11th INTERNATIONAL CONFERENCE

DYNAMICAL SYSTEMS APPLIED TO BIOLOGY AND NATURAL SCIENCES

DSABNS 2020

BOOK OF ABSTRACTS

DIPARTIMENTO DI ECONOMIA E MANAGEMENT
UNIVERSITY OF TRENTO, ITALY

ISBN: 978-989-98750-7-4

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DYNAMICAL SYSTEMS APPLIED TO BIOLOGY
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11th International Conference
Dynamical Systems Applied to Biology and Natural Sciences (DSABNS)

"Gruppo Nazionale per l'Analisi Matematica, la Probabilità e le loro Applicazion"

The conference is partially supported by the SurvEthi project, which is co-funded by the Autonomous Province of Trento and the Italian Agency for Development Cooperation.

This conference has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 792494.

The 11th International Conference DSABNS was held at the Dipartimento di Economia e Management of University of Trento, in Italy, from 4-7 February, 2020. The conference has both theoretical methods and practical applications, covering research topics in population dynamics, epidemiology of infectious diseases, eco-epidemiology, molecular and antigenic evolution and methodological topics in the natural sciences and mathematics.

Local Organizers: Maíra Aguiar, UniTN & BCAM; Giorgio Guzzetta, FBK; Mattia Manica, FEM; Giovanni Marini,FEM; Valentina Marziano, FBK; Stefania Ottaviano, UniTN; Piero Poletti, FBK; Andrea Pugliese, UniTN; Federico Reali, UniTN; Roberto Ros, UniTN; Mattia Sensi, UniTN; Filippo Trentini, FBK.
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Administration Staff: Luca Valenzin, UniTN; Lara Fiamozzini, UniTN.

NB. UniTN: Università degli Studi di Trento, Italy; BCAM: Basque Center for Applied Mathematics, Basque Country, Spain; FBK: Fondazione Bruno Kessler; FEM: Fondazione Edmund Mach; UE: Universidade de Évora, Portugal; VU: Vrije Universiteit Amsterdam, The Netherlands; UNL: Universidade Nova de Lisboa, Portugal; UL: Universidade de Lisboa, Portugal; UT: Università degli Studi di Torino, Italy.

Sponsors: The organizers are grateful for the sponsorship and support of the Università degli Studi di Trento and its Dipartimento di Economia e Management, who have hosted the Conference. We thank the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement with No 792494, the European Society for Mathematical and Theoretical Biology (ESMTB), the Basque Center for Applied Mathematics (BCAM) and the Università degli Studi di Torino for funding, along with the Gruppo Nazionale per l'Analisi Matematica, la Probabilità e le loro Applicazioni (GNAMPA), as well as the SurvEthi project which is co-funded by the Autonomous Province of Trento and the Italian Agency for Development Cooperation.

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SCIENTIFIC PROGRAM

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11th CONFERENCE

"DYNAMICAL SYSTEMS APPLIED TO BIOLOGY AND NATURAL SCIENCES" (DSABNS)

FEBRUARY 4-7, 2020

SCIENTIFIC PROGRAM

DSABNS2020

CONFERENCE VENUE:

DIPARTIMENTO DI ECONOMIA E MANAGEMENT

UNIVERSITÀ DEGLI STUDI DI TRENTO

"Gruppo Nazionale per l'Analisi Matematica, la Probabilità e le loro Applicazioni"

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FEBRUARY 4th 2020						
	Aula Azzurra		Aula 2B		Aula 2C	
08:30 – 9:30	**Registration**					
09:30 – 09:45	**Opening**					
	Chair: Andrea Pugliese					
09:45 – 10:30	BAS KOOIJMAN	PUBLIC LECTURE: 40 YEARS OF DEVELOPMENT AND APPLICATION OF DYNAMIC ENERGY BUDGET THEORY	--	--	--	--
10:30 – 11:15	GIANFRANCO ANFORA	PUBLIC LECTURE: INCORPORATING MATHEMATICAL MODELS AND BIOCONTROL INTO IPM PROGRAMS FOR INVASIVE ALIEN INSECTS	--	--	--	--
11:15 – 11:40	**Coffee Break**					
	“Stochastic Models / Ecology” Chair: Paulo Doutor		**“Mathematical Epidemiology / Population Dynamics” Chair: Alberto D'Onofrio**		**“Mathematical Epidemiology/ Infectious Diseases” Chair: Nico Stollenwerk**	
11:40 – 12:10	CARLOS BRAUMANN	SUB-OPTIMAL HARVESTING POLICIES WITH STEPWISE EFFORT IN A RANDOM ENVIRONMENT	CHIARA POLETTO	HOST CONTACT DYNAMICS SHAPES RICHNESS AND DOMINANCE OF PATHOGEN STRAINS	VALENTINA MARZIANO	PARENTAL VACCINATION TO ACCELERATE THE PROGRESS TOWARDS MEASLES ELIMINATION IN ITALY
12:10 – 12:30	Ozan Kahramanogullari	STOCHASTIC MECHANISMS OF GROWTH AND BRANCHING IN MEDITERRANEAN CORAL COLONIES	Ryosuke Omori	MODELLING STUDY OF THE ASSOCIATION BETWEEN SEXUALLY TRANSMITTED INFECTIONS	Paul Georgescu	ANALYZING THE SPREAD OF A DISEASE WITH DUAL TRANSMISSION MODE VIA A METAPOPULATION MODEL: ROLES OF ACTIVE AND PASSIVE MOVEMENTS
12:30 – 12:50	Uffe Høgsbro Thygesen	OPTIMAL YIELD AND UTILITY IN STOCHASTIC BIOMASS MODELS	Andrea Tomeri	THE EFFECTS OF COMPETION AMONG INFECTORS AND DEPLETION OF SUSCEPTIBLES ON THE REALIZED GENERATION INTERVALS	Gabriel Dimitriu	GLOBAL SENSITIVITY APPROACHES FOR MODELS DESCRIBING HIV DISEASE DYNAMICS
12:50 - 13:10	Patrícia Antunes	ADDITIVE MODELS - AN APPLICATION IN NATURAL SCIENCES	Angela Martiradonna	QUALITATIVE ANALYSIS AND NUMERICAL APPROXIMATION OF AN OPTIMAL CONTROL MODEL FOR INVASIVE SPECIES	Mostafa Adimy	GLOBAL DYNAMICS OF A DIFFERENTIAL-DIFFERENCE SYSTEM: A CASE OF KERMACK-McKENDRICK EPIDEMIC SIR MODEL WITH AGE-STRUCTURED PROTECTION PHASE
13:10 – 14:30	**Lunch**					
	Chair:Anna Marciniak-Czochra					
14:30 – 15:15	ROELAND MERKS	MATHEMATICAL MODELING OF CELL-EXTRACELLULAR MATRIX INTERACTIONS TO EXPLAIN COLLECTIVE CELL BEHAVIOR AND CELL MIGRATION	--	--	--	--
	“Mathematical Epidemiology / Game Theory” Chair: Edy Soewono		**“Delayed Differential Equations / Cancer” Chair: Fabio Milner**		**“Eco-Epidemiology/ Ecology” Chair: Maíra Aguiar**	
15:20 – 15:50	MAX SOUZA	ON THE SPATIAL DISPERTION OF WOLBACHIA IN WILD MOSQUITO POPULATIONS	EZIO VENTURINO	THE INFLUENCE POPULATIONS OF SHAPE ON INTERACTING POPULATIONS	MIMMO IANNELLI	MODELING CORAL REEFS: PROBLEMS IN ECOLOGICAL CONSERVATION
15:50 – 16:10	Rinaldo M. Colombo	CONTROL PROBLEMS AND GAMES IN CONSERVATION LAWS MOTIVATED BY BIOLOGY	Elena Piretto	EGFR TRAFFICKING AND SIGNALLING: INSIGHTS FROM MATHEMATICAL MODELLING	Galina Neverova	INFLUENCE OF HARVEST ON DYNAMICS OF “PREDATOR-PREY” COMMUNITY
16:10 – 16:30	Luciano Andreozzi	ON [NAME] STABLE EQUILIBRIA	Elena A. Martynova	HOW MANY GENES FROM Wnt-CASCADE IDENTIFY tnbc-PATIENTS?	Sangeeta Saha	IMPACT OF FEAR IN A TRI-TROPHIC FOOD CHAIN MODEL INCORPORATING PREY REFUGE
16:30 – 16:50	Amira Kebir	REPLICATOR EQUATIONS FOR STRUCTURED POPULATIONS: HAWK-DOVE GAME APPLICATION	Pirmin Schlicke	A MATHEMATICAL MODEL TO PREDICT GROWTH AND SIZE OF METASTATIC TUMORS UNDER THERAPY	Paolo Freguglia	A DYNAMICAL MODEL FOR SYMPATRIC SPECIATION IN AN ECOLOGICAL NICHE
16:50 – 17:10	Alberto Pinto	NASH EQUILIBRIA IN EVOLUTIONARY COMPETITIVE MODELS OF FIRMS AND WORKERS	Attila Dénes	GLOBAL ANALYSIS OF A CANCER MODEL WITH DRUG RESISTANCE DUE TO LAMARCKIAN INDUCTION AND MICROVESICLE TRANSFER	--	--
	Chair: Nico Stollenwerk					
17:15 – 18:00	LUCIA RUSSO	THE DYNAMICS OF RING NETWORKS OF DYNAMICAL SYSTEMS WITH PERIODICALLY FORCED INPUTS	--	--	--	--
18:00 – 19:30	**Welcome Drinks and Poster Session**					**DSABNS2020**

FEBRUARY 5th 2020						
	Aula Azzurra		**Aula 2B**		**Aula 2C**	
08:45 – 9:00	**Registration**					
	Chair: MaÍra Aguiar					
09:00 – 09:45	HAL SMITH	LOTKA-VOLTERRA PREDATOR-PREY SYSTEMS MODELING VIRUS DYNAMICS IN MARINE ECOSYSTEMS AND HIV INFECTION	--	--	--	--
09:45 – 10:30	ANNA MARCINIAK-CZOCHRA	MECHANISMS OF SYMMETRY-BREAKING AND PATTERN FORMATION DURING DEVELOPMENT: INSIGHTS FROM MATHEMATICAL MODELLING	--	--	--	--
10:30 – 11:00	**Coffee Break**					
	“Mathematical Epidemiology / Vectors and Vector-borne diseases I” Chair: Giorgio Guzzetta		**“Developmental Biology / Reaction-Diffusion” Chair: Rossana Vermiglio**		**“Mathematical Epidemiology / Cell Biology” Chair: Mattia Sensi**	
11:00 – 11:30	ANDREA PUGLIESE	MODELLING THE TRANSMISSION DYNAMICS OF WEST NILE VIRUS IN EMILIA-ROMAGNA REGION (ITALY)	HEIKKI HAARIO	MODEL DISCRIMINATION BY RANDOM PATTERN DATA	NICO STOLLENWERK	FRACTIONAL FOKKER-PLANCK EQUATIONS IN POPULATION BIOLOGY
11:30 – 11:50	Pierre-Alexandre Bliman	FEEDBACK CONTROL PRINCIPLES FOR BIOLOGICAL CONTROL OF DENGUE VECTORS	Cinzia Soresina	BIFURCATIONS IN REACTION CROSS-DIFFUSION SYSTEMS FOR COMPETING SPECIES	Federico Reali	AN EXTHENDED DYNAMICAL MODEL OF α-SYNUCLIEN METABOLISM
11:50 – 12:10	Agnese Zardini	MODELLING THE SPATIO-TEMPORAL RISK OF MOSQUITO-BORNE DISEASES	Sara Sommariva	VALIDATION OF A DYNAMIC SYSTEM MODEL FOR THE COLON–RECTAL CANCER CELLS VIA CHEMICAL REACTION NETWORKS	Giovanni Filatrella	GLOBAL STABILITY ANALYSIS OF BIRHYTHMICITY IN A VAN DER POL TYPE SELF-SUSTAINED OSCILLATOR
12:10-12:30	Kamil Erguler	MODEL-BASED DESIGN AND ANALYSIS OF LIFE TABLE EXPERIMENTS FOR INSECT VECTORS OF DISEASE	Lukas Eigentler	SPATIAL SELF-ORGANISATION ENABLES SPECIES COEXISTENCE IN A MODEL FOR SAVANNA ECOSYSTEM	Simone Rusconi	POPULATION BALANCE APPROACH FOR PREDICTING POLYMER PARTICLES MORPHOLOGY
12:30-12:50	Slimane BenMiled	A CLIMATE-BASED MODEL FOR TICK LIFE CYCLE: AN INFINITE SYSTEM OF DIFFERENTIAL EQUATION APPROACH	Abdelhamid Ainouz	HOMOGENIZATION OF SOME REACTION-DIFFUSION SYSTEMS IN BIOLOGICAL TISSUES	Julia Delacour	A MODEL FOR THE GROWTH OF A p62-UBIQUITIN AGGREGATE INVOLVED IN CELLULAR AUTOPHAGY
12:50-13:10	Sk Shahid Nadim	IMPACT OF VENEREAL TRANSMISSION ON THE DYNAMICS OF VERTICALLY TRANSMITTED VIRAL DISEASES AMONG MOSQUITOES	--	--	Iacopo Ruolo	TFEB TRANSLOCATION DYNAMICS: QUANTITATIVE MODELLING AND EXPERIMENTAL ANALYSIS
13:20	**Lunch and FREE AFTERNOON**					

FEBRUARY 6th 2020						
	Aula Azzurra		Aula 2B		Aula 2C	
08:45 – 9:00	Registration					
	Chair:Maíra Aguiar					
09:00 – 09:45	SUSANNE DITLEVSEN	OSCILLATING SYSTEMS WITH COINTEGRATED PHASE PROCESSES	--	--	--	--
09:45 – 10:30	KONSTANTIN BLYUSS (Skype talk)	STOCHASTIC AND TIME-DELAYED EFFECTS IN AUTOIMMUNE DYNAMICS	--	--	--	--
10:30 – 11:00	Coffee Break					
	“Mathematical Epidemiology / Health Policy” Chair: Valentina Marziano		**“Theoretical and Numerical Methods / General Session I” Chair: Carlos Braumann**		**“Mathematical Models in Population Biology / Infectious Disease Dynamics” Chair: Max Souza**	
11:00 – 11:30	PIERO MANFREDI	THE HARD PART OF THE MEASLES ENDGAME. HINTS FROM BEHAVIOURAL EPIDEMIOLOGY	ROSSANA VERMIGLIO	NUMERICAL APPROXIMATION OF THE BASIC REPRODUCTION NUMBER FOR STRUCTURED POPULATIONS	EZIO VENTURINO	DYNAMICS OF HSV-2 INFECTION WITH A THERAPEUTIC VACCINE
11:30 – 11:50	Rossella Della Marca	RAPID VACCINE OPINION SWITCHING: OPTIMAL AWARENESS CAMPAIGNS VIA DETERMINISTIC AND HEURISTIC ALGORITHMS	Dimitri Breda	PERIODICITY, DELAYS AND NUMERICAL METHODS IN BIOMATHEMATICS: A RECENT ACCOUNT	Dmitry Gromov	TWO-LEVEL EVOLUTION OF CHRONIC VIRAL INFECTIONS AND THE EFFECT OF THE POPULATION-LEVEL CONTROL
11:50 – 12:10	Eunha Shim	MATHEMATICAL MODELING OF PUBLIC HEALTH POLICIES	Monica Salvioli	GAME THEORY OF FISHERIES MANAGEMENT	Bruno M. P. M. Oliveira	FIT OF IMMUNE RESPONSES BY CD4 + T CELLS TRIGGERED BY LCMV INFECTION
12:10-12:30	Alberto Pinto	PERIODIC VACCINATION STRATEGIES IN THE REINFECTION SIRI MODEL	Othman Cherkaoui Dekkaki	VIABILITY ANALYSIS FOR A STOCK-CAPITAL FISHERY MODEL	João Maurício de Carvalho	CANCER DYNAMICS IN HIV INFECTED PATIENTS UNDER DIFFERENT IMMUNE FUNCTIONS
12:30-12:50	Maha Alsharari	INCORPORATION OF AWARENESS PROGRAMS INTO A MODEL OF THE SPREAD OF HIV/AIDS AMONGST PEOPLE WHO INJECT DRUGS (PWIDs)	J. Leonel Rocha	ALLEE EFFECT BIFURCATION IN THE γ-RICKER POPULATION MODEL USING THE LAMBERT W FUNCTION	Sonja Radosavljevic	POVERTY TRAPS IN MULTILEVEL SYSTEMS
12:50-13:10	Hee-Dae Kwon	OPTIMAL CONTROL PROBLEM OF INFLUENZA MODELS WITH INEQUALITY CONSTRAINTS	Do Wan Kim	NON-LOCAL BOUNDARY CONDITION IN A COMPUTATIONAL DOMAIN OF EXTERIOR PROBLEMS	Andrei Halanay	A DELAY DIFFERENTIAL EQUATIONS MODEL FOR THE ACTION OF THE IMMUNE SYSTEM IN MALARIA
13:10 – 14:30	Lunch					
	Chair: Hal Smith					
14:30 – 15:15	REBECCA TYSON	PHASE-SENSITIVE CRITICAL TRANSITIONS IN PREDATOR-PREY SYSTEMS	--	--	--	--
			Aula 2A		Aula 2C	
	“Mathematical Epidemiology / Vectors and Vector-borne Diseases II” Chair: Pierre-Alexandre Bliman		**“Mathematical Epidemiology / Models for Social Behavior” Chair: Paolo Freguglia**		**“Mathematical Models in Population Biology / Predator-Prey Systems” Chair: Angela Martiradonna**	
15:20 – 15:50	EDY SOEWONO	CAUSALITY ANALYSIS OF DENGUE TRANSMISSION IN BANDUNG, INDONESIA	ALBERTO D’ONOFRIO	BEHAVIOUR INDUCED PHASE TRANSITIONS IN EPIDEMIOLOGY OF INFECTIOUS DISEASES	CHRISTIAN KUEHN	MODERN NUMERICAL CONTINUATION METHODS FOR BIOLOGICAL SYSTEMS
15:50 – 16:10	Mahmoud Ibrahim	THRESHOLD DYNAMICS IN A PERIODIC MODEL FOR ZIKA VIRUS DISEASE	José Martins	REINFECTION THRESHOLDS DETERMINED BY THE MAXIMUM CURVATURE OF THE ENDEMIC STATE	Hamlet Castillo Alvino	INTERFERENCE COMPETITION ON GROUP DEFENSE WITH HOLLING TYPE IV COMPETITIVE RESPONSE
16:10 – 16:30	Jai Prakash Tripathi	A SOCIAL INTERACTION MODEL WITH HOLLING TYPE II FUNCTIONAL RESPONSE	Prashant K.Srivastava	IMPACT OF INFORMATION ON TREATMENT AS WELL AS ON DISEASE DYNAMICS	Oksana Revutskaya	COMPLEX DYNAMICS OF DISCRETE-TIME PREDATOR-PREY SYSTEM WITH STAGE-STRUCTURED PREY
16:30 – 16:50	Urszula Skwara	NUMERICAL ASPECTS IN MATHEMATICAL MODELLING OF VECTOR-BORNE DISEASES	Giorgio Martalò	OPTIMAL STRATEGIES MINIMIZING THE CONTROL OPERATION COSTS IN BIOCELL COMPOSTING	Deeptajyoti Sen	DYNAMICAL BEHAVIOR OF PREDATOR-PREY MODEL SUBJECTED TO ALLEE EFFECT IN THE PREDATOR
16:50 – 17:10	Akhil Srivastav	MODELING THE IMPACT OF EARLY CASE DETECTION ON DENGUE TRANSMISSION: DETERMINISTIC VS STOCHASTIC	Romina Travaglini	AN OPTIMAL CONTROL PROBLEM FOR DEGRADATION OF WASTE IN LANDFILLS UNDER ANAEROBIC CONDITIONS	Partha Sarathi Mandal	IMPACT OF ADDITIVE ALLEE EFFECT ON THE DYNAMICS OF A INTRAGUILD PREDATION MODEL WITH SPECIALIST PREDATOR
	Chair: Bas Kooijman					
17:15 – 18:00	BOB W. KOOI	INDIVIDUAL DEB-BASED STRUCTURED POPULATION MODELING	--	--	--	--
19:30:00	CONFERENCE DINNER					**DSABNS2020**

