the system that match the existing experimental results. The goal of this work is twofold: (i) a new algorithmic approach of asymptotic analysis on brain energy metabolism will be introduced, which is not hindered by the complexity of the mathematical model and (ii) the ability of CSP to manipulate neuronal activation will be demonstrated, by identifying the components of the model that influence the duration of the neuronal activation time and the desired levels of selected concentrations.

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A NOVEL VERSION OF THE VON FOERSTER EQUATION TO DESCRIBE POIKILOTHERMIC ORGANISMS CONSIDERING PHYSIOLOGICAL AGE AND REPRODUCTION RATE IN CROP PROTECTION

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Nowadays, forecasts with mathematical models in plant protection against insect pests is widely used. One of the most interesting equations to describe the phytophagous agents' life cycle is the Von Foerster equation (1). More in detail, its main potentiality is to describe a population which evolves through the life stages and over time. On the other hand, the development of poikilothermic organisms is strongly linked to the environmental parameters, which, also, have to be measured day by day with instruments placed in the monitored fields. This means that the development through the stages has to be managed by a specific function, called development rate function which expresses the interaction between the specie and the external environment. In the Von Foerster equation the age increases linearly with time: in other words, it is considered as a time with different scale while in reality it is a quantity which accumulates over time (2). In addition, the exit from the diapause period is not homogeneous, and influences in relevant way the development of the future generations in the year. Our purpose is to reformulate

the problem starting from similar Von Foerster's conditions, but considering also the new-born rate and the development through the stage ruled by the development rate function. In this way, it is possible to insert as a boundary condition of the problem the rate of diapause exit, and the initial population profile as initial condition. The result is an integro-differential equation able to describe the pest generations in the current year. Since there is the need to insert the measured daily average temperature to run the model, a numerical solution is required. Part of the work, has also concerned the validation with field data in the case of the grapevine moth *Lobesia botrana* in Castelli Romani area (Lazio, Italy).

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MODEL OF OPTIMAL TUMOR TREATMENT

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Immunotherapy is increasingly used in the treatment of cancer. If associated with chemotherapy, it can give better results (1). We have already built and analyzed a model of control problem in the framework of viability theory. In this work, the same dynamic corresponds to the constrained optimal control problem where the objective function that will be minimized, is related to the total quantity of tumor as well as to the treatment costs.

Starting from Kuznetsov's model (2) describing the interaction between two populations: tumor cells and effector cells, we insert variable controls corresponding to combined therapy: chemotherapy and immunotherapy, this leads to the following controlled dynamic system :

$$(S) \begin{cases} \dot{T} = a(1 - bT)T - \mu c(t)T - ET \\ \dot{E} = \sigma - dE + \frac{\rho TE}{g+T} - \beta TE - hc(t)E + i(t) \\ E(0) = E_0, \text{ and } T(0) = T_0 \end{cases}$$

Where $c(t)$ describes the amount of chemotherapy agent doses and $i(t)$ the immunotherapy injection. The elaborated model is studied by the deductive method that consists firstly on verifying the existence of optimal solutions and then applying necessary conditions using Pontryagins Maximum/Minimum Principle.

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MEDICAL IMAGE PROCESSING USING NVIDIA DEEP LEARNING GPU TRAINING SYSTEM

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In the last two years applying machine learning to medical imaging, especially deep learning, has achieved the state-of-the-art of performance in medical image analysis and processing. By using deep learning techniques the researchers in medical imaging attributed the availability of machine learning frameworks and libraries to simplify the work of physicians. In our work, we provide a high-level overview of how to build a fully connected deep neural network for medical image classification and segmentation, by using Deep Learning GPU Training System (DIGITS) avoiding rigorous mathematical formalism of neural networks [1]. We use the concept of solving problems by learning from experiences [2]. The goal is to create mathematical models that can be trained to produce useful outputs when fed input data. On the other hand we will demonstrate how to train a fully convolutional network (FCN) to segment and classify lung cancer tissues found in computed tomographic (CT) on abdominal images using DIGITS. [3]

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ON THE DYNAMICS OF A SYSTEM MODELING WATERBORNE DISEASES

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Infectious diseases continue to debilitate and to cause death worldwide (more than 3.5 million deaths a year according to WHO estimates). A small sampling of diseases in common waterborne infections includes Cholera, Giardia, Cryptosporidium, Campylobacter, Typhoid and Paratyphoid fevers, hepatitis A and E, rotavirus. [2]); these can be caused by a variety of pathogenic microbes (bacteria, protozoa, etc.) in contaminated water. Unfortunately, severe waterborne disease outbreaks continue to occur, such as Cholera in Haiti from October 2010 to January 2014 which caused 8531 deaths and 696922 cumulative cases (PAHO's Interactive Report of Cholera Outbreak); the Zimbabwe cholera epidemic from August 2008 to July 2009 which caused more than 98000 cases and 4200 deaths (WHO, 2009). Several different factors must be considered in attempting to understand waterborne disease dynamics, including different transmission pathways. A limitation of current modeling studies in waterborne diseases, however, is that the intrinsic dynamics of the pathogens are poorly addressed, leading to incomplete, and often, inadequate understanding of the pathogen evolution and its impact on disease transmission and spread. Recently, a model describing the transmission dynamics of a waterborne bacterial infection, which sheds light on the importance of the type of intrinsic bacterial dynamics in the pathogen evolution equation has been proposed in "Yang C., Wang J. (2018), *On the intrinsic dynamics of bacteria in waterborne infections*, Mathematical Biosciences, 296, 71-81". Starting from

this paper, we thus formulate the above-mentioned model (with bacterial growth with Allee effect) using a more adequate functional response (to better express the shape of indirect/direct transmission) and on taking into account the diffusivity of each population on the model dynamics. A reaction-diffusion system modeling waterborne disease dynamics in a non-homogeneously mixed population is therefore introduced. The existence of biologically meaningful equilibria and their stability is investigated. Numerical simulations of the obtained results applied to concrete cases are shown.