FEBRUARY 7th 2020						
	Aula Azzurra		**Aula 2B**		**Aula 2C**	
08:45 – 9:00	**Registration**					
	Chair: Bob W. Kooi					
09:00 – 09:45	CONSTANTINOS SIETTOS	CAN DYNAMICAL MODELS IN BIOLOGY AND NATURAL SCIENCES GO BEYOND INFINITY?	--	--	--	--
09:45 – 10:30	MAÍRA AGUIAR	ON THE ORIGIN OF COMPLEX DYNAMICS IN MULTI-STRAIN DENGUE MODELS	--	--	--	--
10:30 – 11:00	**Coffee Break**					
	“Mathematical Epidemiology / Physiological Models” Chair: Paula Patrício		**“Multi-Scale Systems” Chair: Dimitri Breda**		**“Mathematical Epidemiology / Genetics” Chair: Heikki Haario**	
11:00 – 11:30	PAULO DOUTOR	DELAYING AGE OF INFECTION: A PERNICIOUS EFFECT OF VACCINATION	NICO STOLLENWERK	TIME SCALE SEPARATION: COMPARISON OF SINGULAR PERTURBATION AND CENTER MANIFOLD ANALYSIS UNDER SCALING	CLAUDIA FERREIRA	AEDES AEGYPTI AND WOLBACHIA INTERACTION
11:30 – 11:50	Fabio Milner	A MODEL FOR ACUTE MYELOID LEUKEMIA (AML)	Panagiotis Papaioannou	FOREX FORECASTING USING PRINCIPAL COMPONENT ANALYSIS AND LOCAL LINEAR EMBEDDING	Manuel Molina	MATHEMATICAL MODELING OF POPULATION DYNAMICS IN BIOLOGICAL SPECIES
11:50 – 12:10	Giulia Simoni	POPULATION-BASED AND PATIENT-STRATIFICATION APPROACHES APPLIED TO A HUMAN CARDIAC MODEL OF ELECTROPHYSIOLOGY	Alberto Bersani	SINGULAR PERTURBATION TECHNIQUES AND ASYMPTOTIC EXPANSIONS FOR AUXILIARY ENZYME REACTIONS	Torsten Lindström	DESTABILIZATION, STABILIZATION, AND MULTIPLE ATTRACTORS IN SATURATED MIXOTROPHIC ENVIRONMENTS
12:10 – 12:30	Erica Ipocoana	BREATHING AS A PERIODIC GAS EXCHANGE IN A DEFORMABLE POROUS MEDIUM	Evangelos Galaris	USING DATA MINING TO CONSTRUCT DYNAMICAL EQUATIONS FROM AGENT-BASED PEDESTRIAN SIMULATORS	Oksana Zhdanova	MATHEMATICAL MODELLING OF SELECTION BY A SEX-LIMITED FEMALE TRAIT: TO THE QUESTION OF LITTER SIZE POLYMORPHISM IN NATURAL POPULATIONS OF ARCTIC FOXES
12:30 – 12:50	Stefan Schuster	JENSEN'S INEQUALITY AS A TOOL FOR EXPLAINING THE EFFECT OF OSCILLATIONS ON THE AVERAGE VALUES OF VARIABLES	Mattia Sensi	A GSPT APPROACH TO EPIDEMICS ON HOMOGENEOUS GRAPHS	Tatiana Guseva	HOMEOBOX GENES: INVESTIGATING THE DEVELOPMENT OF PINUS SYLVESTRIS (SCOTS PINE)
12:50 – 14:00	**Lunch**					
	“Population Biology / Plant Dynamics” Chair: Mimmo Iannelli		–		**“Mathematical Epidemiology / Disease Control” Chair: Piero Poletti**	
14:00 – 14:30	SARA PASQUALI	A STAGE STRUCTURED DEMOGRAPHIC MODEL FOR INSECT PEST DYNAMICS	--	--	GIOVANNI PUTOTO	USING DIGITAL METHODS IN EPIDEMIOLOGY TO ADDRESS DISEASE CONTROL IN SUB SAHARAN AFRICA: EXPERIENCES AND PERSPECTIVES OF DOCTORS WITH AFRICA CUAMM
14:30 – 14:50	Annalisa Iuorio	MODELLING COMPETITIVE INTERACTIONS AND PLANT-SOIL FEEDBACK IN VEGETATION DYNAMICS	--	--	Margherita Galli	EFFECTIVENESS OF MEASLES SURVEILLANCE IN SOUTH WEST SHOA ZONE OF THE OROMIA REGION, ETHIOPIA
14:50 – 15:10	Fabio Tedone	MODELLING THE ROOT GROWTH: AN OPTIMAL CONTROL APPROACH TO LINK BIOLOGY AND ROBOTICS	--	--	Valentina Veronesi	MODELING THE INFLUENCE OF MALNUTRITION ON MEASLES EPIDEMIOLOGY IN ETHIOPIA
15:10 – 15:30	Indrajit Ghosh	ESTIMATING THE PROPORTION OF SEXUAL TRANSMISSION ON ZIKA VIRUS SPREAD	--	--	Abhishek Senapati	EFFECT OF ADULT MOSQUITO CONTROL ON DENGUE PREVALENCE IN A MULTI-PATCH SETTING: A CASE STUDY IN KOLKATA (2014–2015)
	Chairs:Andrea Pugliese, Piero Manfredi and Constantinos Siettos					
15:30 – 16:15	ROUND TABLE	Novel Coronavirus (2019-nCoV)	--	--	--	--
16:15 – 16:30	**Closing**					**DSABNS2020**

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PUBLIC LECTURES

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INCORPORATING MATHEMATICAL MODELS AND BIOCONTROL INTO IPM PROGRAMS FOR INVASIVE ALIEN INSECTS

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Biological invasions are now considered a major form of human-induced global change, due to trade globalization and the increasing movements of people, goods and vehicles, combined with climatic and environmental variability. In particular, climate change is expected to favour the spread of several species also toward higher altitudes and latitudes. The spotted wing drosophila *Drosophila suzukii* and the brown marmorated stink bug *Halyomorpha halys*, both native to Asia, are polyphagous insects with a broad climate range tolerance, facility to passive transportation and a high invasive potential. They became noxious crop pests anywhere introduced, causing heavy economic losses, and represent a serious threat for agriculture in Trento Province. Since their first detection in Trentino, many efforts have been made to develop nontoxic effective management strategies, nonetheless chemical control remains the principal tool used by farmers to reduce the pest population. There are a number of drawbacks associated with the massive use of pesticides, including increased risk of residues on fruit, worker safety reduction and ecological imbalances resulting in secondary pest outbreaks. Moreover, the use of broad-spectrum chemistries jeopardizes the results obtained with IPM on cultivated fruits. In this context, the development of alternative control methods appears urgent to ensure an economic future for the concerned fruit industry. Possible solutions would only arise from a multidisciplinary approach, from genetics to biological control and mathematical population models, aiming at understanding the fundamental aspects of the ecology of these pests and paving the way for implementing effective and sustainable control strategies. In particular, for *D. suzukii* we have characterized the life history traits of the pest and the population structure after key bottleneck periods, such as winter diapause, in order to better predict serious outbreaks and improve the effectiveness of pest management decisions. We also evaluated the potentiality of the *D. suzukii* indigenous parasitoids in open field and semi-field conditions, and the effectiveness of different biocontrol techniques. A similar approach is ongoing also for *H. halys*, for which adventive populations of the native parasitoids have been recently found in our territory.

40 YEARS OF DEVELOPMENT AND APPLICATION OF DYNAMIC ENERGY BUDGET THEORY

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I started to develop Dynamic Energy Budget (DEB) theory (8) in 1979, with the aim to apply it in physiologically-structured population models for any species of organism on earth (micro-organisms, plants, animals) and evaluate effects of toxicants at the population level, modelled as dynamic changes in (particular toxicant-specific) parameter values. The research program radiated substantially over time to ensure coherence with physiology, ecology and evolution (6; 11), involving many co-workers. Metabolic transformations and behaviour are taken into account by Synthesizing Units (5), that exploit the principle of time conservation within the class of Markov processes, while a food-depending aging module (12; 13) specifies the bottom-line exit dynamics. Attention has been given to a wide range of topics, such as surface area-volume relationships, cytoplasm-mitochondria interactions, organ size and function dynamics, including tumour development, isotope dynamics, mixotrophy, parasitism and symbiosis. A large number of popular seemingly-unrelated empirical models turn out to be special cases of DEB theory, or very good numerical approximations, such a Kleiber's "law" (1932), stating that respiration is proportional to body weight to the power of (about) 3/4, and Lavoisier's indirect calorimetry (1780), stating that heat production equals a weighted sum of dioxygen consumption and carbon dioxide and nitrogen-waste production. This is remarkable, since DEB theory makes no direct assumption about respiration, but still specifies it (and water dynamics) by closing the balances for chemical elements. Being firmly based on mass and energy conservation and other thermodynamic principles (20), I discuss arguments to expect that DEB theory will have no alternatives with a similar level of generality and simplicity (14). Simplicity is required for testing generality, due to practical limitations on data availability, and even the present level of simplicity motivated the development of advanced parameter estimation methods (18; 17). At the same, such a theory must be detailed enough to respect biodiversity for links to evolution; a fine balance indeed. Meanwhile some 850 publications (3) have been written about the theory and its applications by a rapidly expanding community of research workers from all over the world. The Add-my-Pet collection (1) of data, parameters and implied properties has been set up to test the generality of the theory for animals. This collection now has over 2000 species from all larger animal phyla; model predictions for some 3e4 data sets have a mean relative error of 0.07, supporting the generality of the theory. Apart from a priory predictable patterns in the co-variation of parameter values on plain physical grounds (4), patterns have been identified that relate to ecological and evolutionary adaptations, such as metabolic acceleration (9), 'waste-to-hurry'(8), supply-demand (15) and altricial-precocial spectra (1). We also found explanations for some remarkable findings, such as why the allocation fraction of mobilised reserve to soma follows a beta-distribution among animal species, with perplexing accuracy (16). The mean value of this parameter of all species is larger than 0.9, while a value around 0.45 maximizes reproductive output (10). My expectation is that DEB theory will eventually affect the way we think about ecology and evolution, in satisfying harmony with an army of early workers in this field (19).

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ON THE ORIGIN OF COMPLEX DYNAMICS IN MULTI-STRAIN DENGUE MODELS

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Dengue fever epidemiological dynamics shows large fluctuations in disease incidence, and several mathematical models describing the transmission of dengue viruses have been proposed to explain the irregular behavior of dengue epidemics. Multi-strain dengue models are often modelled with SIR-type models where the SIR classes are labeled for the hosts that have seen the individual strains. The extended models show complex dynamics and qualitatively a very good result when comparing empirical data and model simulations. However, modeling insights for epidemiological scenarios characterized by chaotic dynamics, such as for dengue fever epidemiology, have been largely unexplored. The problem is mathematically difficult and to make the urgently needed progress in our understanding of such dynamics, concepts from various fields of mathematics as well the availability of good data for model evaluation are needed.

In this talk, I will present a set of models motivated by dengue fever epidemiology and compare different dynamical behaviors originated when increasing complexity into the model framework.

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STOCHASTIC AND TIME-DELAYED EFFECTS IN AUTOIMMUNE DYNAMICS

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Among various causes of autoimmunity, a particularly important role is played by infections that can lead to a breakdown of immune tolerance. In this talk, I will discuss a model of immune response to a viral infection, and subsequent onset of autoimmunity, with particular account for cytokines and different types of T cells. Of particular biological relevance is the analysis of stochastic oscillations around deterministically stable states, as well as the effects of stochasticity on dynamics of the system in a bi-stable regime. I will show how variance of stochastic fluctuations and their coherence depend on system parameters (1). To make the model more realistic, it is important to also consider the effects of time delays associated with various processes involved in the development of immune response. I will discuss a method for deriving stochastic delayed differential equations and a corresponding numerical simulation algorithm, and will show how it can be used to simulate stochastic dynamics in a time-delayed model of autoimmunity (2).

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OSCILLATING SYSTEMS WITH COINTEGRATED PHASE PROCESSES

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I will present cointegration analysis (2; 2) as a method to infer the network structure of a linearly phase coupled oscillating system. By defining a class of oscillating systems with interacting phases, a data generating process is derived with a specified coupling structure of the network that resembles biological processes. In particular we study a network of Winfree oscillators (3), for which we present a statistical analysis of various simulated networks, where we conclude on the coupling structure: the direction of feedback in the phase processes and proportional coupling strength between individual components of the system. We show that we can correctly classify the network structure for such a system by cointegration analysis, for various types of coupling, including uni-/bi-directional and all-to-all coupling. I will also touch upon how to deal with high-dimensional systems. Finally, we analyze a set of EEG recordings and discuss the current applicability of cointegration analysis in the field of neuroscience. The talk is based on the papers (1; 4).

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INDIVIDUAL DEB-BASED STRUCTURED POPULATION MODELING

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In unstructured or compartmental population models the state of the population is described by one or a set of ordinary differential equations for one or a few scalar variables as a function of time. Examples are number of individuals or total biomass. In structured models time depending individual variables such as age, size, mass or energy content are taken into account (10). The dependent variables that describe the state of the population and are not scalars but a density function of these independent of all the individuals that make up the population. They can be considered as emerging properties of the group of co-specific individuals living an a bounded spatial homogeneous well-mixed environment.

The individual model used is the DEB model described in (8; 7). The Add-my-Pet collection (1) contains estimated parameters of over 2000 species from all larger animal phyla. Besides age, structural biovolume, energy reserves and maturation are the individuals state variables.

The population model will be formulated for the whole life-cycle consisting of three life-stages: embryo, juvenile and adult including the criteria for the transitions, like in the physiologically structured populations approach (11). We will assume that reproduction occurs simultaneously for all individuals and periodically, for instance with fish populations as a specific short period of the year with spawning related to mating success but also by food availability for the offspring.

The resulting model is called the Cohort Projection Model (CPM) since each individual lives in one cohort as a group of individuals that are born at the same time. It is related to a projection matrix formulation, especially the Integral Projection Model (IPM) (2; 9) method which is intermediately between the continuous-time and the well known discrete matrix projection model. Recently in (12) this approach was applied based on a previous version of the DEB model.

The CPM-method was already used in (5; 6) with the DEB model for asexual microorganisms having one juvenile life stage that propagate by binary fission in (4; 3). In a case study the results for the marbled electric ray fish *Torpedo marmorata* population are shown where all model parameter values are taken from the Add-my-Pet collection (1).

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MECHANISMS OF SYMMETRY-BREAKING AND PATTERN FORMATION DURING DEVELOPMENT: INSIGHTS FROM MATHEMATICAL MODELLING

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Cells and tissues are objects of the physical world, and therefore they obey the laws of physics and chemistry, notwithstanding the molecular complexity of biological systems. A natural question arises about the mathematical principles at play in generating such complex entities from simple laws. In this talk, I show how different pattern formation concepts may stand challenges arising from the current experimental research. Specifically, Turing-style morphogen-based models are compared to mechano-chemical models exhibiting de novo pattern formation. The latter are using geometric singular perturbation allowing separating fast and slow-scale subsystems. Patterning potential of mechano-chemical interactions is investigated using two classes of mathematical models coupling dynamics of diffusing molecular signals with a model of tissue deformation. The first class of models is based on energy minimization that leads to 4-th order partial differential equations of evolution of infinitely thin deforming tissue (pseudo-3D model), coupled with a surface reaction-diffusion equation. The second approach (full-3D model) consists of a continuous model of large tissue deformation coupled with a discrete description of spatial distribution of cells to account for active deformation of single cells. We discuss analytical and numerical challenges of the proposed models and compare the resulting patterns of tissue invagination and evagination to those observed in developmental biology.

MATHEMATICAL MODELING OF CELL-EXTRACELLULAR MATRIX INTERACTIONS TO EXPLAIN COLLECTIVE CELL BEHAVIOR AND CELL MIGRATION

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During embryonic development, the behavior of individual cells must be coordinated to create the large scale patterns and tissue movements that shape the whole embryo. Apart from chemical signals exchanged between cells, a prominent role is played by the extracellular matrix (ECM); these are the hard or jelly materials (e.g. collagens, fibronectin) that form the micro-environment of many cells in tissues. To get a better grip on the role of the extracellular matrix in determining the behavior of cells, we are developing mathematical and computational approaches to analyse the interactions off the mechanics of cells and the extracellular matrix (ECM) (1; 2; 3). The cell models are usually based on the Cellular Potts model, whereas the ECM is model is based on a variety of approaches, including the finite-element model and molecular dynamics. I will show how these mathematical approaches help to elucidate the regulation of cell migration and collective cell behavior during angiogenesis and other mechanisms, including immune cell migration.

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THE DYNAMICS OF RING NETWORKS OF DYNAMICAL SYSTEMS WITH PERIODICALLY FORCED INPUTS

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Networks describe how dynamical systems interact. A cell, or node, represents a component subsystem, and a connection represents an input from one cell to another. Applications are widespread and they include gene regulation networks, food webs, and neural networks, naming just a few. Networks often display patterns of synchrony, in which clusters of cells behave in the same manner. A related phenomenon, occurring when the system oscillates periodically, is phase-locking: cells behave the same way, except for a time delay. Coupled cell systems and symmetry group theory provide a general mathematical context for studying networks. The theory provides a classification, for any network, of all possible rigid patterns of synchrony and phase-locking: those that persist when the model equations are perturbed. It also provides methods for finding these patterns in a given model. Stability of synchronous states and periodic regimes in symmetric network can be analyzed with systematic methods based on a group theoretical approach. In this talk, I analyze transitions between symmetric and asymmetric regimes in ring networks with periodically forced connections. In particular, the network consists of a ring where the connections are periodically switched (ON/OFF) with a circular law. I consider, as an example, a sequence of n reactors where the feed position is periodically shifted according to a permutation law. I analyze the symmetry-breaking phenomena which are consequence of interaction between the natural and external forcing action. As the main parameters are varied due to the presence of Neimark-Sacker bifurcations, the system exhibits periodic regimes where the periods are exact multiples of the period of the forcing or quasi-periodic regimes. In addition to the standard phenomenon of frequency locking, we observe symmetry breaking bifurcations. While in a symmetric regime all the reactors in the network have the same time history, symmetry breaking is always coupled to a situation in which one or more reactors of the ring exhibit a greater temperature than the others. I found that symmetry is broken when the rotational number of the resonant limit cycle, which arises from the Neimark-Sacker bifurcation, is an specific ratio. Symmetry locking and resonance regions are computed through the bifurcation analysis to detect the critical parameters which mark the symmetry-breaking transitions. Finally, I will present numerical results when the dynamical systems of the network are PDEs.

CAN DYNAMICAL MODELS IN BIOLOGY AND NATURAL SCIENCES GO BEYOND INFINITY?

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Many mathematical models in the form of Ordinary (ODEs) and/or Partial Differential Equations (PDEs) trying to approximate the dynamics of biological and natural systems may in certain regimes reach infinity, i.e. blow up in finite time. Take for example the celebrated integrate-and-fire (IF) model that constitutes the backbone of many models in computational neuroscience or many population dynamics models. This ”peculiar” behaviour for a physical/biological/natural sytem rises various fundamental questions: are these equations well-defined? are the selected variables the appropriate for the modelling of the systems dynamics? are there solutions beyond inifnity? To answer these questions we have addressed a numerical framework that can be applied both to ODEs and PDEs (1) that, upon suitable singular transformations allows the system to “go beyond infinity”, with the solution becoming again not-singular. Thus we can study the dynamics “around infinity”, bypasssing the numerical problems that are asociated with the singularity at infinity. The proposed approach sets the stage for the systematic analysis of both the numerics and the physics of dynamics that go to infinity in finite time for a broader set of such problems.

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LOTKA-VOLTERRA PREDATOR-PREY SYSTEMS MODELING VIRUS DYNAMICS IN MARINE ECOSYSTEMS AND HIV INFECTION

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Marine ecosystems may contain diverse populations of bacteria which are supported by relatively few limiting nutrients and which are predated upon by an equally diverse set of bacteriophages (viruses). The network defined by which virus kill which bacteria strongly influences the overall persistence of the marine community (1; 2; 3).

The dynamics of virus and immune response within a host can also be viewed as a complex ecological system. The immune response predates on the pathogen, and distinct viral strains compete for a target cell population, while immune response populations compete for the virus since their proliferation occurs upon pathogen recognition. For example, during HIV infection an extensive family of CTL immune cells recognize specific viral proteins presented on the surface of infected cells to effectively mediate their killing. However HIV can rapidly evolve resistance to CTL attack at different epitopes. The ensuing battle creates a dynamic network of interacting viral strains and immune response variants with variable levels of (strain) reactivity (4).

It is unsurprising that similar mathematical models can be used to better understand the role of the predation network structure on the ultimate bio-diversity of the community in each of these cases. The models we consider consist of systems of Lotka-Volterra-like ordinary differential equations. The talk will describe recent joint work with colleagues Dan Korytowski and Cameron Browne on the dynamics of such models.

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PHASE-SENSITIVE CRITICAL TRANSITIONS IN PREDATOR-PREY SYSTEMS

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Global change is expected to lead to climate changes that include greater intensity and more autocorrelation in environmental noise. Many recent studies have noted that the greater variability associated with global change often has more impact than the change in average behaviour (temperature, precipitation, etc). In this presemtatopm we explore how changes in climate variability could interact with a system that is already oscillating, namely, predator-prey systems. We explore tipping points, likelihood of extinction, and early warning signals for such climatically-forced systems, and the implications for conservation.

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SUB-OPTIMAL HARVESTING POLICIES WITH STEPWISE EFFORT IN A RANDOM ENVIRONMENT

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In a randomly varying environment, we can describe the evolution of a fished population size using stochastic differential equations. Previously (see (2; 5; 6)), we have compared the profit performance of two harvesting policies, one with variable harvesting effort, called optimal policy, and the other with constant harvesting effort, called optimal sustainable policy. The former is characterized by fast and abrupt variations of the harvesting effort associated with the frequent variations in population size due to the random environmental fluctuations. This type of policy is inapplicable due, for instance, to the logistics of the fisheries being incompatible with abrupt and frequent changes in the harvesting effort. It also poses social problems during the periods of no or low harvesting effort. Furthermore, this type of policy requires the knowledge of the population size at each instant and estimating population size is an inaccurate, lengthy and expensive task. The optimal sustainable policy considers the constant application of the same harvesting effort and leads to population sustainability, as well as to the existence of a stationary probability density for the population size (see (1)). This policy has the advantage of being easily applicable and there is no need to estimate the population size at every instant. The performance of the two policies was compared in terms of the profit over a finite time horizon. Using data based on a real fished population, we show that there is only a slight reduction in profit by using the optimal sustainable policy (based on constant effort) instead of the inapplicable optimal policy (based on variable effort).

Since the optimal variable effort policy is not applicable, we present here *step-*

wise policies (see (3; 4)), which are sub-optimal policies where the harvesting effort is determined at the beginning of each year (or of each biennium) and kept constant throughout that year (or biennium). These policies are not optimal and pose social problems common to the optimal policies, but have the advantage of being applicable, since the changes in harvesting effort are much less frequent and are compatible with the fishing activity. Furthermore, even though estimating population size is still required, that needs to be done less frequently. We present the comparison in terms of profit of these stepwise policies with the two previously mentioned policies.

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BEHAVIOUR INDUCED PHASE TRANSITIONS IN EPIDEMIOLOGY OF INFECTIOUS DISEASES

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Phenomena concerning the spread and control of infectious diseases (IDs) can be read, from theoretical physics viewpoint, as phase changes and phase transitions (PTs). This is an increasingly important concept in Mathematical Epidemiology (ME) (2). It is enough to think that the kinetic of PTs as well as the spatial progression of an epidemics are characterized by traveling waves (TWs) (1). TWs are so intimately connected to the epidemiology of IDs that an epidemic TW was described in the IV–the century B.C by the greek historian Thucydides.

Nowadays it is increasingly understood that models of ME must include human behaviour (3), a major factor impacting on the spread, prevention and control of IDs.

In this talk we will illustrate by means of two case studies how human behaviour can induce phase transitions that can deeply impact on the spread, control and prevention of infectious diseases.

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DELAYING AGE OF INFECTION: A PERNICIOUS EFFECT OF VACCINATION

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We study the effect of vaccination in the population, for what we call a childhood disease, where we assume the following: the disease has mild complications for infants but it is relatively dangerous for adults (as an example we have Zika virus that can provoke severe complications in the fetus when a pregnant woman is infected). It is well known that a sufficiently high level of vaccination decreases the effective reproduction number of such diseases, eventually making it smaller than one, conferring herd-immunity to all the population.

Yet, before achieving herd-immunity, partial vaccination of population decreases transmission causing a delay on the average age at infection. So, for a sufficiently high level of vaccination but not high enough, the average age at infection of the individuals may be where the effects of the disease are most dangerous.

We relate the average age at infection with the level of vaccination and characterize that relation.

AEDES AEGYPTI AND *WOLBACHIA* INTERACTION

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Laboratory and field tests have been highlight the importance of choosing an optimal *Wolbachia* strain to ensure the success of colonization and persistence of the released *Aedes aegypti* infected mosquito. Thresholds for vertical infection transmission and male sterilization depend on bacterial density and its distribution in mosquitoes tissue, which also affects strongly mosquito fitness. Temperature variation during mosquito development phase is an important factor that can affect the feasibility of this novel technique to control dengue transmission. In this context, a mathematical model is proposed to assess the factibility of dengue control transmission using a transinfection of *Aedes aegypti* with a *Wolbachia* strain. This model takes the form of a delay-differential system with two delays. The strength of this approach is measured by the fact that it can address several aspects of the problem, through scenarios construction where model parameters are setting according to mosquito genetic background, its ability to transmit the bacteria to the next generation, and its competence to block virus replication. The persistence of both infected and wild population is explored in the context of mosquito's fitness, host-symbiont interaction, and temperature change. Surprisingly, the model predicts that mosquito population extinction can occur in a region of the parameter space where the reproductive number of the wild population is bigger than one and migration of mosquitoes from surrounding areas is not allowed.

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MODEL DISCRIMINATION BY RANDOM PATTERN DATA

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Mathematical models allow establishing a connection between a pattern observed on a macroscopic scale and a hypothetical underlying mechanism. But different mechanisms may result in a similar pattern. As a topical example, in developmental biology the de novo formation of periodic structures similar to purely chemical Turing patterns can also be obtained using mechano-chemical models with only one diffusing morphogen (2). A computational approach allowing model calibration to a certain pattern will enable not only model identification based on experimental data but also comparison of different mechanisms. However, model parameter identification by pattern data only is challenging. Patterns obtained with fixed model parameter values but small random perturbations of the initial data will significantly differ in location and shape, while being of the "same" type. In this sense, for unknown initial values, each model parameter corresponds to a family of patterns rather than a fixed solution. This rules out the use of standard estimation methods such as least squares. Most typically, one has to resort to tedious and subjective hand-tuning. Here we present a solution for such problems. We consider classical Turing-type reaction-diffusion systems and one-dimensional mechano-chemical models of pattern formation with different coupling mechanisms between mechanical and chemical parts. The problem of parameter identification for these models is analogous to the identification of chaotic systems: in both cases slightly different initial values lead to different solutions which, however, can be considered to belong to the same family of solutions. So we modify a recently developed statistical approach for parameter studies of chaotic systems to the non-chaotic reaction-diffusion systems and mechano-chemical models. We demonstrate how the approach provides a cost function that enables a statistically sound identification of the model parameters by steady-state pattern data only, without known initial values or transient data. This is the situation often faced in experimental work. The accuracy of the cost function is verified by adaptive MCMC methods.

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MODELING CORAL REEFS
PROBLEMS IN ECOLOGICAL CONSERVATION

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Mathematical modeling of coral growth is naturally embedded in discrete-time population theory and, since there is experimental evidence that crowding effects influences the recruitment process, we need to consider non-linear models for a realistic description to be used in the long term perspective.

In the talk we will present results and problems within a collaboration that aims to build realistic models, based on experimental data, for producing possible scenarios on the long term behavior of various gorgonians populations. Different themes will be discussed such as conservation of endangered species (*Corallium rubrum* (1; 2)), climate changes and ocean acidification (*Pocillopora damicornis* (3)), ecological shift in community structure (*Eunicea flexuosa-Porites astreoides* (4)).

Future work aims to provide more refined models in connection with the different populations. In turn collection of data is oriented to provide basic information to be included into the models.

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MODERN NUMERICAL CONTINUATION METHODS FOR BIOLOGICAL SYSTEMS

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Numerical continuation methods allow for effective computations for a wide variety of parameter dependent problems. They are particularly well-suited to produce parametric diagrams, e.g., to illustrate the dependence of a steady state for an ODE upon input parameters. Yet, their uses are much broader as recently many new techniques have been developed. In my talk, I shall outline, how to utilize these techniques via biological examples in the context of epidemic models given by ODEs (4; 6), for competing neuronal populations and predator-prey models given by SDEs (5; 8; 10; 2), for random ODEs (1), and for various reaction-diffusion PDEs (7; 9; 3; 11).

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THE HARD PART OF THE MEASLES ENDGAME. HINTS FROM BEHAVIOURAL EPIDEMIOLOGY

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The dramatic difficulties faced by the measles global elimination plan might be symptomatic, beyond the "objective" difficulties that are intrinsic to measles elimination compared to other vaccine preventable infectious disease, of globally changing perceptions and attitudes about infection and vaccination, of which industrialised countries might just represent the tip of the iceberg. Modern behavioural epidemiology (BE) (2) models aid to unfold the complexities underlying such phenomena and give insight on the determinants of vaccine uptake under endgame conditions, and on the related communication efforts and key related parameters. In this work we consider a general BE model capturing the sources of conflict between private and public interest that might be detrimental for herd immunity as a public good. The model analysis provides a number of useful formulas for vaccine uptake under elimination condition. We use such formulas, and the underlying critical parameters, to provide a number of hints on the complexity of the measles endgame whose understanding will be critical to win the hardest challenge of the endgame, namely to maintaining high levels of vaccine uptake in situation of increasingly generalised absence of measles infection. In particular, we will (i) clarify the determinants of vaccine coverage during endgame phases, (ii) disentangle, within public health communications on the topic, the distinct role played by the type and content of the communication vs its intensity, (iii) identify how the communication priorities will evolve during the various stages of the endgame depending on the setting considered.

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PARENTAL VACCINATION TO ACCELERATE THE PROGRESS TOWARDS MEASLES ELIMINATION IN ITALY

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High-income countries are experiencing measles reemergence as the result of suboptimal vaccine uptake and marked immunity gaps among adults. In 2017, the Italian Government introduced mandatory vaccination at school entry for ten infectious diseases, including measles. However, sustainable and effective vaccination strategies targeting adults are still lacking.

We propose a vaccination strategy to be introduced on top of the current policy, which consists of offering vaccination to the parents of all of the children who receive any measles vaccine dose. The “current” and the “parental” immunization strategies are simulated trough a model of household demography informed with detailed socio-demographic data. The effectiveness of each vaccination program is evaluated in terms of its impact on the overall and age-specific susceptibility to infection of the Italian population, on the effective reproduction number over the period 2017-2045, and on the amount of time required to achieve measles elimination.

We show that the current policy would reduce measles susceptibility in the age segments of the population characterized by higher contact rates, resulting in

a remarkable decrease in the infection transmission potential and making measles elimination a realistic target (Figure 1). However, if only 50% of unvaccinated children are vaccinated at school entry, disease elimination would probably be achieved only after 2045. Offering vaccination to the parents of children who receive a measles vaccine dose could progressively reduce by 17-35% the immunity gaps among individuals who are between 18 and 45 years of age in 2018 and would increase the probability of measles elimination before 2045 from 12.0% (estimated in the absence of this additional policy) to 78.9-96.5% (Figure 1).

Although the proposed policy can reach only a fraction of susceptible adults, that is those with children in the measles-vaccination age group, the obtained results suggest that this strategy may be both feasible and effective. In particular, a key advantage of this policy is that it does not require targeted activities to recruit parents, thus resulting in a relatively simple implementation protocol.

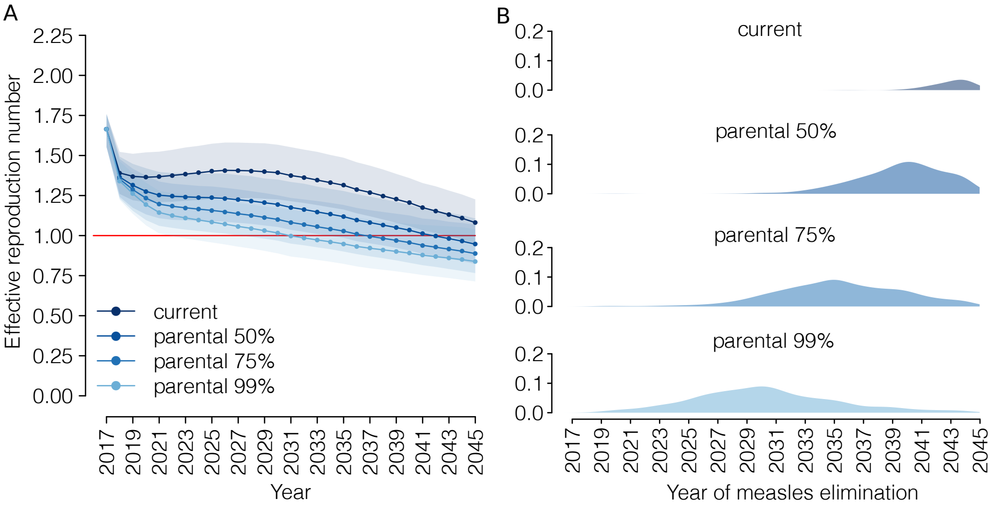

Figure 1: Progress towards measles elimination. (A) Mean effective reproduction number over time, as estimated by the model under the "current" vaccination program (50% coverage) and under different coverage scenarios for the "parental" vaccination program. Shaded areas represent the 95% CI associated with model estimates. The red line represents the measles elimination threshold; elimination is achieved when the effective reproductive number is smaller than 1. **(B)** Probability associated with different time at measles elimination, as obtained by 1000 model realizations under the "current" vaccination program (50% coverage) and under different coverage scenarios for the "parental" vaccination program.

A STAGE STRUCTURED DEMOGRAPHIC MODEL FOR INSECT PEST DYNAMICS

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Insect pests are insects causing damage to crops, farm animals and human health. It is then important to have a good knowledge of their temporal dynamics to usefully apply phytosanitary treatments. Often pesticides are effective only for a particular insect life stage. This suggests to consider the insect population as a stage structured population.

Here a physiologically based demographic model is used to describe the temporal dynamics of the stage structured insect pest population. Each individual of the population is characterized by a physiological age, that is a percentage of development in a stage. The physiological age is considered as a random variable driven either by a Wiener process allowing regression or by a Gamma process that guarantees a non-decreasing behaviour of the physiological age. The model gives the abundance of the population in each stage in time and physiological age. It is represented by a system of Fokker-Planck partial differential equations taking into account the dispersion effects of the individuals during the development. The model includes the stage-specific biodemographic functions (development, mortality and fecundity) describing the biology of the species. The biodemographic functions depend on environmental variables, mainly temperature. A reliable population dynamics model requires a good estimate of the biodemographic functions. The estimation can be easily obtained using a least square method when data on the biology of the species are available from literature. This is not often the case for the mortality, then a statistical estimation method based on population abundance data is considered.

The model is used to describe the dynamics of an insect pest for which field data are available.

HOST CONTACT DYNAMICS SHAPES RICHNESS AND DOMINANCE OF PATHOGEN STRAINS

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The interaction among multiple microbial strains affects the spread of infectious diseases and the efficacy of interventions. Genomic tools have made it increasingly easy to observe pathogenic strains diversity, but the best interpretation of such diversity has remained difficult because of relationships with host and environmental factors. We focused on host-to-host contact behavior and use stochastic modeling and network theory to quantify its effect on strain richness and dominance (1). We systematically compared multi-strain spread on various network models illustrating properties found in real-world examples. We then analyzed the spread of *Staphylococcus aureus* in a hospital, leveraging on a combined dataset of carriage and close proximity interactions. We found that contact dynamics has a profound impact on strain populations. Contact heterogeneities reduce strain diversity by limiting the number of circulating strains and leading few strains to dominate over the others. Conversely, strong community structure increases strain richness. In the *S. aureus* example, network structural and temporal properties could account for a large part of the variability observed in strain abundance. These results show how stochasticity and network structure affect the population ecology of pathogens and warn against interpreting observations as unambiguous evidence of epidemiological differences between strains.

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MODELLING THE TRANSMISSION DYNAMICS OF WEST NILE VIRUS IN EMILIA-ROMAGNA REGION (ITALY)

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West Nile virus (WNV) transmission was much greater in 2018 than in previous seasons in Europe. Focusing on Emilia-Romagna region (northern Italy), we analyzed detailed entomological and epidemiological data collected in 2013-2018 to quantitatively assess environmental drivers of transmission and explore hypotheses to better understand why the 2018 epidemiological season was substantially different than the previous seasons. In particular, in 2018 WNV was detected at least two weeks before the observed circulation in 2013-2017 and in a larger number of mosquito pools. Transmission resulted in 100 neuroinvasive human cases, more than the total number of cases recorded between 2013 and 2017.

We used temperature-driven mathematical models calibrated through a Bayesian approach to simulate mosquito population dynamics and WNV infection rates in the avian population. We then estimated the human transmission risk as the probability, for a person living in the study area, of being bitten by an infectious mosquito in a given week. Finally, we translated such risk into reported WNV human infections.

The estimated prevalence of WNV in the mosquito and avian populations were significantly higher in 2018 with respect to 2013-2017 seasons, especially in the eastern part of the region. The high mosquito prevalence resulted in a much greater predicted risk for human transmission in 2018, which was estimated to be up to four times higher than previous seasons. Our modelling results suggest that such greater WNV circulation might be explained by exceptionally high spring temperatures, which have likely amplified WNV transmission at the beginning of the 2018 season.

This study provides new important insights into the ecology of WNV in southern Europe and represents a first quantitative assessment of the dependency between temperature and infection that can explain why WNV circulation in 2018 was significantly higher than in previous years.

USING DIGITAL METHODS IN EPIDEMIOLOGY TO ADDRESS DISEASE CONTROL IN SUB SAHARAN AFRICA: EXPERIENCES AND PERSPECTIVES OF DOCTORS WITH AFRICA CUAMM

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Novel digital methods in epidemiology are increasingly used in Africa and concurrent with major changes in the burden, dynamics and distributions of diseases, both infectious and chronic. These methods include, among others: GPS for geolocation and navigation, mathematical modelling, digital computation and data storage, genomic sequencing and analysis. Doctors with Africa CUAMM, an Italian NGO operating in various african countries, has recently experienced some of these methods in collaboration with their developers, by applying them in real life settings such as: Ebola outbreak in Sierra Leone, measles vaccination in Ethiopia, distribution of maternal care units in Tanzania, malaria control in South Sudan. Aim of the contribution is to learn from these experiences by showing the potential impact of these new approaches to ensure that are addressing questions that are most relevant in disease control.

CAUSALITY ANALYSIS OF DENGUE TRANSMISSION IN BANDUNG, INDONESIA

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Investigation of dengue incidence data from the Borromeus Hospital in Bandung from the years 2008-2017 is done. This hospital is serving as one of the primary preferences of dengue patients, and we assume the data represent half of the total dengue incidences in Bandung. The data contains the address, age, gender, and length of stay in hospital of each patient. It is interesting to observe that the average stay in hospital decreases from 4.1 days in 2008 to 4.1 days in 2016. From the normalized distribution data in each district, it is shown that Coblong and Bandung Wetan are two most endemic districts with much higher incidences than the rest of the districts. Causality analysis indicates that the neighboring districts granger-caused the incidences in Coblong and Bandung Wetan districts, but not the other way.

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ON THE SPATIAL DISPERTION OF WOLBACHIA IN WILD MOSQUITO POPULATIONS

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Systematic introduction of Wolbachia in wild populations is now considered an important strategy of controlling dengue and other diseases transmitted by *Aedes aegpty*. However, one important component in this strategy is the assumption of an efficient dispersal of Wolbachia in the target population, and recent data suggests that this might not be the case in general. In order to access this risk, we consider a simplified population dynamics model for *Aedes aegpty* and how that for typical parameters regime this dispersion can be considerably slowed and, in some extreme cases, even counteracted.

TIME SCALE SEPARATION: COMPARISON OF SINGULAR PERTURBATION AND CENTER MANIFOLD ANALYSIS UNDER SCALING

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To analayse time scale separation for model reduction to lower dimensional effective models we compare singular perturbation and center manifold analysis, giving special attention to the scaling of small parameters appearing in the dynamic equations.

Examples shown are models for vector borne diseases, SISUV and SIRUV models, as examples of low dimensional analytically treatable models. The first, the SISUV model, is naturally a singular perturbation problem, not the other one, the SIRUV model, which initially appears in the form of a regular perturbation problem, but leading to singular behaviour due to the non-linearity of the dynamics, making it an initially harder problem than models with naturally appearing classical singular pertubation form.

The main result is that in lowest order in the naturally small parameters, the SIRUV model gives in lowest order a $V(S, I) = \frac{\vartheta}{\nu} \cdot \frac{M}{N} \cdot I$ as required for effective SIR models for human disease dynamics only, whereas the SISUV model gives in lowest order a Holling type II functional form $V(S, I) = \frac{\frac{\vartheta}{\nu} I}{N + \frac{\vartheta}{\nu} I} \cdot M$ where the saturation still matters due to eventually large numbers of infected I because of the long recovery period in the SISUV model (as opposed to the SIRUV model). In this respect the SISUV model is a sketching model for e.g. malaria with long re-appearing disease, wheras the SIRUV model with its short recovery time is a sketching model for e.g. dengue fever and other fast recovering vector-borne diseases.

The scaling analysis of the spectral gap of eigenvalues around the endemic fixed point, as required in center manifold analysis, can be extended to numerical analysis of spectral gaps also in Lyapunov spectra as signs of time scale separation and possible model reduction, applied to multi-strain epidemiological models as examples of not only higher dimensional models but also with complex dynamical behaviour, i.e. bifurcations into chaos with positive Lyapunov exponents.

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FUNCTIONAL FOKKER-PLANCK EQUATIONS 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 disentagling 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 multistrain epidemiological systems, i.e. where no explicit static fitness functions have to be given, with discrete or continuous trait space. Further implications are given for data analysis of empirical systems, since we have readly the stochastic formulations obtained.

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DYNAMICS OF HSV-2 INFECTION WITH A THERAPEUTIC VACCINE

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Herpes-Simplex Virus type 2 (HSV-2) is a lifelong infection (1; 2) which can be treated with episodic and suppressive antiviral treatments, (4; 5) although none of the currently available therapies can clear the virus from the body of an infected person. Most individuals with initial episode experience symptomatic recurrences, (3), with especially high rates in individuals with an extended first episode of symptomatic disease. Therefore there is an interest in developing therapeutic vaccines. Due to the limited data from clinical trials of HSV-2 therapeutic vaccines, (1; 2; 6) models have been of limited help in evaluating the impact of vaccination. In this study, we propose a simple compartmental deterministic model for the dynamics of HSV-2 and extend it to include vaccination. The proposed model is relatively simple with few parameters and does not address the complexity of the disease and variability of individual and infection characteristics. However, it can illustrate the potential effect of vaccination and build the foundation for future studies that involve more heterogeneous characteristics of the disease and individuals.

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THE INFLUENCE OF SHAPE ON INTERACTING POPULATIONS

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We model various types of two-population interactions. We focus on different population social behaviors, by assuming e.g. that prey gather in herds and/or predators in packs, or individuals of both populations live gathering together. In this way, the individuals staying on the outermost parts of these sets are the ones benefiting or suffering most from the interactions with the other population. The ones present in the inside show instead the reverse feature. Mathematically, this mechanism is modeled by a functional response expressed as a power of the population size. This allows to implicitly account for space, without the recourse to partial differential equations.

Novel features arising in the model outcomes are: population extinction in finite time; occurrence of persisting limit cycles arising with different assumptions than a Holling-type II underlying dynamics, that models instead a feeding satiation phenomenon; coexistence equilibrium levels being higher or lower than the corresponding ones for the classical models, if the interactions are respectively of damaging type or instead beneficial; the principle of competitive exclusion not necessarily holding, as in suitable conditions tristability is discovered.

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NUMERICAL APPROXIMATION OF THE BASIC REPRODUCTION NUMBER FOR STRUCTURED POPULATIONS

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The basic reproduction number, commonly denoted R_0, plays a fundamental role in many ecological and epidemiological models of population dynamics, where it is defined as the spectral radius of the next generation operator (1). In this general setting R_0 has not an explicit expression, and numerical methods are needed for its practical computation. We address the problem by reducing the relevant operators to matrices through the pseudospectral collocation and then by computing the (dominant) eigenvalues of the resulting matrices. The approach is illustrated for two classes of models, respectively from ecology and epidemiology. Some numerical tests give evidence of the convergence properties and potentialities of the approach.