A SYSTEM OF DIFFERENTIAL EQUATIONS DESCRIBING EFFECT OF IGF-1 ON HORMONAL DYNAMICS OF THE BOVINE ESTRUS CYCLE

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The bovine estrus cycle lasts on average 21 days (1) and is governed by changes in the hormonal environment. During the estrus cycle, there are on average 2 or 3 waves of follicles emerging which mature and then regress or ovulate (2).

To date there exist several models describing the estrus cycle. We have developed a model first proposed by Boer *et al.* (2017) (2) by incorporating the metabolic hormone IGF-1 into the estradiol and inhibin equations as well as modifying equations describing the hormones GnRH, LH and FSH. This results in a new model containing 12 ordinary differential equations and one algebraic equation describing hormone concentrations, dominant follicle and *corpus luteum* growth during the estrus cycle. Because the exact mechanisms are often unknown, Hill functions are used to model stimulatory or inhibitory effects of the hormone. A novel aspect of this model is the consideration of the liver which is important since the liver is the main organ producing IGF-1. The concentrations of IGF-1 are modelled using an algebraic equation.

This system is further used for investigating the relationship between IGF-1 levels and the follicle mass and estrus cycle length. We expect this new simplified model to be at least as good as the model of Boer *et al.* despite containing fewer equations.

Also, since our new model incorporates IGF-1, which is a metabolic hormone, our new system can describe and predict the effect of nutritional factors on hormones, *corpus luteum* and follicles.

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Piero Manfredi	Dep of Economics and Management, Pisa University	Italy	piero.manfredi@unipi.it;	Contributed talk
Piero Salatino	Department of Chemical, Materials and Industrial Production Engineering, Università degli Studi di Napoli Federico II	Italy	piero.salatino@unina.it;	Public Lecture
Roberta De Luca	University of Naples Federico II, Department of Mathematics and Applications "R. Caccioppoli"	Italy	roberta.deluca@unina.it;	Attendance Poster (joint with Dr. Torciccollo)
Rosalba Cacciapuoti	Università degli Studi di Napoli Federico II,	Italy	osalb.cacciapuoti@studenti.unina.it;	Attendance
Rossana Vermiglio	Department of Mathematics, Computer Science and Physics, University of Udine	Italy	rossana.vermiglio@uniud.it;	Invited Lecture
Rossella Della Marca	Department of Mathematical, Physical and Computer Sciences, University of Parma	Italy	rossella.dellamarca@unipr.it;	Poster
Ryosuke Otori	Research Center for Zoonosis Control, Hokkaido University	Japan	omori@czc.hokudai.ac.jp;	Contributed talk

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Salvatore Cuomo	Department of Mathematics and Applications, University of Naples Federico II		salvatore.cuomo@unina.it;	Invited Lecture
Sebastian-Aurelian Stefaniga	West University of Timisoara, Computer Science Department	Romania	sebastian.stefaniga@e-uvt.ro;	Poster
Slimane ben Miled	BIMS Lab, Pasteur Institute of Tunis, Tunis el Manar University	Tunis	slimane.benmiled@fst.utm.tn;	Contributed talk
Soukaina Sabir	University Mohammed V in Rabat	Morocco	souky.sabir@gmail.com;	Poster
Stefano Mazzoleni	Dipartimento di Agraria, Università degli Studi di Napoli Federico II	Italy	stefano.mazzoleni@unina.it;	Public Lecture
Svetlana Bunimovich	Ariel University	Israel	svetlanabu@ariel.ac.il;	Attendance
Tatiana Guseva	Siberian Federal University	Russia	dianema2010@mail.ru;	Contributed talk
Tatiana Shpagina	Siberian Federal University, School of Fundamental Biology and Biotechnology	Russia	shpagusa@mail.ru;	Attendance
Ulyana S. Zubairova	Institute of Cytology and Genetics SB RAS	Russia	ulyanochka@bionet.nsc.ru;	Contributed talk
Urszula Skwara	Maria Curie-Skłodowska University	Poland	uskwara@poczta.umcs.lublin.pl;	Contributed talk
Victory Fedotovskaya	Siberian Federal University, Russia	Russia	viktoria.fedotovskaia@gmail.com;	Poster
Vincenzo Capasso	Department of Mathematics, University of Milano	Italy	vincenzo.capasso@unimi.it;	Invited Lecture
Vladislav Biriukov	Siberian Federal University, Krasnoyarsk	Russia	ladislav.v.biriukov@gmail.com;	Poster
Walid Ben Aribi	Faculty of Sciences of Bizerte, University of Carthage	Tunisia	ben.aribi.walid89@gmail.com;	Poster
Yuliya Kyrychko	Department of Mathematics, University of Sussex	UK	y.kyrychko@sussex.ac.uk;	Invited Lecture
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