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DYNAMICAL SYSTEMS APPLIED TO BIOLOGY

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NASH EQUILIBRIA IN EVOLUTIONARY COMPETITIVE MODELS OF FIRMS AND WORKERS

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The object of this paper is to study the labour market using evolutionary game theory as a framework. The entities of this competitive model are firms and workers, with and without external regulation. Firms can either innovate or not, while workers can either train or not. Under the most simple model, called *normal* model, the economy stucks in a *poverty trap*, where workers do not train and firms do not innovate. This Nash equilibria is stable even when both entities follow the optimum strategy in an on-off fashion. This fact suggests the need of an external agent that promotes the economy in order not to follow in a poverty trap.

Therefore, an evolutionary competitive model is introduced, where an external regulator provides loans to encourage worker training and firm innovation. This model includes poverty traps but another Nash equilibria, where firms and workers jointly innovate and train.

The external regulator, in a three-phase process (loans, taxes and inactivity) achieves a common wealth, with a propsperous economy, with innovative firms and trained workers.

This talk was presented by Alberto Pinto.

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GLOBAL DYNAMICS OF A DIFFERENTIAL-DIFFERENCE SYSTEM: A CASE OF KERMACK-McKENDRICK EPIDEMIC SIR MODEL WITH AGE-STRUCTURED PROTECTION PHASE

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In this work, we are concerned with an epidemic model of susceptible, infected and recovered (SIR) population dynamic by considering an age-structured phase of protection with limited duration, for instance due to vaccination or drugs with temporary immunity. The model is reduced to a delay differential-difference system, where the delay is the duration of the protection phase. We investigate the local asymptotic stability of the two steady states: disease-free and endemic. We also establish when the endemic steady state exists, the uniform persistence of the disease. We construct quadratic and logarithmic Lyapunov functions to establish the global asymptotic stability of the two steady states. We prove that the global stability is completely determined by the basic reproductive number.

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HOMOGENIZATION OF SOME REACTION-DIFFUSION SYSTEMS IN BIOLOGICAL TISSUES

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In this talk I shall derive a macro-model for the diffusion of species in biological tissues which can be viewed as poro-elastic materials. It is assumed that at the micro-scale, these tissues contain highly heterogeneous components periodically distributed. The macro-model is then obtained by the use of the two-scale convergence technique (1).

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INCORPORATION OF AWARENESS PROGRAMS INTO A MODEL OF THE SPREAD OF HIV/AIDS AMONGST PEOPLE WHO INJECT DRUGS (PWIDs)

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Mathematical modelling techniques have been used extensively during the HIV epidemic. Injecting drug use is an increasing cause of HIV transmission in most countries worldwide. The media plays an important role in spreading health awareness by changing mixing behaviour. The published studies show some of the mathematical models which have been used to explore the effect of media awareness programs on the spread and control of infectious disease (1).

In this talk, we have developed a mathematical model of the effect of disease awareness programs on the prevalence of HIV amongst people who inject drugs (PWIDs), building on the models developed by (2) and (3). A system of differential equations has been deduced to describe the improved model that reduces the spread of the diseases through the effect of awareness of disease on sharing needles and syringes amongst the PWID population. The model supposes that PWIDs clean their needles before use rather than after.

We perform an equilibrium and stability analysis for this model. Our discussion has been focused on two ways of studying the effect of awareness programs in disease transmission models. The key biological parameter of our model is the basic reproductive number R_0. We find that there is a critical threshold parameter $R_0 = 1$ which determines the behaviour of the model. We have shown that the system has a unique equilibrium solution, then we have shown that if $R_0 \leq 1$ then the disease-free equilibrium is globally asymptotically stable, so whatever the initial fraction of infected individuals the disease will die out as time becomes large. If there is no disease initially present then there will never be any disease. If $R_0 > 1$ then there is the disease-free equilibrium and additionally a unique endemic equilibrium. If there is disease initially present and $R_0 > 1$ then the system tends to the unique endemic equilibrium. We also showed that the disease-free equilibrium is locally asymptotically stable if $R_0 < 1$, neutrally stable if $R_0 = 1$ and unstable if $R_0 > 1$. In the case that $R_0 > 1$ we showed that the endemic equilibrium was locally asymptotically stable too. Our analytical results are confirmed by using simulation with realistic parameters values.

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INTERFERENCE COMPETITION ON GROUP DEFENSE WITH HOLLING TYPE IV COMPETITIVE RESPONSE

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Species competition is present under many different forms and strategies including aggressiveness (2), (3). In particular, group defense has been observed among these mechanisms (10) (8) for both vertebrate or invertebrate animals. We redive a model that extend the classical interference competition model (4) (see also (1)) by incorporating a Holling type IV term (6), (7) that we call *Holling type IV competitive response on group defense*. In our framework the competition model takes into account the increase on the time spent to snatch resources to other species' individuals due to group defense strategy (of the other species). It can be seen as a continuation of our previous work (9), where the so called Holling type II competitive response was introduced in the classical interference competition model to incorporate the time spent in interfering with competitors. The resulting model expands the outcomes allowed by the classical Lotka-Volterra competition model by,

1. Enlarging the range of parameter values that allow coexistence scenarios.
2. Displaying dynamical scenarios not allowed by the classical model in the form of multi-stable scenarios: bi/tri-stable conditional coexistence (species can either coexist or one/any pf them go extinct), bi/tristable unconditional coexistence (there exist two or three possible coexistence steady states).

Our results lighten the balance between intra/inter species competitive pressure that is behind competing species coexistence that starting from the outcomes (11), (12). Besides, the model presented herein displays stable alternative states in which the species coexist unconditionally as a result of the group defense strategy. This mechanism is an alternative explanation to empirical observations (5).

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ON [NAME] STABLE EQUILIBRIA

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A large population of individuals play repeatedly a symmetric game and settles on a compact set of Nash equilibria $\mathcal{N}$. Occasionally, they experiment with new strategies and, although initially the new strategies may earn a larger payoff, they cannot coexist stably among themselves. This happens either because they cannot settle on a different Nash equilibrium, or because they cannot enter a stable cycle of invasions. The population is thus pushed back towards the original set of equilibiria $\mathcal{N}$. In this case we say that the set $\mathcal{N}$ is [name] stable. We study the stability properties of [name] stable equilibria under the Best Response and the Replicator Dynamics. A set of NE that is [name] stable is not necessarily asymptotically stable under either dynamics. However, if initially most of the population play pure strategies that appear in $\mathcal{N}$, eventually only these strategies survive, in a combination that belongs to $\mathcal{N}$. In many applications, being [name] stable turns out to be more important than being evolutionarily stable.

ADDITIVE MODELS - AN APPLICATION IN NATURAL SCIENCES

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Here we will focus on some recent results concerning Additive Models. These models are given by the sum of a fixed term $X\underline{\beta}$ with known matrix X and w random independent terms $X_i\underline{Z}_i, i = 1, ..., w$. The components of the $Z_1, ..., Z_w$ are independent and identical distributed with cumulants $\chi_{i,r}$. We are interested in getting a better understanding of these cumulants and we will estimate them in order to obtain confidence ellipsoids for these models. An application in Natural Sciences is given to illustrate the theory.

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A CLIMATE-BASED MODEL FOR TICK LIFE CYCLE: AN INFINITE SYSTEM OF DIFFERENTIAL EQUATION APPROACH

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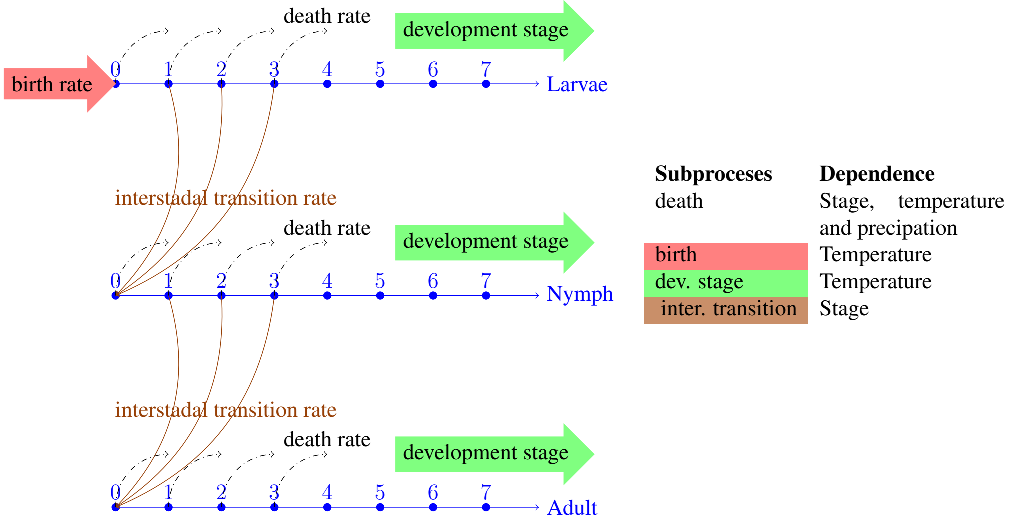
The distribution of ticks is essentially determined by the presence of climatic conditions and ecological contexts suitable for their survival and development.

We develop a general tick biology model to study the major trends due to climate change on tick population dynamics under different climate conditions. One of the main difficulty is that life cycle depends strongly on temperature and humidity.



Subproceses	**Dependence**
death	Stage, temperature and precipation
birth	Temperature
dev. stage	Temperature
inter. transition	Stage

Figure 1: A schematic diagram for the model, identifying the input parameters and the model output (predicted number of ticks of each stage).

We build a model that explicitly takes into account stage into each physiological state through a system of infinite differential equations where tick population density are structured on an infinite discrete set. We suppose that intrastate development process is temperature dependent (Arrhenius temperatures function) and that Larvae hatching and Adult mortality are temperature and precipitations dependent.

We analysed mathematically the model and have explicit the R_0 of the tick population. Therefore, we performed a numerical analysis of the model under three different climate conditions (tropical, Mediterranean and subarctic climates) and using climatic data from two different periods, $1901-1925$ and 90 years later, $1991-2015$.

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SINGULAR PERTURBATION TECHNIQUES AND ASYMPTOTIC EXPANSIONS FOR AUXILIARY ENZYME REACTIONS

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The complex intracellular signal transduction networks can be decomposed into simpler moduli, where fundamental reactions, like the Goldbeter-Koshland switch (which models, for example, the phosphorylation-dephosphorylation cycle) (1; 2), the competitive inhibition (3) and the double phosphorylation mechanism (4), play fundamental roles for the cell fate. It is then fundamental to capture the analytic features of these reactions, in order to predict, in perspective, the behaviour of the networks in terms of their characteristic parameters. This is one of the main reasons for the application of the so-called total quasi-steady-state approximation (tQSSA) (5), which has gained more and more attention in the last two decades for its ability to approximate in a very efficient way the behaviour of the reactants in many enzyme reactions and for a very wide range of parameter values.

In this talk we show some recent results related to the application of singular perturbation techniques in the framework of the total quasi-steady-state approximation (tQSSA) for the approximation of the so-called auxiliary or coupled enzyme reactions (6).

We determine the uniform expansions up to the first order in terms of appropriate perturbation parameters, related to the initial conditions and to the kinetic parameters characterizing the reactions. These results can be very useful for the determination of the kinetic parameter values, by means of the interpolation of experimental data with the explicit (though approximated) formulas we found.

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FEEDBACK CONTROL PRINCIPLES FOR BIOLOGICAL CONTROL OF DENGUE VECTORS

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Controlling diseases such as dengue fever, chikungunya or zika by spreading the parasitic bacterium Wolbachia in mosquito populations which are their vectors, is considered a promising tool to reduce their spread. While description of the conditions of such experiments has received ample attention from biologists, entomologists and applied mathematicians, the effective scheduling of the releases remains an interesting issue for Control theory. Having in mind the important uncertainties on the dynamics of the two populations in interaction, we attempt here to identify general ideas for building release strategies, applicable to various models and situations. These principles are exemplified by the design of interval observer-based feedback control laws whose stabilizing properties are demonstrated theoretically and numerically when applied to a 4-dimensional ODE model retrieved from (1). Crucial use is made of the theory of monotone systems (2; 3).

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PERIODICITY, DELAYS AND NUMERICAL METHODS IN BIOMATHEMATICS: A RECENT ACCOUNT

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Periodicity is common in natural phenomena. And delays are not so uncommon if we accept the challenge of dealing with complex, yet more realistic models. Numerical analysis is then mandatory when the target is either simulating, analyzing stability or detecting bifurcations. Based on the recent works (1; 2; 3), in this talk an up-to-date account is given of the interplay of these three characters, with an eye on applications in biomathematics.

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CANCER DYNAMICS IN HIV INFECTED PATIENTS UNDER DIFFERENT IMMUNE FUNCTIONS

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It is known that cancer is more prevalent among people infected with the human immunodeficiency virus (HIV) than in the general population (1; 2). Individuals in the final stage of the HIV infection, i.e., with acquired immune deficiency syndrome (AIDS) are more vulnerable to the emergence of various types of cancers. The most common are: Kaposi sarcoma, non-Hodgkin lymphoma (NHL) of high-grade pathologic type and of B cell or unknown immunologic phenotype, and invasive cervical carcinoma (3). In this paper we propose a mathematical model incorporating HIV and cancer growth dynamics, and immune response, under highly antiretroviral therapy (HAART) and chemotherapy. The model is analysed theoretical and numerically. The simulations reveal distinct patterns with respect to two immune functions and for different values of some important parameters, namely, the elimination rate of cancer cells by T cells, HIV infection rate and HAART. We discuss the obtained results from a biological point of view.

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CONTROL PROBLEMS AND GAMES IN CONSERVATION LAWS MOTIVATED BY BIOLOGY

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In recent years, several analytical results were obtained that ensure well posedness and stability of a variety of problems where conservation laws play a key role. On this basis, we now have the analytic tools to study new models and to tackle various control problems, or even games.

In this talk, we address the modeling of vaccination strategies and that of consensus dynamics. First, in both cases, a detailed description of the modeling framework is provided, highlighting well posedness results as well as qualitative properties of the solutions, the latter with the help of numerical integrations. Then, we deal with the optimal control problems that naturally arise in choosing vaccination policies. In the case of consensus problems, we have to face hyperbolic differential games.

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VIABILITY ANALYSIS FOR A STOCK-CAPITAL FISHERY MODEL

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This work is based on C. Clark, F.Clarke and G. Munro fishery model, (1), where the dynamic is the evolution of both stock and capital controlled by the investment and the part of the capital dedicated to the harvest. The contribution consists of substituting the profit maximization objective by constraints on the states of the model. In this new formulation, we give conditions on the parameters of the model which guarantees the non-emptiness of the viability kernel, which means the determination of the biggest set of initial conditions on which investment and exploitation sustainable policies could be defined. At the center of this result, we find the viability theory introduced by Aubin (1), which consists of studying the existence of controls yielding admissible states. Thus, we build the viability kernel corresponding to the studied model, under the conditions cited above.

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A MODEL FOR THE GROWTH OF A p62-UBIQUITIN AGGREGATE INVOLVED IN CELLULAR AUTOPHAGY

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The formation of p62-Ubiquitin aggregates is a key step in cellular autophagy (See (1)), a process that has raised a lot of interest these last years among cell biologists (See e.g. (2)). In this talk, we will present a model that describe the growth of a p62-Ubiquitin aggregate through a three-dimensional nonlinear ODE system. We will begin by introducing our new model for the growth of a p62-Ubiquitin aggregate, which was designed in collaboration with S. Martens and G. Zaffagnini (MFPL, University of Vienna). We will then present the three-dimensional nonlinear ODE system that has been derived from this model. Finally, we will show numerical simulations exhibiting the existence of three regimes, that we will study using some dynamical systems tools e.g. Blow-up (See (2)). This last analysis has been done in collaboration with P. Szmolyan (Technical University of Vienna). This is a joint work with Marie Doumic (LJLL, Sorbonne University) and Christian Schmeiser (WPI, University of Vienna).

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GLOBAL ANALYSIS OF A CANCER MODEL WITH DRUG RESISTANCE DUE TO LAMARCKIAN INDUCTION AND MICROVESICLE TRANSFER

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Development of resistance to chemotherapy in patients with cancer strongly effects the patients' outcome. Due to chemotherapeutic agents, Darwinian selection induces intrinsic resistance. Besides this, Lamarckian induction resulting in drug resistance may take place, when resistance emerges upon changes taking place inside the cells as a result of the therapeutic drug. A recent discovery in cancer research uncovered a third possibility, indicating that this phenotype conversion can occur via the transfer of microvesicles from resistant to sensitive cells, mimicking the spread of an infectious agent. We present a model describing the evolution of sensitive and resistant tumour cells considering Darwinian selection, Lamarckian induction and microvesicle transfer. We identify three threshold parameters which determine the existence and stability of the three possible equilibria. Using a simple Dulac function, we give a complete description of the dynamics of the model depending on the three threshold parameters. Numerical simulations are shown to demonstrate the possible effects of increasing drug concentration, and we characterize the possible bifurcation sequences.

GLOBAL SENSITIVITY APPROACHES FOR MODELS DESCRIBING HIV DISEASE DYNAMICS

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HIV (Human Immunodeciency Virus) is a virus that attacks cells that help the body fight infection, making a person more vulnerable to other infections and diseases. First identified in 1981, HIV is the cause of one of humanity’s deadliest and more persistent epidemics. If left untreated and, without antiretroviral treatment, HIV can lead to the onset of AIDS (Acquired Immunodeficiency Syndrome) – the last stage of HIV infection that occurs when the body’s immune system is badly damaged because of the virus. A large variety of mathematical models have been proposed to describe HIV infection and disease dynamics (1; 2; 3; 4; 5; 6; 7).

This talk presents several global sensitivities approaches applied to different models describing Human Immunodeciency Virus (HIV) infection and disease dynamics. The mathematical models defined by ODEs systems describe HIV pathogenesis with cytotoxic T-lymphocytes and infected cells in eclipse phase (1; 2), as well as the disease dynamics by capturing all three stages of infection (7). The global sensitivity studies are illustrated by graphical objects (sensitivity heat maps, parameter sensitivity spectra), as well as results of the elementary effects method, and active subspace method applied on these models.

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SPATIAL SELF-ORGANISATION ENABLES SPECIES COEXISTENCE IN A MODEL FOR SAVANNA ECOSYSTEMS

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The savanna biome is characterised by a continuous vegetation cover, comprised of herbaceous and woody plants. The coexistence of species in arid savannas, where water availability is the main limiting resource for plant growth, provides an apparent contradiction to the classical principle of competitive exclusion. Previous theoretical work using nonspatial models has focussed on the development of an understanding of coexistence mechanisms through the consideration of resource niche separation and ecosystem disturbances, but has ignored effects of spatial interactions.

In this talk, we propose that a spatial self-organisation principle, caused by a positive feedback between local vegetation growth and water redistribution, is sufficient for species coexistence in savanna ecosystems. We present a spatiotemporal ecohydrological PDE model, based on the Klausmeier reaction-advection-diffusion system for vegetation patterns, to suggest two mechanisms that enable species coexistence. Firstly, a stability analysis of the system's single-species patterns, performed through a calculation of their essential spectra, provides an insight into the onset of coexistence states. We show that a stable solution branch in which both species coexist bifurcates off the single-species solution branch as the single-species state loses its stability to the introduction of a second species. We present a comprehensive existence and stability analysis to establish key conditions, including a balance between the species' local competitive abilities and their colonisation abilities, for species coexistence in the model. Secondly, we show that coexistence can also occur as a metastable state. Such a long transient behaviour is caused by the small growth rate of perturbations to a spatially uniform coexistence equilibrium, whose size is controlled by the average fitness difference between both species, a measure of the species' competitiveness in a spatially uniform setting.

MODEL-BASED DESIGN AND ANALYSIS OF LIFE TABLE EXPERIMENTS FOR INSECT VECTORS OF DISEASE

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Life tables can help identify physiological differences in distinct development stages and detect potential vulnerabilities for conservation or control. However, cataloguing mortality, development, and fecundity by following each individual could be challenging due to interweaving generations and development stages in insects. Therefore, the information needed for life tables depend heavily on carefully designed experiments concentrating on a single development stage at a time.

Here, we propose the use of age- and stage- structured population dynamics modelling to aid in the design and analysis of life table experiments (1). We use a hypothetical case, a simulated population with known life parameters, to demonstrate that model-based inference can correctly identify life parameters from the longitudinal observations of laboratory-reared insect populations. The analysis reveals not only the differential physiological behaviour of each development stage, but also identifies the degree to which each parameter can be inferred from the data. We validate this method against the traditional approach by inferring correctly the life table of a well-studied disease vector, *Culex quinquefasciatus*, from the unprocessed experimental observation of its population dynamics (2).

In this study, we present a novel model-based approach to identify life table parameters from incomplete longitudinal observations. We demonstrate that the method is effective, robust, and easily adjustable to fit the specific requirements of different species and experimental setups.

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GLOBAL STABILITY ANALYSIS OF BIRHYTHMICITY IN A VAN DER POL TYPE SELF-SUSTAINED OSCILLATOR

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The properties of a multi-limit cycles variation of the van der Pol self sustained oscillator with random excitations are reviewed (7; 8; 9). Birhythmicity refers to the coexistence of two attractors characterized by two different amplitudes and two frequencies: depending on the initial conditions, the system can produce self–oscillations at two distinct periods (4). Such hysteretic behavior has been sometimes observed in biological systems (1), glycolytic oscillations (4) or circadian rhythms (6) . As a prototype of birhythmic oscillations, we consider a model that has been introduced to analyze enzymatic substrate reactions in brain (2; 3; 10). The global stability properties of birhythmicity can be investigated through the effect random excitations, such as a Gaussian white noise, on the attractors global stability. Noise makes the two limit cycles metastable, and induces switches between the two attractors. The mean escape time from each limit-cycle can give an estimate of the effective activation energy barrier through the slope of the (log of the) escape time as a function of the inverse of the noise intensity. Several properties can be retrieved, most importantly that the trapping barriers of the two frequencies can be very different, thus leaving the system on the same attractor for an overwhelming time. We conclude that although birhythmicity *per se* refers just to the occurrence of two frequencies, actual observation is subject to much more restrictive conditions. Moreover, the system is analytically particularly tractable by means of stochastic averaging; thus the effect of external periodic drive, noise correlation and the coherence of the oscillations, or time delayed feedback, can be analyzed (1; 7; 8; 9; 10).

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A DYNAMICAL MODEL FOR SYMPATRIC SPECIATION IN AN ECOLOGICAL NICHE

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The speciation phenomenon is the process used by the evolution to allow the populations to become distinct species (1). The speciation is the primary cause of the complexity of the ecological network. The biologists have classified four modes to explain the speciation process based on the extent to which speciating populations are isolated from one another: allopatric, peripatric, parapatric, and sympatric (2). Sympatric speciation concerns the rise of a new species from a surviving ancestral species while both continue to inhabit the same ecological niche or geographical region. In sympatric speciation, reproductive isolation evolves within a population in a ecological niche without the aid of geographic barriers Different models have been proposed for alternative modes of sympatric speciation. The most popular was first put forward by John Maynard Smith in 1966 (3): Maynard Smith suggested that in a given population homozygous individuals may, under particular environmental conditions, have a greater fitness than those with alleles heterozygous for a certain trait. Then, under the mechanism of natural selection the homozygous individuals would be favored over heterozygous one, eventually leading to speciation in the population (4). In this framework we assume an effective description of the speciation process based on a dynamical model for the populations in an ecological system (5) (6). Our basic assumptions is the existence of an ancestral population in an ecological niche with finite resources that can express two phenotypes. In presence of particular environmental conditions one of the phenotypes has the propensity to separate from the original population in the reproduction process: i.e. the sexual segregation of the new population is explained by a fitness advantage from a evolutionary point of view. Thene new individual may give rise to a new species in the ecosystem according to the sympatric speciation. Due to the finite resources in the niche the populations are continuously competing each other and their number fluctuates according to the changes of the environmental conditions. The effect of natural selection is introduced in the model by a pointwise stochastic perturbations of the environmental conditions that increase the struggle for life of the populations in the niche. We study the dynamical properties of th system and we prove the existence of a threshold values in the environmental stress in order to observe the speciation process. The analytical arguments are illustrated by numerical results and we also discuss some biological implication of the model and the validation problem using empirical data.

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USING DATA MINING TO CONSTRUCT DYNAMICAL EQUATIONS FROM AGENT-BASED PEDESTRIAN SIMULATORS

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A fundamental challenge in the field of applied mathematics, especially over the last few years revolves around the processing and analysis of big-data coming from experiments or large-scale simulations. In particular, one of the main targets in the field is the data-driven construction of low dimensional mathematical models in a closed form, usually in the form of ordinary (ODEs) and/or partial differential equations (PDEs), which can be then analysed using all our theoretical and numerical analysis arsenal. Here, we apply a data-mining non-parametric statistical learning based approach to construct ODEs in a closed form from data produced by an agent-based simulator of pedestrian dynamics. We access the efficiency of the approximation by comparing the obtained interaction potentials that govern the dynamics of the ODEs with the ones driving the detailed simulation.

The work described in this abstract was also presented during the poster session of the DSABNS 2020.

EFFECTIVENESS OF MEASLES SURVEILLANCE IN SOUTH WEST SHOA ZONE OF THE OROMIA REGION, ETHIOPIA

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Measles is one of the most contagious vaccine-preventable diseases and it is a major cause of child mortality in sub-Saharan Africa [1]. Repeated measles epidemics occurred between 2013 and 2017 in the South West Shoa Zone (SWSZ) of the Oromia Region in Ethiopia. A first outbreak was observed during the first months of 2013. Measles transmission was interrupted by a vaccination campaign conducted between May and June 2013. Immunization efforts were only partially effective in preventing measles circulation and sustained measles epidemics re-emerged in 2015, lasting up to March 2017.The high heterogeneity in the access to well-resourced hospitals has the potential of reducing the effectiveness of epidemic surveillance, which is still strongly dependent on clinical investigation of patients recovered in well-resourced hospitals [2]. It is therefore important to assess the ability of the surveillance system to measure the number of measles cases occurring in the community and to timely detect ongoing measles outbreaks. The proposed analysis provides quantitative estimates of possible delays and potential failures of the current surveillance system in detecting large measles epidemics in the future by using, a dynamic multi-patch transmission, calibrated on the time series of hospitalized measles cases. Model estimates obtained so far suggest that the surveillance system took about 4 months to detect an epidemic starting from the district where the central hospital is located. These results highlight a high risk that persistent silent transmission could characterize future measles outbreaks, undermining the potential containment of large epidemics.

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ANALYZING THE SPREAD OF A DISEASE WITH DUAL TRANSMISSION MODE VIA A METAPOPULATION MODEL: ROLES OF ACTIVE AND PASSIVE MOVEMENTS

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In order to investigate the spread of a disease between a larger urban city and a comparatively smaller satellite city, we formulate a metapopulation model which explicitly integrates vector-borne and sexual transmission and distinguishes between two distinct types of movements, active and passive. After finding the basic reproduction number of the model by means of the next generation method as being the spectral radius of a comparatively higher-dimensional matrix, we provide explicit estimations in terms of community-specific reproduction numbers which are somewhat less computationally intensive. We then perform a correlation analysis along with numerical simulations which lead to the conclusion that the disease is primarily transmitted via the vector-borne mode rather via the sexual transmission mode and that sexual transmission by itself can neither initiate nor sustain an outbreak.

The fact that active movements have comparatively little influence upon the global basic reproduction number of the model indicates that although travel restrictions restriction from the urban city to the satellite city may reduce the prevalence of the disease in the satellite city, significant control measures targeting the densely populated cities will be required in order to eradicate the disease in the entire region. After gauging the effects of mobility, we explore the potential effects of optimal control strategies relying upon several distinct restrictions on population movement.

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ESTIMATING THE PROPORTION OF SEXUAL TRANSMISSION ON ZIKA VIRUS SPREAD

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The recent Zika virus outbreak has been spreading rapidly which in turn makes it a global public health hazard. Zika virus may cause serious health problems like microcephaly and GBS. One rare property of the Zika virus compared to most vector-borne diseases is the fact that the virus is transmitted both by mosquitoes and by direct sexual contact. To quantify the amount of sexual transmission, we formulate and analyze a compartmental model of Zika virus spread considering both vector-borne and sexual transmission (see Fig. 1).

We showed the positivity and boundedness of solutions, global stability of the disease-free equilibrium, existence of endemic equilibria and an analytic expression for R_0. We fitted the proposed model to Zika case data from Colombia. We estimate the reproduction numbers, namely direct (sexual) transmission, vector transmission and the basic reproduction number (R_0). The analysis revealed that the sexual transmission contribution to R_0 is [14.62% (95% CI 3.6926.2)] for the proposed model. For this model, the estimated R_0 to be 1.94 (95% CI 1.672.11), the direct transmission reproduction number to be 0.4 (95% CI 0.11 0.66), and the vector transmission reproduction number to be 1.52 (95% CI 1.331.64). Further, to shed some light on controllability, we performed global sensitivity analysis and analyzed some contour plots. From this study, we conclude that sexual transmission may increase the risk of Zika, but it is not sufficient to create an outbreak by itself (1).

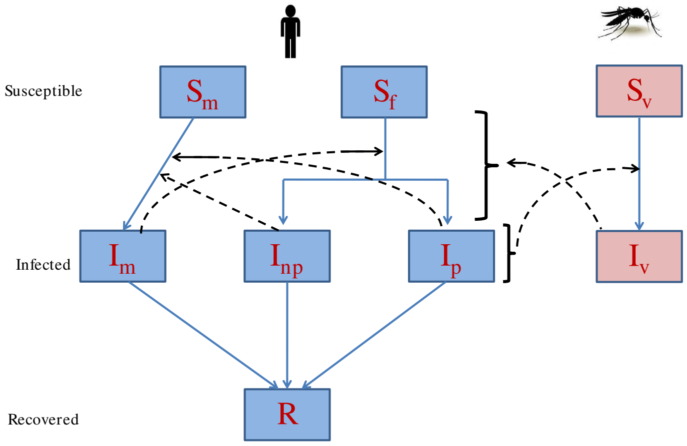

Figure 1: Flow diagram for the Zika virus model involving sexual and vector transmission. Blue nodes are human compartments and red nodes are vector populations. Solid blue lines represent the conversion rate and dashed black lines represent the infection rate. S_m - susceptible male, S_f - susceptible female, I_m - infected male, I_{np} - infected non-pregnant female, I_p - infected pregnant female, R - recovered human, S_v - susceptible vector, I_v - infected vector.

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TWO-LEVEL EVOLUTION OF CHRONIC VIRAL INFECTIONS AND THE EFFECT OF THE POPULATION-LEVEL CONTROL

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In this contribution, we consider a two-level model model of the dynamics of a multiple strain infection. This research is motivated by a need for mathematical models that not only integrate within-host genetic diversity and genotypic (resp., phenotypic) evolution with epidemiological dynamics, but also consider the joint effects of therapeutic and prophylactic controls. We attempted to balance the complexity of the model to be usable as a data analysis tool with the desire to understand the mathematical and statistical properties of the model using analytical methods. Our model accounts for within-host evolution among multiple phenotypes characterized by variable contagiousness, resistance to prophylactic measures, and resistance to therapeutic measures. The used framework allows for new phenotypes to emerge in chronic infection and later spread within the population. In addition to the disease dynamics, we consider the epidemiological and evolutionary effects of both therapy for infected persons and chemo-prophylaxis-type measures for uninfected persons. We thoroughly analyze the structural properties of the model and present a number of results aimed at facilitating parameter identification and validation of the model. In particular, we characterize and analyze the behavior of the basic reproduction number R_0 under different assumptions about the model structure and study how the endemic equilibrium state depends on the systems parameters. We also present a sensitivity analysis along the lines described in (1) and make suggestions aimed at improving the intervention strategies design for combating the disease.

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HOMEOBOX GENES: INVESTIGATING THE DEVELOPMENT OF *PINUS SYLVESTRIS* (SCOTS PINE)

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Homeobox genes play an important role in the processes of the organism developing and have been discovered in plants, fungi, and vertebrates [1]. The aim of the work is to examine the development of Scots pine (*Pinus sylvestris* L.) at the homeobox-containing genes level using the differential gene expression approach.

Previously, the WUSCHEL- related homeobox gene family in *Pinus pinaster* was analyzed [2].

To date, there are a great number of tools and methods for the de novo transcriptome analysis [3]. *P. sylvestris* sequencing data deposited in the NCBI BioProject database under accession number PRJNA531617 (SRR8996768-SRR8996761) provided by the Norwegian Institute of Bioeconomy Research was used as a source of this study [4]. *P. sylvestris* transcriptome was assembled using reads from five tissue types (needle, phloem, vegetative bud, embryo and megagametophyte) from six non-related individuals of *P. sylvestris*. For the *de novo* transcriptome assembly reads were preliminarily trimmed with the Q¿ 30 using Trimmomatic-0.36 and assembled using Trinity software (version 2.8.4). HMMER software (version 3.2.1) was used for the homeobox domain identification in the assembled transcripts using a hidden Markov model of homeodomain which was downloaded from the PFAM database (Accession number PF00046, ID Homeodomain). To estimate transcript abundance and perform differential expression

(DE) analysis, align_and_estimate_abundance perl script, RSEM, as well as bowtie programs (version 1.2.3), were used. Also, cross-sample TMM normalization was performed. Finally, the EdgeR package (R version 3.5.0, Bioconductor version 3.8) was used for statistical analysis and identifying significantly differentially expressed transcripts.

Assembled transcriptome comprises of 775,502 transcripts with the mean GC content of 40.19%. The N50 value for transcripts was 1,273 bp, while the median contig length was 360 bp. 417 homeobox-containing transcripts were selected for further analysis,254 transcripts were annotated using the UniProt database (e-value ¡1e-3).

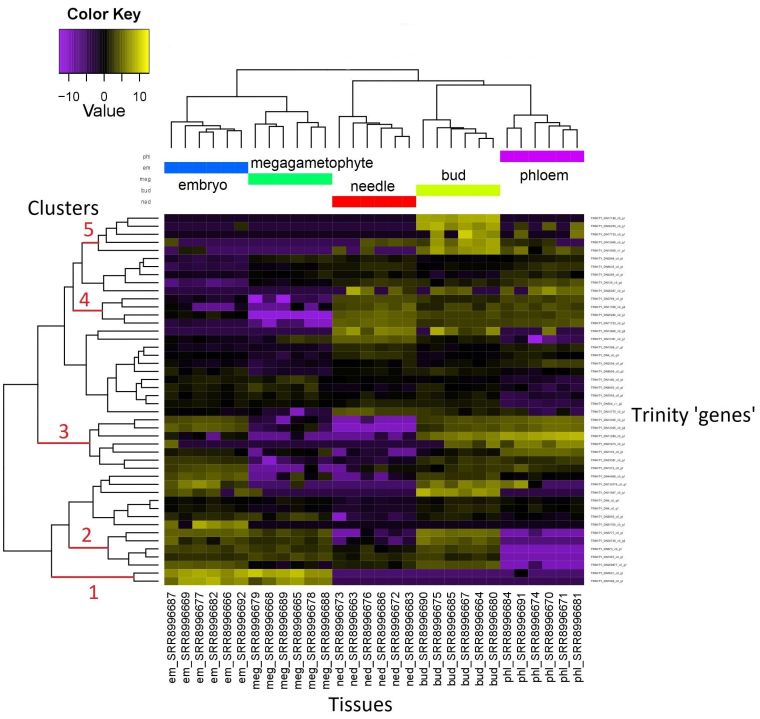

Figure 1: Heatmap of gene expression, five tissues of *Pinus sylvestris*

46 statistically significantly differentially expressed trinity "genes" were identified (adjusted p-value¡0.03) (figure 1) and visualized as a heatmap. Five resulting clusters of DE transcripts were analyzed. In the first cluster, two transcripts encoding proteins involved in early and late embryo development were found, which were upregulated at embryo and megagametophyte stages and downregulated at other stages. The second cluster comprises transcripts encoding transcriptional factors (TF) involved in seed and leaf development as well as in cell differentiation, downregulated in phloem tissue. In the third cluster, transcripts annotated

as proteins responsible for multicellular organism development, phloem histogenesis, auxin-mediated morphogenesis, plant organ development, regulation of leaf morphology and involved in meristem formation were observed. These transcripts are downregulated in needle and megagametophyte tissues. Transcripts in cluster four included proteins involved in the detection and cellular response to the cytokine stimulus and leaf morphogenesis. Transcripts of this cluster are significantly upregulated in needles and downregulated in megagametophyte tissues. Cluster five comprises five transcripts encoding proteins determining cotyledon morphogenesis, response to gibberellin, cell differentiation and positive regulation of transcription. These transcripts are upregulated in bud tissue.

Thus, the presented results gain a more comprehensive understanding of the *P. sylvestris* development process.

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A DELAY DIFFERENTIAL EQUATIONS MODEL FOR THE ACTION OF THE IMMUNE SYSTEM IN MALARIA

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The approach in (3) combined with a physiological modeling of erythropoiesis (see (1)) is completed with the action of the immune system on the lines in (2). The existence of equilibria and their stability is discussed.

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THRESHOLD DYNAMICS IN A PERIODIC MODEL FOR ZIKA VIRUS DISEASE

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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 non-autonomous model with time-dependent mosquito birth, death and biting rates, which shown that the global dynamics is determined by the basic reproduction number R_0 which is defined through the spectral radius of a linear integral operator. If $R_0 < 1$, then the disease free periodic solution is globally asymptotically stable and if $R_0 > 1$, then the disease persists. Although a regular periodic recurrence of Zika has not been observed yet, it is expected that this might be altered by the climate change. We show numerical examples to study what kind of parameter changes might lead to a periodic recurrence of Zika.

BREATHING AS A PERIODIC GAS EXCHANGE IN A DEFORMABLE POROUS MEDIUM

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We represent the mammalian lungs as a deformable viscoelatic porous medium surrounded by a deformable viscoelastic tissue.

Following (1), the hysteretic pressure-volume relationship is described by the Preisach operator in the constitutive equation. We consider breathing as an isothermal time-periodic process with gas exchange between the interior and exterior of the body. The evolution of the system is governed by the mass conservation principle and the momentum balance equation. The mathematical problem consists in solving a PDE system with the time derivative of the Preisach hysteresis operator in the mass balance equation, in the spirit of (2). The main result, in (3), consists in proving the existence of a periodic solution under an arbitrary periodic forcing and suitable hypotheses.

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MODELLING COMPETITIVE INTERACTIONS AND PLANT-SOIL FEEDBACK IN VEGETATION DYNAMICS

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Plant-soil feedback has been proved to play an important role in the formation of vegetation patterns for a single species (1). In real-life, however, plants rarely grow in monoculture; hence multi-species scenarios are more realistic. In these cases, additional effects between different species - such as competition and interaction - must be considered. Moreover, plant-soil feedback is recognised as a causal mechanism for plant-species coexistence (2).

Using a mathematical model consisting of four PDEs, we investigate mechanisms of *inter-* and *intra-specific* plant-soil feedback on the coexistence of two competing plant species. In particular, the model takes into account both negative and positive feedback influencing the growth of the same and the other plant species. Both the coexistence of the plant species and the dominance of a particular plant species are examined with respect to all model parameters. Analytical and numerical results reveal the emergence of spatio-temporal patterns.

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STOCHASTIC MECHANISMS OF GROWTH AND BRANCHING IN MEDITERRANEAN CORAL COLONIES

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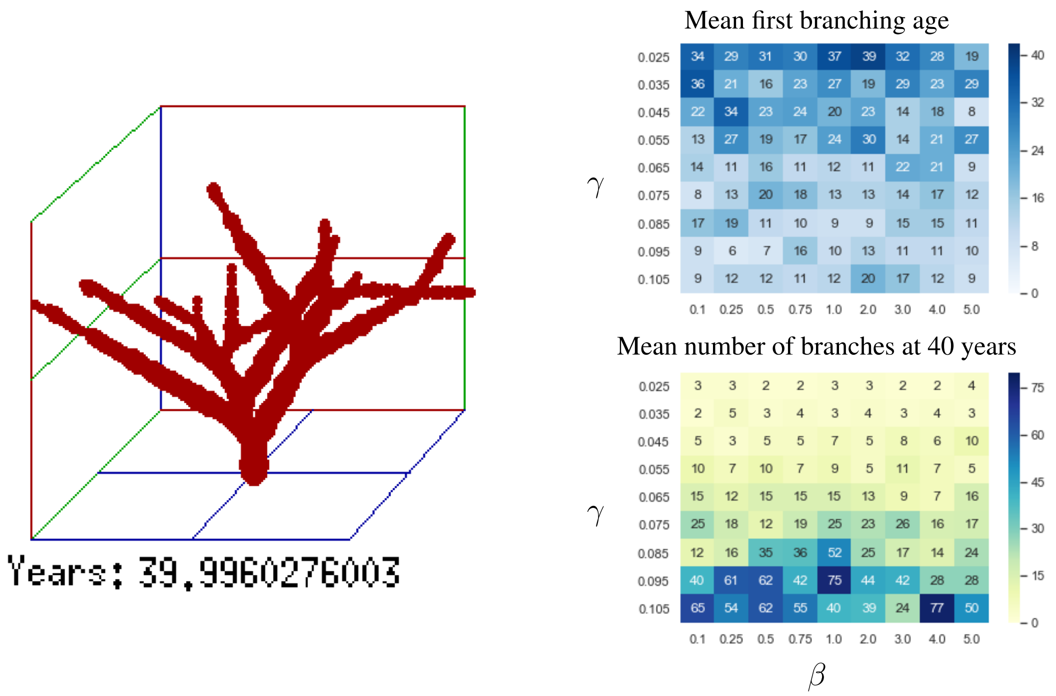
One of the fundamental questions in biology is concerned with the mechanisms that govern phenotype as a result of the interplay between the genetic material and the physical environment of the organisms. This is because the environment can strongly influence the developmental process. In particular, in the growth of marine sessile organisms such as seaweeds, sponges, and corals, there is a strong impact of the physical environment on the growth process, leading to a variety of structural forms (2).

The red coral *Corallium rubrum* is an octocoral species, endemic to Mediterranean and adjacent Atlantic rocky bottoms, which can be found between 10 and 800 m depth. This slow-growing species has a life span that can exceed 100 years. The skeleton of branching colonies is composed of calcium carbonate deposited by the polyps. The colonies exhibit wide variability in growth forms, which are linked to local environmental conditions. Due to extensive harvesting and increase in water temperature, this long-lived and slow-growing species, which has an important role in the three-dimensional structuring of coralligenous assemblages, is at risk of local extirpation in the coastal Mediterranean. Despite many conservation projects that focus on *Corallium rubrum*, little is known about the modular growth mechanisms of its colonies. In particular, theoretical models, which can be used for restoration and guide conservation policies, are lacking.

To this end, we present a simple stochastic model, based on three rules and accurately captures the phenotypic variability of the structures observed in the field



Mean first branching age

	0.1	0.25	0.5	0.75	1.0	2.0	3.0	4.0	5.0
0.025	34	29	31	30	37	39	32	28	19
0.035	36	21	16	23	27	19	29	23	29
0.045	22	34	23	24	20	23	14	18	8
0.055	13	27	19	17	24	30	14	21	27
0.065	14	11	16	11	12	11	22	21	9
0.075	8	13	20	18	13	13	14	17	12
0.085	17	19	11	10	9	9	15	15	11
0.095	9	6	7	16	10	13	11	11	10
0.105	9	12	12	11	12	20	17	12	9

Mean number of branches at 40 years

	0.1	0.25	0.5	0.75	1.0	2.0	3.0	4.0	5.0
0.025	3	3	2	2	3	3	2	2	4
0.035	2	5	3	4	3	4	3	4	3
0.045	5	3	5	5	7	5	8	6	10
0.055	10	7	10	7	9	5	11	7	5
0.065	15	12	15	15	15	13	9	7	16
0.075	25	18	12	19	25	23	26	16	17
0.085	12	16	35	36	52	25	17	14	24
0.095	40	61	62	42	75	44	42	28	28
0.105	65	54	62	55	40	39	24	77	50

Figure 1: **Left:** A screenshot from a representative video `https://youtu.be/FAH1DgqUO8w`. **Right:** The mean first branching age and the mean number of branches at 40 years age in 10 simulations in response to variations in branching rate (β) and calcium carbonate accumulation rate (γ). The branching age is measured as the simulation time at the generation of the first branching unit.

(2). Our model is based on the notion that the growth process can be described as calcium carbonate deposition and branching structures result from the deposition of fork layers on top of the previously deposited layers. As a result of this, and with the inclusion of stochasticity, the same processes, driven by the three rules of our model, result in an infinite number of different realisations of colony structures.

We show that the variations in structures due to the changes in model parameters are representative of the differences in environmental factors that affect the colony development. Repeated simulations on our model with varying parameters suggest that branching and growth are conflicting processes for the colony that may be prioritised in accordance with the environmental conditions (Figure 1). Our analysis provides an overview of how such stochastic models can provide insights into the structure and development of modular organisms.

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REPLICATOR EQUATIONS FOR STRUCTURED POPULATIONS: HAWK-DOVE GAME APPLICATION

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In this work, we describe a structured replicator equation model that includes a finite number of strategies and a finite number of physiological states. The population state distribution is considered to be a result of the environmental conditions; whereas, the strategies arise from behavioral plasticity. Our aim is to understand how a state-dependent fitness can affect the existence, stability and distribution of the strategies. As the first result, we prove the existence of an equilibrium point that describes a population with a mix of pure strategies over a partition of the structure set and provide a sufficient condition for its local asymptotic stability. Then, we extend the analysis to a particular case of a structured Hawk-Dove game. We prove that the forms of the cost, gain, and initial population function by the size can shift the population from one of complete coexistence to one with pure strategies.

NON-LOCAL BOUNDARY CONDITION IN A COMPUTATIONAL DOMAIN OF EXTERIOR PROBLEMS

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Physical problems of interest are often defined in unbounded domains, for example, so are the electromagnetic problems and flow problems in infinite domains. The point here is how to calculate the numerical solution more accurately using the non-local boundary condition proposed by Jo, et al.(1) The key idea comes from the Axial Green function Methods which starts in 2008 by the paper (5). The Axial Green function Methods enable us to calculate the electromagnetic field(2) and the Stokes flow(4) in arbitrary domains, including the convection-dominated problem(3) in complicated domains. While these previous works are conducted in bounded domains, the problems in unbounded domain is in fact most interesting. They have asymptotic behaviors at far boundaries, for instance, $u(\mathbf{x}) \sim u_0(\mathbf{x}) + C\,u_1(\mathbf{x})$ as $\mathbf{x}$ goes to infinity. As usual, the leading behavior u_0 and the next one u_1 are prescribed but the constant C is not determined a priori. Using the non-local boundary condition, we finally compute the unknown constant C as well as the numerical solution $u^h(\mathbf{x})$ in a smaller computational region compared to the larger truncated computational region on which artificial Dirichlet or Neumann boundary condition is given.

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OPTIMAL CONTROL PROBLEM OF INFLUENZA MODELS WITH INEQUALITY CONSTRAINTS

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Recently, A control theoretic approach is applied to minimize the number of infective individuals as well as the costs associated with vaccination and treatment (1; 2). In this talk, we consider various optimal control problems to derive an efficient vaccination strategy for influenza outbreaks. First, an optimal control problem of a SEIAR model is considered with control strategies include vaccination, antiviral treatment, and social distancing such as school closures. We also investigate an optimal control problem of a SIR reaction-diffusion system with inequality constraints. This control problem reflect realistic restrictions associated with limited total vaccination coverage and the maximum daily vaccine administration. The results of numerical simulations show that the optimal vaccine strategy varies regionally according to the spreading rate of the disease.

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DESTABILIZATION, STABILIZATION, AND MULTIPLE ATTRACTORS IN SATURATED MIXOTROPHIC ENVIRONMENTS

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The ability of mixotrophs to combine phototrophy and phagotrophy is now well recognized and found to have important implications for ecosystem dynamics. In this paper we examine the dynamical consequences of the invasion of mixotrophs in a model that is a limiting case of the chemostat. The model is a hybrid of a competition model describing the competition between populations of autotroph and mixotroph for limiting resources, and a predator-prey type model describing the interaction between populations of autotroph and herbivore. Our results show that mixotrophs are able to invade in both autotrophic environments and environments described by interactions between autotrophs and herbivores. The interaction between autotrophs and herbivores might be in equilibrium or cycle. We find that invading mixotrophs have the ability to both stabilize and destabilize autotroph-herbivore dynamics depending on the competitive ability of mixotrophs. The invasion of mixotrophs can also result in multiple attractors.

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IMPACT OF ADDITIVE ALLEE EFFECT ON THE DYNAMICS OF A INTRAGUILD PREDATION MODEL WITH SPECIALIST PREDATOR

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In this presentation, we consider a intraguild predation model in which predator is specialist, the growth of shared prey population is subjected to additive Allee effect and there is Holling-Type III functional response between IG prey and IG predator. We analyze the impact of Allee effect on the global dynamics of the system with the prior knowledge of the dynamics of the model without Allee effect. Our theoretical and numerical analysis suggest that: 1. Trivial equilibrium point is always locally asymptotically stable and it may be globally stable also. Hence, all the populations may go to extinction depending upon initial conditions; 2. Bistability is observed between unique interior equilibrium point and trivial equilibrium point or between boundary equilibrium point and trivial equilibrium point; 3. Multiple interior equilibrium points exist under certain parameters range. We also provide here a comprehensive study of bifurcation analysis by considering Allee effect as one of the bifurcation parameter. We observed that Allee effect can generate all possible bifurcations such as transcritical bifurcation, saddle-node bifurcation, Hopf bifurcation, Bogdanov-Taken bifurcation and Bautin bifurcation. Finally, We compared our model with the IGP model without Allee effect for better understanding the impact of Allee effect in the system dynamics.

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RAPID VACCINE OPINION SWITCHING: OPTIMAL AWARENESS CAMPAIGNS VIA DETERMINISTIC AND HEURISTIC ALGORITHMS

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Hesitancy and refusal of vaccines preventing childhood diseases are spreading due to 'pseudo–rational' behaviours: parents overweight real and imaginary side effects of vaccines and do not fully perceive the actual risks linked to the disease. The complex dynamics ruling vaccine uptake has been modelled as an imitation game (1) or, equivalently, as 'infection of ideas' (3), augmented by terms modelling the switching of vaccine position (from 'anti' to 'pro') thanks to awareness campaigns enacted by the Public Health Systems (1). Here we investigate the noteworthy case, of great relevance in the age of social networks, where the opinions rapidly change, so that the system (in absence of the awareness campaigns) can be reduced to the phenomenological model proposed in (2), where the vaccine uptake rate was an increasing function of the prevalence. After briefly investigating how the above mentioned campaigns influence the dynamics of the system, we study the problem of minimizing the total cost of the disease spread and control. It is formed by different 'sub–costs': that related to the disease burden, the vaccination costs and the economic burden to enact the awareness campaigns. We numerically explore the impact of human behaviour on the control and spread of the target disease via both deterministic and heuristic methods. For the latter, we also provide a statistical assessment. Finally, results are compared with those obtained in the case of slow opinion switching dynamics.

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OPTIMAL STRATEGIES MINIMIZING THE CONTROL OPERATION COSTS IN BIOCELL COMPOSTING

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We present a recent optimal control problem for composting in biocell (2), whose aim is to find suitable strategies that minimize the total costs due to the control operation and to the minimization of soluble substrate concentration. The problem is based on a mathematical model, taking account of (i) degradation of soluble substrate by an aerobic bacterial biomass; (ii) solubilization of insoluble substrate; (iii) biomass decay phenomenon. The control is acted by monitoring the effects of oxygen concentration in the cell atmosphere on the degradation term. The operation cost is modeled by linear and quadratic function of the effort. We will show that optimal strategies in the linear case lead to a higher reduction of soluble substrate and to a major effort with respect to the quadratic case.

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REINFECTION THRESHOLDS DETERMINED BY THE MAXIMUM CURVATURE OF THE ENDEMIC STATE

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The reinfection SIRI model describes the spreading of an epidemics in a population of susceptible, infected and recovered individuals, where after an initial infection the recovered individuals only have partial immunity and may be infected again. Using the SIRI model, Gomes et al. introduced the reinfection threshold concept for epidemic models. Here, we extend the notion of reinfection threshold. Our extension is based on the maximum curvature of the endemic state graph, that can be used to define the beginning point and the end point of the reinfection region.

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QUALITATIVE ANALYSIS AND NUMERICAL APPROXIMATION OF AN OPTIMAL CONTROL MODEL FOR INVASIVE SPECIES

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Invasive species cause huge amounts of environmental, economic, social and cultural damage in Europe and worldwide. Improving measures to control them is an ongoing challenge, and mathematical modeling and optimization are becoming increasingly popular as a tool to assist management (1; 2; 4). We analyse an optimal control model for the control of invasive species which aims to find the best temporal resource allocation strategy for the population reduction, under a budget constraint (3). We derive the optimality system in the state and control variables and we use the phase-space analysis to provide qualitative insights about the behaviour of the optimal solution. We pay special attention to the nature of the optimal trajectories in long time intervals and the explore the Turnpike property of the problem (5). Finally, we introduce a numerical scheme for the solution of the state-costate nearly-Hamiltonian system, based on exponential-Lawson symplectic Runge-Kutta schemes applied in a forward-backward procedure.

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HOW MANY GENES FROM Wnt-CASCADE IDENTIFY *tnbc*-PATIENTS?

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Burst cancer is widely spread pathology, worldwide. Some types of cancer are hard to detect and cure, *tnbc* is among them. Molecular genetics methodology may contribute a lot in the problem. We studied the Wnt-cascade gene expression database of three types of patients: *tnbc* (118 entries), *non-tnbc* (852 entries) and healthy women (112 entries). The database was provided by Prof. Vladimir Katanaev from Geneva University. Due to database inconsistency, few genes have been removed from the consideration, so that we dealt with 68 genes. Standard techniques of statistical analysis fail to distinguish properly *non-tnbc* from *tnbc* patients (2). We used elastic map technique that provides almost perfect clustering for *non-tnbc*, *tnbc* and healthy patients. It has been found that an incomplete set of genes provides similar (or even the same) clustering, as the full set of them does. Hence, we tried to identify the minimal set of genes still providing the clustering with high resolution of *non-tnbc*, *tnbc* and healthy patients. Obviously, such minimal subset could be ambiguous. To figure out the minimal subset of genes still yielding the reasonable clustering with good determination of those three groups of patients, we generated a series of subsets of various abundance of the genes involved into the clustering implementation. Each series comprises as many, as 50 different samplings from the original database. The number of genes included into the samplings varied from 68 (a single set of genes) through 34, 16, 8 and 4. It was found that three sets of 8 genes yield the clusterings with minor deviations from that one provided over the complete set of genes. Other subsets of this capacity failed to provide a proper clustering. This fact means that the set of genes of Wnt-cascade is redundant, from the point of view of revealing the pathology standing behind the difference in genes expression. Obviously, the cascade set may not be claimed as redundant, from the point of view of functioning of the network. Apparently, this duality conspires the good identification of *tnbc* patients with linear statistics techniques.

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A MODEL FOR ACUTE MYELOID LEUKEMIA (AML)

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Idasanutlin (RG7388) is a potent and selective MDM2 antagonist showing promising responses in phase 1 studies in relapsed/refractory AML. The drug is presently undergoing Phase I and II clinical trials. RG7388 was generally well tolerated with GI toxicity being the most commonly reported adverse event. In laboratory cultures of MOLM-13 wild type cells it was observed that using increasing dosages of RG7388 led, within 96 days, to a complete replacement of wild type (drug-sensitive) cells by mutant (drug-resistant) cells. We propose a model for the growth of the two strains of cells in such cultures that is designed to elucidate whether the replacement is due to the natural mutation of the wild type cells or rather to the use of RG7388 for AML treatment.

MATHEMATICAL MODELING OF POPULATION DYNAMICS IN BIOLOGICAL SPECIES

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The motivation behind this research is to investigate mathematical models to describe the population dynamics of biological species. In particular, we focus the attention on populations of large and long-lived raptor species. These species are mainly characterized by the lifetime stability of their breeding pairs and by a marked philopatry. The methodology based on population viability analysis (PVA), usually considered in conservation biology and in the management of threatened or endangered species, requires information about several variables (sizes, ages, mortality rates, growth rates, environmental variables, etc.) In practice, real data about such variables are difficult to obtain. Mathematical models based on other methodologies have not been sufficiently developed for these raptor species. Recently, in order to describe the demographic dynamics of such biological species, we have introduced a class of mathematical models, based on branching processes, see (1). Unlike other classes of models developed in the literature, we have considered the most realistic practical situation where the coexistence in the population of individual from different generations is assumed. By considering such a class of stochastic models, we now study several statistical questions of ecological interest. As illustration, we apply the proposed methodology to describe the population dynamics of some Eurasian black vulture colonies located at the region of Extremadura (Spain) which appear to be both the largest and densest breeding colonies worldwide.

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IMPACT OF VENEREAL TRANSMISSION ON THE DYNAMICS OF VERTICALLY TRANSMITTED VIRAL DISEASES AMONG MOSQUITOES

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Despite centuries of enormous control efforts, mosquito-borne diseases continue to show upward trend of morbidity. According to WHO reports, malaria caused 438000 deaths in the year 2015 and dengue cases has been increased 30-fold over the last five decades. To control these diseases, it is necessary to understand the transmission dynamics of them among mosquitoes. There are some vertically transmitted mosquito-borne diseases which can also be spread among mosquitoes through sexual contact (e.g., dengue, zika, chikungunya). Recent experimental observations indicate that for virus persistence in mosquito population, the role of venereal transmission can not be ignored. It is therefore important to investigate which transmission route is more responsible for the persistence of the virus when there is no host. To this aim, we propose and analyze a novel compartmental model considering mosquito population only. To the best of authors knowledge, this is the first attempt to take into account both vertical and sexual transmission of the virus in a mathematical model. Expression representing the basic reproduction number is derived using Jacobian approach. Local stability conditions for disease-free equilibrium and complete infection equilibrium are obtained. Global sensitivity analysis of the system is performed with respect to an epidemiologically important response. While investigating the impact of sexual transmission in presence of vertical transmission, we observed that sexual transmission route has the potential to drive the equilibrium from disease free to endemic states. Further numerical experiments reveal that the virus will have higher half life in fertilized infected female mosquitoes for vertical transmission only than for venereal transmission alone. Furthermore, when both transmission

pathways are active, a variety of parameters indicate threshold like behavior of the infection.

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INFLUENCE OF HARVEST ON DYNAMICS OF "PREDATOR-PREY" COMMUNITY

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We propose a time-discrete model of "predator prey" community to describe dynamics of a community like arctic fox mouse rodents. (2) The community is under anthropogenic impact, which is realized as a harvest of some part of predator or prey population. The model takes into account seasonality of the life cycles of predator and prey populations. In addition, each of the species under consideration has an age structure represented by two stages of development. Prey population growth is limited by density-dependent regulation of birth rate. Limiting the survival of juveniles is observed in predator population. Harvesting is assumed to be discretely timed with intervals equal to the reproduction period, with a yield proportional to population size.

The bifurcations, dynamic modes and a possibility of its shifting are studied for the model proposed. It has been shown the stability loss of a non-trivial fixed point is realized according to both the Neimark-Sacker scenario and the Feigenbaum one.

The study of anthropogenic impact influence on community dynamics shows harvest of some share of the prey's population from the community leads to an expansion of stability area of non-trivial stationary state. Consequently, harvest of prey population results in sustainable coexistence of community species (Figure). The harvest of part of prey population has little effect on the dynamics of the predator population. The changes are mainly associated with areas of multistability, in which the community dynamics depends on the initial population sizes. With high values of reproductive potentials of both populations, the community dynamics can adapt to the dynamics of both prey and predator, depending on their initial population sizes. Increasing harvest rate leads to multistability domain contraction, and as a result, expansion of parametric space area, in which fluctuations of prey population size are initiated by the predator (Figure).

In the case of the predator population harvest, stability domain of the nontrivial

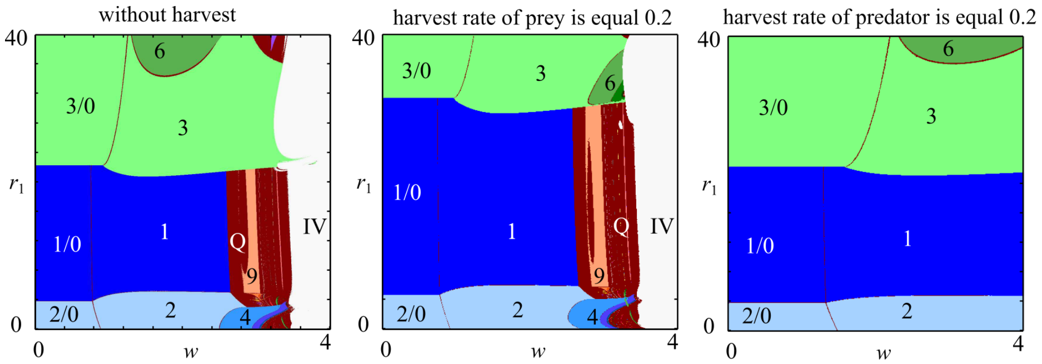

Figure 1: Dynamic mode maps of predator-prey model with harvest. The figures correspond to the period of observed cycle. Q is a quasi-periodic dynamics, C is chaotic dynamics. 1/0, 2/0, 3/0 are stable semi-trivial solutions: 1, 2, 3 are periods of cycles observed in prey population, 0 corresponds to extinction of predator population. IV is infeasible parameter value area where the model loses its meaning. r_1 and w are birth rates of prey and predator populations, respectively.

fixed point expands along the parameter characterizing the birth rate of predator (Figure). Accordingly, a situation, where a predator determines the prey population dynamics, is possible only at high values of predator reproductive potential. With an increase in harvest rate an expansion of parametric areas is observed, where variation in the current population sizes leads to a change in the species determining the dynamics of the community. In particular, when the values of demographic parameters and interaction coefficients are fixed, for some current population sizes of community the predator suits to the periodic dynamics of the prey, while for others the predator initiates quasiperiodic fluctuations in the prey population.

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FIT OF IMMUNE RESPONSES BY CD4$^+$ T CELLS TRIGGERED BY LCMV INFECTION

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We fit an ODE model of immune response by CD4+ T cells to a time series of data from mice infected with lymphocytic choriomeningitis virus (LCMV). We considered two clonotypes of CD4+ T cells, gp61 and NP309 LCMV epitopes. The model also includes the presence of regulatory T cells (Tregs) and interleukine-2 (IL-2) density. This model is able to fit both the immune activation phase triggered by the LCMV infection and the subsequent relaxation phase, with a smooth transition from faster to slower death rates.

Acknowledgements
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MODELLING STUDY OF THE ASSOCIATION BETWEEN SEXUALLY TRANSMITTED INFECTIONS

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To understand the dynamics of sexually transmitted infections (STIs), understanding sexual behavior is important. However, quantification of sexual behavior is difficult due to its nature. Indeed, our analysis showed no clear trend between HIV prevalence and the estimated sexual behavior (1). Instead of sexual behavior, the use of STIs prevalences as a bio-marker of other STIs was proposed. To assess the accuracy, we analyzed the association between sexually transmitted infections. An individual-based mathematical model was constructed to describe temporal sexual contact network (2) and STI transmissions of HIV, herpes simplex virus type 2 (HSV-2), gonorrhea, chlamydia, and syphilis. Model was parametrized with representative biological and behavioral data. A total of 500 varied sexual networks were simulated, on each of which STI transmission was also simulated. Associations were assessed on model-simulated STI prevalences. Regressions were conducted to evaluate the predictability of HIV prevalence from each of the other STI prevalences. Sexual networks affect different STIs in both similar and variable ways, leading to rich dynamics and varying associations between STIs. Still, knowledge of the prevalence of one STI can be predictive of that of another STI. This outcome is specially relevant for HIV, as prevalence of other STIs can be used as an objective biomarker for HIV epidemic potential.

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FOREX FORECASTING USING PRINCIPAL COMPONENT ANALYSIS AND LOCAL LINEAR EMBEDDING

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We employed Principal Component Analysis (PCA) and Local Linear Embedding (LLE) to construct embedded Foreign Exchange Rate (FOREX) portfolios whose performance was accessed by trading simulations. For our analysis we used a data-set of 20 FOREX pairs spanning the time period between 01-01-1997 and 26-06-2017. Our aim was to try to forecast the embedded time series using Exponential Moving Average (EMA), but also ARIMA and Recurrent Neural Networks (RNN). The trading simulations provided high scores in terms of sharpe ratios compared to the classical equally weighted and risk parity portfolios. Furthermore, we show that the LLE outperforms the PCA embedding when using RNN for forecasting, while it provides almost the same results when using EMA and ARIMA models.

PERIODIC VACCINATION STRATEGIES 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. Here, we introduce the dynamical evolution of the morbidity risks and observe the arise of periodic vaccination strategies.

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EGFR TRAFFICKING AND SIGNALLING: INSIGHTS FROM MATHEMATICAL MODELLING

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One of the most important tyrosine kinase receptors, mediating signals for proliferation, differentiation and development is the epidermal growth factor receptor (EGFR). Human cancer is often characterized by dysfunctional EGFR signalling induced by the overexpression of the receptor and/or the upregulation of its ligands. The EGFR fate and signalling are regulated by several mechanisms of which the major is the endocytosis. EGFR can be internalized through two internalization pathways depending on the ligand dose, *i.e.*, the clathrin-mediated endocytosis (CME) and the non-clathrin endocytosis (NCE). They regulate the recycling or degradation fate of the receptors. Particularly, NCE is related to EGFR degradation whereas CME is mainly linked to receptor recycling and sustained signalling, see Figure 1.

In this contribution, preliminary results will be provided on the development of a novel mathematical model of EGFR trafficking to test hypotheses on the principal mechanisms regulating the different EGFR endocytosis pathways and their impact on EGFR signalling propagation. The extended dynamical model is built starting from an early activation model (EAM) (1), consisting of a system of ordinary differential equations (ODEs), focusing on the first two minutes after EGF stimulation. The extended model herein presented fits *ad hoc* data from wet-lab experiments and provides a more accurate quantitative description of the EGFR phosphorylation and ubiquitination processes. Moreover, it includes for the first time a preliminary description of the EGFR internalization processes. The current

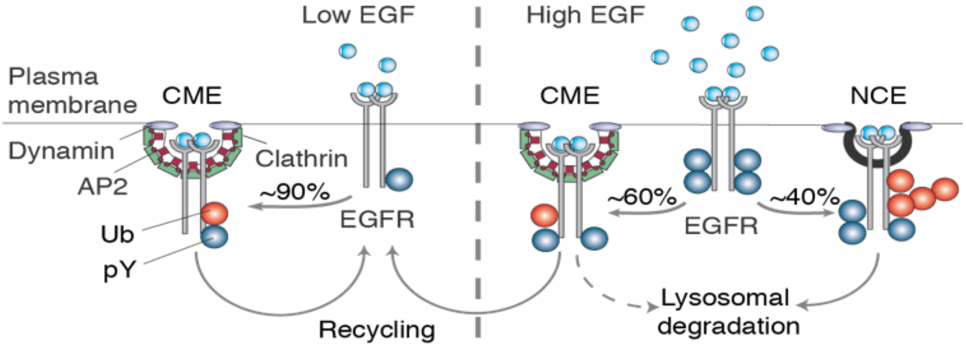

Figure 1: EGFR is internalized either via CME or NCE: CME is activated at low EGF doses and it is mainly involved in EGFR recycling and sustaining signalling; the NCE is activated only at high EGF concentrations, and it leads primarily to receptor degradation and signals extinction, representing a mechanism to protect cells from overstimulation.

model allows simulating the system for longer time periods and provides a unique opportunity for building a computational framework to investigate how EGFR signalling/endocytosis dysfunction could contribute to the tumorigenic process.

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POVERTY TRAPS IN MULTILEVEL SYSTEMS

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Social-ecological systems are defined as coupled human-nature systems, where society and nature co-evolve rather than externally influence one another. The ecological aspect of such systems is often traced through population dynamics (representing stock growth) or through nutrient flow, the epidemiological component is introduced through disease dynamics, but the social aspect presents significant challenge for modelling. Great diversity of human activities and ways in which people affect environment and respond to changes in the ecosystem require tailored approach and careful choice of systems variables. Human activities, such as agricultural production or fishing, can be influenced by social norms, institutional decisions and individual behaviour, habits and opinion dynamics. This may require considering more than one level of organization, i.e. including individual, community or even country level and cross-level interactions in models.

We illustrate social-ecological modelling on the example of poverty traps, which are defined as undesired self-reinforcing mechanisms that keep individuals or communities below threshold of economic well-being. The ecological part in our models is represented by nutrient dynamics and the economic component is based on agricultural production. The social aspect includes decision making on individual and community levels and interactions between these two levels. Using stability and bifurcation analysis, we investigate how within and cross-level interactions shape long term behaviour of the multilevel system.

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AN EXTENDED DYNAMICAL MODEL OF α-SYNUCLIEN METABOLISM

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α-synuclein (α-syn) is a 140 amino acid protein that is abundantly expressed in the nervous system and contributes to the control of neurotransmitter release (1). In addition, aggregates of misfolded α-syn are the main component of Lewy bodies, fibril-like agglomerates. High abundances of Lewy bodies impair the production of dopamine leading to severe neurogenerative diseases such as Parkinson's disease (PD) or Lewy Body dementia (2).

Under normal conditions, α-syn metabolism rarely promotes the formation of aggregates, such as dimers or oligomers, which, in the long run, lead to the formation of Lewy bodies. However, different external factors as oxidative stress or the mutation of genes such as SNCA, LRRK2, and Parkin result in promoting the aggregation of α-syn (2). As a consequence, these risk factors increase the likelihood of developing the diseases of several folds.

In recent years, different mathematical models have been proposed to provide a dynamical description of α-syn metabolism and the formation of aggregates (3). However, most of these models could not depict the entire α-syn metabolism and its interactions with the cellular environment. To provide a complete picture of the α-syn dynamics, to elucidate the processes that lead to its aggregation, and to better characterize its interaction with the other cellular processes, we introduce an enhanced dynamical model of α-syn metabolism, which combines and extends existing mechanistic models. We parametrize the model by combining the existing knowledge and the available literature data. Moreover, we explore the α-syn dynamics by using a combination of stochastic and deterministic simulations (4).

Through sensitivity analysis (5) and in-silico experiments, we quantify the effect of different causes in perturbing or affecting the course of the aggregation. In this way, we can provide a cause-effect map that includes several risk factors for the accumulation of α-syn. Moreover, the model can support the development of new drugs and identify relevant metabolic processes for the occurrence of Lewy body related diseases. Potentially, the model may provide a tool to in-silico asses the effect of candidate therapeutics to ameliorate patient conditions or slow down the progress of neurodegeneration.

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COMPLEX DYNAMICS OF DISCRETE-TIME PREDATOR-PREY SYSTEM WITH STAGE-STRUCTURED PREY

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The study of biological communities, such as predator-prey or host-parasite systems, is one of the most important environmental problems. Predator-prey interactions are crucial to formation of the species composition in a community and their dynamics. In particular, predator-prey interactions can cause fluctuations in the numbers of both interacting species and can amplify such fluctuations if they exist due to other causes. In this work, we present a new look at the problem of complex dynamics that can arise between a prey and a predator.

The paper investigates dynamic modes of the predator-prey model with age structure for prey. We use a slight modification of the Nicholson-Bailey model to describe the interaction between predator and prey. We assume the population size is regulated by decreasing juvenile survival rate with growth of age class sizes. Conditions for sustainable coexistence of interacting species are described. It is shown that the coexistence of species becomes possible if there are a transcritical or saddle-node (tangential) bifurcations. Due to the saddle-node bifurcation there is bistability in the system of interacting species: predator either coexists with prey or dies depending on the initial conditions. It is shown, with changing parameters values and transition through the stability domain boundary the stability loss of the model fixed point may occur according to both scenarios: the period doubling and the Neimark-Sacker bifurcation. In the first case period doubling bifurcation leads to occurrence of stable fluctuations of sizes. In the second case the dynamics of population sizes begins to demonstrate quasiperiodic dynamics.

We studied the oscillation scenarios of interacting population, influences of reproduction, survival and self-regulation rates of population prey and age-dependent predation as well as variations in the current number on transitions between different dynamic modes. It is shown that an increase in the birth rate of the prey under intraspecific competition can lead to a dynamics destabilization and to complex oscillations appearance in numbers. Besides, age-dependent predation has a stabilizing influence. The anthropogenic impact on the community and its components, including deratization and harvesting, has been studied. It was found that in the model parametric space there arise the areas of multistability, which are not related to bistability of semi-trivial and non-trivial fixed point. Consequently, even a small variation of the current population size leads to more complex behavior of the interacting species, and can give a significant change in both the observed dynamic mode and the coexistence scenario of the species.

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ALLEE EFFECT BIFURCATION IN THE γ-RICKER POPULATION MODEL USING THE LAMBERT W FUNCTION

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The classical discrete Ricker population model was proposed for modeling fish populations, see (1). Since then this overcompensatory model has been used in several studies with applications to different types of populations, see, for example, references in (2). In the definition of the classical discrete Ricker population model, given by the difference equation $x_{n+1} = r\ x_n\ e^{-\delta x_n}$, is assumed that the survival function for generation n is density-dependent, while the birth or growth rate is density-independent. However, in several applications of this model to biology and ecology there are circumstances which lead to non constant density-dependent birth or growth functions. This phenomenon can be caused by several factors: difficulty to find mates, environmental modification, predator satiation, cooperative defense, among others. This model is classified in several studies as relatively inflexible, since it has only two parameters.

In this work it is considered the discrete-time population model whose dynamics of the population x_n, after n generations, is defined by the difference equation,

$$x_{n+1} = b(x_n)\ x_n\ s(x_n), \text{ with } n \in \mathbb{N} \tag{1}$$

where $b(x_n) = x_n^{\gamma-1}$ is the per-capita birth or growth function (a cooperation or interference factor), with $\gamma > 0$ the cooperation parameter or Allee effect parameter, $s(x_n) = e^{\mu-\delta x_n}$ is the survival function for generation n or the intraspecific competition, with $\mu > 0$ the density-independent death rate and $\delta > 0$ the carrying capacity parameter. In particular, we consider the γ-Ricker population model defined by Eq.(1) written in the form,

$$x_{n+1} = r\ x_n^{\gamma}\ e^{-\delta x_n} := f(x_n) \tag{2}$$

where $r = e^{\mu}$, γ and δ are positive real parameters and $f : [0, +\infty[\to [0, +\infty[$. This stock-recruitment model is usually called γ-Ricker model or γ-Ricker map.

The particular case $\gamma = 1$ is known as the classical overcompensatory Ricker model, which was introduced by Ricker in the context of stock and recruitment in fisheries, see (1). The limit case $\delta \to 0^+$ corresponds to the Cushing model. Throughout this work, the parameters space is denoted by,

$$\Sigma_0 = \left\{ (r, \gamma, \delta) \in \mathbb{R}^3 : \; r, \gamma, \delta > 0 \text{ and } \; \gamma \neq 1 \right\}. \tag{3}$$

The main purpose of this talk is to present the dynamical study and the bifurcation structures of the γ-Ricker population model. Resorting to the Lambert W function, the analytical solutions of the positive fixed point equation for the γ-Ricker population model are explicitly presented and conditions for the existence and stability of these fixed points are established. The use of the Lambert W function, generally defined as the real analytic inverse of the function $W(x) = xe^x$, allows us to obtain a deeper insight and a new point of view of the behavior of the γ-Ricker population model. This procedure proves to be extremely useful, since the fixed points expression of the γ-Ricker population model is an implicit condition.

Another main focus of this work is the definition and characterization of the Allee effect bifurcation for the γ-Ricker population model, which is not a pitchfork bifurcation. Consequently, we prove that the phenomenon of Allee effect for the γ-Ricker population model is associated to the asymptotic behavior of the Lambert W function in a neighborhood of zero. The theoretical results describe the global and local bifurcations of the γ-Ricker population model, using the Lambert W function in the presence and absence of the Allee effect. The Allee effect, *snap-back repeller* and big bang bifurcations are investigated in the parameters space considered. Numerical studies are included.

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TFEB TRANSLOCATION DYNAMICS: QUANTITATIVE MODELLING AND EXPERIMENTAL ANALYSIS

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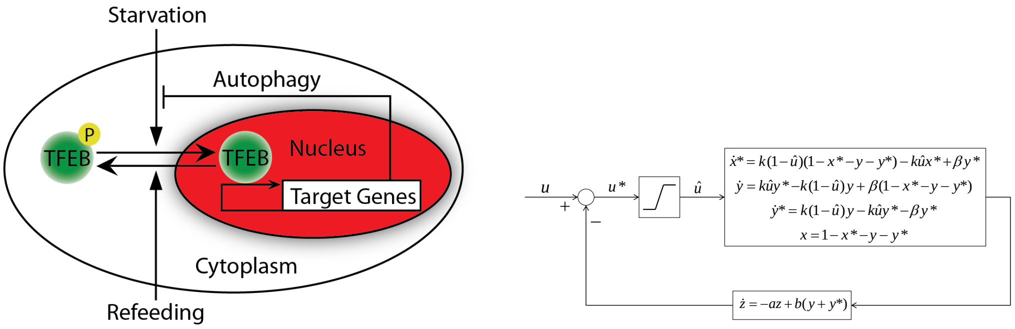
Mammalian cells can be described as dynamical systems. They detect, adapt and respond to time-varying inputs, such as environmental cues, secreted molecules and mechanical stimuli. In particular, we focused on their response upon starvation stimulus. Under nutrient stress, cell metabolism adapts to sustain cell survival by initiating autophagy. During autophagy, cytoplasmic components, damaged proteins and entire organelles are degraded and recycled to generate building blocks for the synthesis of proteins that are essential for survival.

The Transcription Factor EB (TFEB) plays a pivotal role in organelle biogenesis and cell metabolism. TFEB acts as a global controller of autophagy (as well as of lysosomal biogenesis, lysosomal exocytosis, lipid catabolism, energy metabolism, and in the modulation of the immune response). TFEB is often deregulated in different types of cancer, suggesting that the pharmacological modulation of TFEB activity may represent a relevant therapeutic approach for a wide number of diseases (1).

As shown in Figure 1 (a), under nutrient-rich conditions, TFEB is phosphorylated and sequestered in the cytoplasm. Upon amino-acid starvation, TFEB is dephosphorylated and can freely translocate to the nucleus where it transcriptionally activates lysosomal and autophagic pathways (2; 3). Phosphorylation of TFEB in the nucleus has been reported as responsible for its nuclear export (1).

Here, we investigated the dynamics of TFEB shuttling between the cytoplasm and the nucleus upon starvation and feeding stimuli.

We derived a nonlinear dynamical model to describe TFEB translocation. The



(a) *TFEB nuclear-cytoplasmic shuttling.* (b) *Closed-loop model of TFEB translocation.*

Figure 1: (*a*) TFEB is phosphorylated and sequestered in the cytoplasm under normal feed condition. In the absence of amino-acids, TFEB is dephosphorylated and translocates into the nucleus, where it activates the transcription of its target genes. In turn, these genes activate autophagy to modulate the starvation response. (*b*) The translocation model is represented by a system of nonlinear differential equations of the third order. A feedback action has been hypothesized to explain the overshoot experimentally observed.

model consists of two compartments (nucleus and cytoplasm), where two species (de/phosphorylated TFEB) were considered for each. Both de/phosphorylation and transport were modeled as first order kinetics whereas the input (the nutrients concentration) acts by changing the de/phosphorylation rates. The model parameters were inferred from the available experimental data of (1).

We experimentally measured the response of TFEB upon starvation by means of a microfluidics platform, observing two characteristic dynamics. The first is the rapid translocation of TFEB from the cytoplasm to the nucleus (of the order of minutes) upon switching from feeding to starvation, and can be explained by the open-loop model proposed above. The second is an overshoot dynamics (of the order of hours), and can be explained by hypothesizing the presence of a negative feedback action closing the loop (Figure 1 (b)).

The closed-loop model was based on biological reasonable hypotheses and recapitulated the whole dynamics behaviour observed experimentally. We investigated the TFEB response to starvation in deep by using different drugs (Torin 1, Bafilomycin A1, Cycloheximide) to prove this hypothesis. At present, further analysis is required in order to confirm our thesis.

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POPULATION BALANCE APPROACH FOR PREDICTING POLYMER PARTICLES MORPHOLOGY

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Polymer particles morphology can be defined as a pattern of phase-separated domains comprising a multi-phase polymer particle (1). Properties of a polymer particle strongly depend on its morphology, and thus the control of particle morphology is a key factor for success in producing high-quality polymers materials, such as coatings, adhesives and additives (2).

Currently, an accurate prediction of particles morphology is still a challenge due to its complexity. Several modelling approaches, describing the dynamics of the morphology of a single particle, have been suggested in the last few years (3; 4; 5). However, the single-particle approaches only provide a partial view of realistic systems, containing millions of particles. Furthermore, such models are computationally demanding even with the use of High Performance Computers.

In contrast to currently available computationally expensive and restricted single-particle approaches, we recently proposed (6) a Population Balance Equations (PBE)-based model to predict the size distribution of polymer agglomerates, composing the morphology of interest. The PBE model provides a view of the whole population of polymers particles, taking into account the relevant kinetic and thermodynamic effects behind the morphology formation (7).

The numerical treatment of such a model is not trivial due to the following difficulties. First, reactants and particles concentrations may be coupled, leading to a challenging integration of the resulting system of equations. Then, numerical solutions require substantial computational resources since, in practical engineering processes, the computed solution may extend over several orders of magnitude and can exhibit very sharp moving fronts.

We propose three novel numerical approaches which help to obtain accurate and efficient numerical solutions of the introduced model. While the Optimal Scaling (OS) (8) procedure, designed for the dimensionless reformulation of equations expressed in physical units, assures computationally tractable orders of magnitude for the PBE terms, the novel Generalised Method of Characteristics (GMOC) allows for the integration of PBE models with coupled dynamics. Finally, the Laplace Induced Splitting Method (LISM) combines a splitting integration scheme with Laplace induced analytical solutions to enhance accuracy and speed of the numerical treatment.

We discuss the main features of OS, GMOC and LISM methodologies and present numerical results demonstrating the potential of the proposed techniques.

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IMPACT OF FEAR IN A TRI-TROPHIC FOOD CHAIN MODEL INCORPORATING PREY REFUGE

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A tritrophic food chain model is proposed in this work where consumer (or, predator) hunt for prey species (or, source) with Holling type-III functional response and the functional response between consumer and predator (or, top-predator) follows Beddington-DeAngelis response. It is assumed that the birth rate of the prey population is affected and in fact, is reduced due to the fear of predation. Incorporation of prey refuge term implies that only a fraction of prey is available to the consumer for consumption. Positivity and boundedness of the system guarantee that the proposed model is biologically well-posed. Analytical results show that there are some parametric restrictions under which the system is permanent. By Routh-Hurwitz criterion, the local stability conditions of the equilibrium points have been analyzed and on the other hand, Lyapunov LaSalle theorem proves that the locally stable equilibrium points are globally stable under some parametric restrictions. Also , Matlab supports the analytical findings with the help of diagrams. The occurrence of one dimensional as well as two-dimensional bifurcations have been shown and conditions for the existence of a limit cycle in the system through Hopf bifurcation also have been stated. The numerical figures depict that the prey refuge has both stabilizing and destabilizing effect on the system. Both the analytical and numerical results suggest that a minimum amount of fear is needed to make the system steady.

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GAME THEORY OF FISHERIES MANAGEMENT

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Fish populations subject to heavy exploitation are expected to evolve over time smaller average body sizes. In this work we use evolutionary game theory to show how fisheries management should be adjusted to mitigate the potential negative effects of such evolutionary changes.

We present the game of a manager versus a fish population, where the former adjusts the harvest effort and the net size to maximize profit, while the latter responds by evolving their size at maturation to maximize their fitness. We analyze three strategies: i) ecologically enlightened (leading to a Nash equilibrium in game-theoretical terms); ii) evolutionarily enlightened (leading to a Stackelberg equilibrium) and iii) domestication (leading to team optimum). In order to determine the impact that incorporating evolution into the management decision framework can have in terms of profit, we calculate the manager's profit at the three equilibria. Domestication results in the largest size for the fish and the highest profit for the manager. With the Nash approach the manager tends to adopt a high harvest rate and a small net size that eventually leads to smaller fish. With the Stackelberg approach the manager selects a bigger net size and scales back the harvest effort to preserve both the long term size of the fish and the profit.

Overall, our results encourage fishery managers to take evolutionary dynamics into account and advocate the use of evolutionary game theory as a tool for providing insights into the eco-evolutionary consequences of exploiting evolving resources.

A MATHEMATICAL MODEL TO PREDICT GROWTH AND SIZE OF METASTATIC TUMORS UNDER THERAPY

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The identification and quantification of metastases is necessary to find the optimal treatment for an individual patient suffering from cancerous diseases. Due to limited possibilities of medical imaging techniques, it is currently technically too difficult to find metastases of very small sizes. These micro metastases though can highly influence the treatment success. About 90% of cancer deaths do not occur due to primary tumors and their resulting symptoms but metastases, of which most are undiscovered at the time point of primary diagnosis (1). Mathematical models capable of describing metastases growth are therefore of high clinical interest to assist choosing an appropriate treatment setting.

A McKendrick-von Foerster equation introduced by Iwata et al. (2) was modified to describe different scenarios and aspects of the metastatic seeding process. The numerical implementation of those scenarios facilitated a possible comparison to clinical data of lung cancer patients under treatment, from whom model parameters could be gathered. The model is defined in a continuous setting which allows it to also model the transition of a single primary tumor towards a metastatic disease, thus indicating the metastatic cascade necessary to develop multiple metastatic tumors.

The resulting prognostic possibilities were used to quantify the total metastatic burden at the time point of primary diagnosis retrospectively for those patients and to forecast their further development and seeding behaviour. In these sets of clinical data, the framework could correctly predict sizes of metastases which were not yet discovered at the primary diagnosis. Further analysis included *in silico* experiments of different therapeutic schedules with differing medications and time plans.

The work described in this abstract was also presented during the poster session of the DSABNS 2020.

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JENSEN'S INEQUALITY AS A TOOL FOR EXPLAINING THE EFFECT OF OSCILLATIONS ON THE AVERAGE VALUES OF VARIABLES

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Nonlinear oscillatory systems, playing a major role in biology, do not exhibit harmonic oscillations. Therefore, one might assume that the average value of any of their oscillating variables is unequal to the steady-state value. However, it is known that for Lotka-Volterra systems, these values do equal each other. Also for a number of mathematical models of calcium oscillations, the average cytosolic calcium concentration (not, however, the average concentration in the intracellular store) has this property. We show that this also holds for the Higgins-Selkov model of glycolytic oscillations and the smallest chemical system with Hopf bifurcation, while it does not hold for the Goodwin oscillator often used to describe circadian oscillations.

Moreover, we apply Jensens inequality to analyze under which conditions the average value during oscillations is lower or higher than the steady-state value. Jensens inequality states that for a (strictly) convex function, the function value of the average of a set of argument values is lower than the average of the function values of the arguments from that set. By analytical calculations, we derive that, if the Ca2+ efflux is a strictly convex (concave) function of the cytosolic Ca2+ concentration, then oscillations lower (increase) the average Ca2+ concentration in comparison to the unstable steady state.

We discuss our results in view of the question which advantages oscillations may have in biology. For example, the implications of the findings for the decoding of calcium oscillations are outlined.

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DYNAMICAL BEHAVIOR OF PREDATOR-PREY MODEL SUBJECTED TO ALLEE EFFECT IN THE PREDATOR

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Implementation of prey-predator interaction in mathematical form has a long history after discovering the pioneer work by Lotka and Volterra. This model provides a more realistic description about predation, reproduction, mortality term etc. It is recognized that population can subjected to Allee effect when the population density is small (4; 3). Introduction of Allee effect can change the dynamics of the model, particularly affect the persistence of the species. Previous studies mostly focused on the dynamics where Allee effect occurs in prey growth (2). In this talk I will consider the prey-predator model where Allee effect occurs in the numerical response of predator without affecting the functional response. Biologically there are many reason such as lack of mating partners, pollen deficiency, sperm limitation, cooperative breeding mechanisms etc to arise this situation (1; 4; 5). At first we consider a generic mathematical formulation of Allee effect and then consider the local and global bifurcation structure of the model with three different type of parameterisations of the Allee effect. Finally we show that regardless of parameterisations, Allee effect in predator results system destabilization and extinction of the predator population.

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EFFECT OF ADULT MOSQUITO CONTROL ON DENGUE PREVALENCE IN A MULTI-PATCH SETTING: A CASE STUDY IN KOLKATA (2014–2015)

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Dengue is one of the deadliest mosquito-borne disease prevalent mainly in tropical and sub-tropical regions. Controlling the spread of this disease becomes a major concern to the public health authority. World Health Organization (WHO) adopted several mosquito control strategies to reduce the disease prevalence. In this work, a general multi-patch non-autonomous dengue model is formulated to capture the temporal and spatial transmission mechanism of the disease and the effectiveness of different adult mosquito control strategies in reducing dengue prevalence is evaluated. During the period (2014–2015) the dengue situation of Kolkata which is one of the most dengue affected city in India is considered in our study. Depending on geographical location, Kolkata is divided into five regions and our model is fitted to the monthly dengue cases of these five regions during the above-mentioned period. By considering control specific characteristics such as efficacy, environment persistence of the mosquito control strategies, we study the efficiency of three adult mosquito controls and their combined effect in reducing dengue prevalence. From our study, it is observed that control with higher environment persistence performs better in comparison to the controls having low environment persistence. It is also observed that, spatial coupling between the regions plays a key role in the effectiveness of the control strategies.

A GSPT APPROACH TO EPIDEMICS ON HOMOGENEOUS GRAPHS

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We begin this talk by introducing the basic dynamics of epidemics on homogeneous graphs (1). We then build on the SIR model proposed in (1) by allowing recovered individuals to become susceptible again at a small rate $\epsilon\delta$: this choice introduces a distinction between fast and slow processes. We introduce the so called "pairwise approximation", which lets us reduce the complexity of the model by only looking at nodes and edges. Lastly, we look at the $\epsilon \to 0$ limit system, deduce from it information on the system with $\epsilon > 0$ small enough, and present some numerical simulations.

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MATHEMATICAL MODELING OF PUBLIC HEALTH POLICIES

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Mathematical modeling of infectious diseases and the evolution of pathogens can contribute to the prediction of health policy effectiveness and best practices. Integrating mathematics, epidemiology, economics, and evolutionary biology, this interdisciplinary research generates predictions that could not be made by these disciplines alone, and has important impacts on these fields as well as for policy makers world-wide. Health policies must be developed to maximize the benefit to the public and to balance health, social, and economic considerations. Achieving this aim requires combining molecular, individual, population, and national scales with evolutionary perspectives to understand the importance of trade-offs between disease control and the risk of pathogen replacement.

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POPULATION-BASED AND PATIENT-STRATIFICATION APPROACHES APPLIED TO A HUMAN CARDIAC MODEL OF ELECTROPHYSIOLOGY

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Mathematical models of cardiac electrophysiology are usually defined to represent average data from voltage-clamp experiments of ionic membrane current (1). It is only recently, with the advancement of the computational capabilities, that new modeling techniques have been developed to account for the individual variability that typically affects these biological processes. Among these techniques, the most common is the population-based approach that identifies a set of key model parameters that can be varied to address the scientific question in different phenotypical conditions. In parallel with the development of this population approach, several computational strategies have emerged with the purpose to elucidate the role of each model parameter for specific physiological behaviors. This could be addressed with a parameter sensitivity analysis that, in the context of electrophysiology, is usually performed with multivariate regression methods (2). The combination of these two approaches with clustering techniques allows an integrative understanding of the individual variability of disease progression, as well as the response to drug actions, thus could play an essential role in the advancement of precision medicine (3).

We used the population-based approach to generate a group of virtual patients, representing the healthy and the heart failure (HF) phenotypes (4; 5), by considering a human cardiac model of electrophysiology (6). We employed a novel-defined computational pipeline for patient stratification to identify the key mechanisms responsible for the stratification and highlight the importance of including additional phenomenological functions in the mathematical model to better represent the variability of the disease phenotypes. Besides, we compared the results of a global sensitivity analysis (GSA) (7), performed by coupling a sampling algorithm (8) with a logarithmic sensitivity approach (9), with the results of two linear-regression sensitivity algorithms (10; 11). Both the two regression approaches proved to work well even with a complex non-linear system, providing similar results to the ones computed with GSA, but with considerable advantages in terms of computational cost.

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NUMERICAL ASPECTS IN MATHEMATICAL MODELLING OF VECTOR-BORNE DISEASES

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The periodic outbreaks of vector-borne diseases still constitute one of the most serious global health and economic problems. According to the World Health Organization (WHO), every year there are more than 700 000 deaths from diseases such as malaria, dengue, yellow fever, Chagas disease, chikungunya, Zika, worldwide. Distribution of vector-borne diseases depends on demographic, environmental and social factors. Human mobility, urbanization and climate changes increase the probability of getting an infection and cause diseases also in places where they were previously unknown. For example, from September 2012 to March 2013, the autonomous region of Madeira in Portugal, reported the first dengue outbreak with more than 2000 cases. Mathematical modelling is a very important tool for studing epidemic spreading and the prediction of possible scenarios. We consider stochastic models described by master equation [2] and stochastic differential equations [1]. We discussed analytical and numerical aspects of this subject.

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VALIDATION OF A DYNAMIC SYSTEM MODEL FOR THE COLON–RECTAL CANCER CELLS VIA CHEMICAL REACTION NETWORKS

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Each cell function is regulated by a complex signaling network that translates extracellular signals into cellular responses and whose alteration underline diseases as cancer (1).

From a mathematical perspective, this process can be modelled through a chemical reaction network (CRN) (2), i.e. through a graph whose nodes are the involved chemical species and the edges are the chemical reactions. By applying mass action kinetics, the concentration dynamics of the species in a CRN gives rise to a polynomial system of ordinary differential equations (ODEs).

Here we study and validate the CNR for the G0-G1-S transition of colon-rectal cancer cells presented by Tortolina and colleagues (3), involving 419 chemical species and 850 chemical reactions. In particular, we study the corresponding system of ODEs, by characterizing moiety conservation laws, asymptotic steady states, and numerical solutions. We then simulate the steady state of a physiological cell and quantify its alteration due to various combinations of loss and gain of function mutations. We validate our model by comparing our results with those in the literature on the effect of each mutation.

Our study represents the first step of a mathematical tool for the design of targeted drugs.

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BIFURCATIONS IN REACTION CROSS-DIFFUSION SYSTEMS FOR COMPETING SPECIES

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The Shigesada–Kawasaki–Teramoto model (SKT) was proposed to account for stable inhomogeneous steady states exhibiting spatial segregation (4), which describes a situation of coexistence of two competing species. Despite the fact that the reaction part does not present the activator–inhibitor structure, the cross-diffusion terms are the key ingredient for the appearance of spatial patterns. We provide a deeper understanding on the conditions required on both the cross-diffusion and the reaction coefficients for non-homogeneous steady states to exist, by combining a detailed linearized analysis with advanced numerical bifurcation methods via the continuation software `pde2path` (5). We report some numerical experiments suggesting that, when cross-diffusion is taken into account, there exist positive and stable non-homogeneous steady states outside of the range of parameters for which the coexistence homogeneous steady state is positive (1). In 1D and 2D, we pay particular attention to the fast-reaction limit (2) by computing sequences of bifurcation diagrams as the time-scale separation parameter tends to zero. We show that the bifurcation diagram undergoes major deformations once the fast-reaction systems limits onto the cross-diffusion singular limit. Furthermore, in 2D we find evidence for time-periodic solutions by detecting Hopf bifurcations, we characterize several regions of multi-stability, and improve our understanding of the shape of patterns (3).

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MODELING THE IMPACT OF EARLY CASE DETECTION ON DENGUE TRANSMISSION: DETERMINISTIC VS STOCHASTIC

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Dengue fever is a mosquito-borne tropical disease caused by the dengue virus. It is spread by several species of female mosquitoes of the Aedes type. There are rapid dengue diagnostic kits commercially available in the market. Early detection of dengue is possible using this kit and one can get cured from dengue disease without much complications [1]. Keeping in view the fact that early detection can influence the transmission dynamics of dengue disease, a nonlinear mathematical model is formulated and analyzed to study the dynamics of dengue. The basic reproduction number R_0 of the proposed model is computed and all possible equilibria of the model are obtained. Stability analysis for different equilibria of the proposed model is discussed in detail. The nontrivial equilibrium exists only when the basic reproduction number $R_0 > 1$ and it is locally asymptotically stable under some restriction on parameters. The sensitive analysis is performed to identify the key parameters associated with the basic reproduction number R_0. Further the ODE model is converted to stochastic model and results of stochastic and deterministic models are compared using numerical simulation[2, 3].

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IMPACT OF INFORMATION ON TREATMENT AS WELL AS ON DISEASE DYNAMICS

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In this work we shall highlight the impact of control interventions: information of the disease (non-pharmaceutical) and treatment (pharmaceutical) on the infectious disease dynamics. With improvement of medical facilities and technology, it is important to use the available resources to their maximum and achieve the best output. Also, it has been also observed that due to presence and spread of a disease, the information about disease spreads via media in the population. This information induces behavioral changes in susceptible population which take protective measures (such as use of masks, sanitizer, protections etc.) to avoid contracting infection. Hence this information induced behavioural change can be used as a control intervention [1]. The question is how can we use this control intervention to reduce load on treatment, which is usually limited? For this, we propose and analyse compartment models which highlight impact of information on treatment and disease dynamics. We perform stability analysis of infection free and infected equilibria. Global stability of infected equilibrium is established under certain parametric conditions. We also note that the system undergoes backward and hopf bifurcation and there is possibility of existence of multiple equilibria, which employs that system consists of rich and complex dynamics. We further develop an optimal control problem and find the optimal profiles of control interventions using Pontryagin Maximum Principle [2]. We observe that the effect of information is significant during initial phase of disease spread and reduces the peak of infective even in absence of any other control. The treatment on the other hand not only reduces the peak of infective but also the infectivity period. We numerically discuss various optimal control scenarios for certain set of parameters. We also perform cost analysis and find that a suitable combination of both the control interventions is economically most viable option and does not only reduce disease prevalence but also minimize total cost.

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MODELLING THE ROOT GROWTH: AN OPTIMAL CONTROL APPROACH TO LINK BIOLOGY AND ROBOTICS

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A plant's root grows into the soil driven by attractive targets (e.g. nutrients or water) while avoiding obstacles. Under non-stressful biological and chemical conditions, root growth mainly depends on the mechanical strength of the surrounding soil and the presence of obstacles at the root tip. To overcome the resistance of the surrounding environment, plants have developed motion strategies to reduce soil friction. Due to the complexity of the soil, it is difficult to set laboratory experiments to investigate these motion strategies. I will present an optimal control problem that minimises the energy spent by a growing root subject to physical constraints imposed by the surrounding soil. A new framework for biological systems with dynamical constraints arises. The well-posedness of such a system will be briefly addressed. The optimal problem proposed allows us to investigate the motion strategy adopted by plant roots to facilitate penetration into the soil, which we hypothesis to be a circumnutation movement. By numerically solving the proposed optimal control problem, we validate the hypothesis that root growth in soil can be well described by circumnutation motion and that this process arises from the mechanical stress originated at the root's tip. The proposed formalisation could be applied to replicate such a biological behaviour in robotic systems, characterising the design of efficient autonomous bio-inspired devices for soil exploration.

OPTIMAL YIELD AND UTILITY IN STOCHASTIC BIOMASS MODELS

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Optimal management of exploited ecosystems such as fisheries is a subject in theoretical ecology of great interest to society. Here, we consider the problem of optimal harvest strategies in a stochastic continuous-time biomass model of a fish stock; specifically, the stochastic logistic growth model and a variant thereof, the Pella-Tomlinson model. Similarly to previous related works (e.g. (1; 2) and references therein) we frame the problem as one of optimal control for stochastic differential equations and use the stationary Hamilton-Jacobi-Bellman equation to identify the optimal Markov (i.e., state feedback) strategy. We first consider the problem of maximizing the yield and extend recent results (2) regarding the resulting "bang-bang" policy where the fishery is either closed or unrestricted, depending on the current biomass. Next, we consider concave utility functions. In the case of stochastic logistic growth and a square root relationship between catch and utility, the optimal solution is found analytically: The optimal fishing effort is proportional to the biomass and is independent of the intensity of the process noise, which however reduces the expected profit in steady state. We then consider the Pella-Tomlinson model, where solutions must be found numerically, and show that the asymmetry in the growth curve is also found in the resulting optimal harvest strategy. We finally extend the system to two coupled stochastic differential equations, describing predator-prey dynamics, where each species is harvested. For this system solutions must be found numerically. The optimal harvest policies depend on the relative value of predators vs. prey but tend to remove predator-prey cycles in the unfished system.

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THE EFFECTS OF COMPETION AMONG INFECTORS AND DEPLETION OF SUSCEPTIBLES ON THE REALIZED GENERATION INTERVALS

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The realized generation interval, i.e. the time difference between the infection times of two connected individuals in the same epidemic tree, is a quantity of utmost importance in the analysis and prediction of an infectious epidemic. Two observation schemes can be used to describe generation intervals over time: the *forward* and the *backward* that assume, respectively, the infector's and infectee's point of view. For an SIR dynamic in a closed population, the mean realized generation interval varies over the course of an epidemic spread, in each of the aforementioned schemes. Little is known about the cause of these fluctuations which are commonly argued to be a consequence of the depletion of susceptible or competition among infectors. Nevertheless, a precise definition of competition and depletion is lacking in literature as well as a study that investigates their impact on the realized generation interval. Here, we present a theoretical framework, based on the notion of the effective contact process, where competition among infectors and depletion of susceptibles are naturally defined. Through a simulation study, we quantify their effects on the mean realized generation interval in relation to the reproduction number and infectious period distribution. Results suggest that competition and depletion jointly affect the mean realized generation interval and their effects are emphasized for a high value of the reproduction number as well as a high variance of the infectious period distribution. Furthermore, we simulate the levels of competition and depletion in different locations, such as household or workplace, showing how the realized generation intervals depends on the selected structure of contacts. This highlights the importance of the developed framework which is suitable to describe generation intervals in structured populations.

AN OPTIMAL CONTROL PROBLEM FOR DEGRADATION OF WASTE IN LANDFILLS UNDER ANAEROBIC CONDITIONS

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We propose a recent mathematical model (2) for the degradation of the organic fraction of solid waste in a batch bioreactor by means of an anaerobic bacterial population. The time variation of a two components substrate (soluble and insoluble) and a bacterial population (biomass) is governed by a system of ordinary differential equations describing: anaerobic digestion, hydrolysis, i.e. solubilization of the insoluble substrate, and biomass decay. The evolution of the system is monitored by controlling the effects of leachate recirculation that can stimulate or inhibit the hydrolytic process. The main aim is to find the best strategies optimizing an objective functional, that balances the minimization of leachate recirculation cost, modeled by a linear or quadratic function, and the minimization of substrate components at the final time. The minimization problem can be reformulated by typical tools of Pontryagins theory and solved numerically by a classical descent gradient method. Results show the occurrence of different optimal strategies: constant (*bang*), piecewise constant (*bang-bang*) or *singular* controls. A sensitivity analysis for varying parameters and different initial configurations will be presented.

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A SOCIAL INTERACTION MODEL WITH HOLLING TYPE II FUNCTIONAL RESPONSE

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In this paper, we formulate and analyze a series of dynamical system models of the dilation of crime. These population models of social interactions have been constructed based on predator-prey interaction models with Holling type II functional response and assuming two different types of population in a particular community/society: criminal minded and non-criminal minded. According to law policy for crime control, we scrutinize the dynamic behavior of the model system concerning law enforcement on the criminal minded population. Analytical expressions for the existence of all the equilibrium points and their stability have been investigated. Geometrical interpretations have also been given using different isoclines for existence and stability of equilibria. The ex- pressions obtained for the existence and stability of equilibrium points have been used to examine, in particular, the effects of coefficient of law of enforcement and the logistic growth term on the prevalence of crime. It is observed that for a threshold value of law enforcement, a stable limit cycle exists. More precisely thresholds for law enforcement and carrying capacity have been explicitly explained. In particular, a threshold of law of enforcement is determined beyond which the associated place/community could be made crime free. A threshold value R_0 have also been introduced for our model systems. The threshold value (R_0) is similar to basic reproduction number in epidemiology. It is obtained that when $R_0 < 1$, crime free equilibrium is stable. Theoretical results have been supported via numerical simulations.

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MODELING THE INFLUENCE OF MALNUTRITION ON MEASLES EPIDEMIOLOGY IN ETHIOPIA

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Measles and severe acute malnutrition (SAM) represent two of the major causes of deaths in children under 5 years of age in Ethiopia. In recent years, recurrent measles outbreaks have been reported in several areas of the country, including the Oromia Region. The majority of cases was reported among under-5 children. According to the World Health Organization, every month over 25,000 children in this age group are admitted to Ethiopian hospitals due to SAM. The aim of this study is to investigate measles spread between 2015 and 2018 in five different districts of the South West Shoa Zone, in the Oromia region, and to understand the potential role of malnutrition in determining the current burden of measles disease.

We analyzed patient records related to measles and different diagnosis of SAM as collected at the Woliso hospital between 2015 and 2018 to estimate: i) the prevalence of SAM across the different districts; ii) the case fatality rate (CFR) among measles patients in the presence and in the absence of an additional diagnosis of SAM. We developed a multi-patch ordinary-differential equations model for measles transmission to estimate the measles infection incidence across the different districts and evaluate possible spatial heterogeneity driven by local prevalence of SAM. The model is calibrated by means of a Markov Chain Monte Carlo approach applied to the monthly measles case patients recorded at the Woliso hospital between 2015 and 2018.

We found that the prevalence of SAM in the main hospital catchment area ranges from 1.5% in Woliso Town to 14.2% in Amaya. The estimated CFR of measles patients also affected by SAM is 11.6% (95%CI: 3.9-25.1), which is significantly higher than the one estimated for measles patients not affected by SAM: 1.7% (95%CI: 1.1-2.5). Modeling results show that the measles attack rate in the considered period ranges between 0.94% in the Woliso Town woreda to 2.57% in the Woliso Rural woreda. Our results suggest that, as SAM increases the measles CFR among severe cases, SAM might have caused indirectly about 34.16% of measles deaths.

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MODELLING THE SPATIO-TEMPORAL RISK OF MOSQUITO-BORNE DISEASES

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The study of the spatio-temporal variation in the mosquito population density represents a crucial ingredient to assess the risk of vector-borne disease outbreaks (1; 3) as well as the spread of potential epidemics (4). The carried-out analysis aims at providing estimates of the abundance of Ae. albopictus and Ae. aegypti mosquitoes and of the spatio-temporal risk of Dengue and Chikungunya outbreaks at continental scales. The proposed model is calibrated on mosquito capture data collected in Italy (1; 2), in US and in Brazil (5) and by using local eco-climatic data, including detailed temperature and precipitation records (6). For each day of the year, we estimate the absolute number of female adult mosquitoes per hectare at a spatial scale of 250m x 250m. Obtained results are used to estimate the transmission potential associated with Dengue and Chikungunya (1; 4) in Europe and the Americas at the same spatial resolution. Model results can support public health authorities in designing and planning surveillance and control measures aimed at containing and preventing the spread of mosquito-borne diseases in humans.

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MATHEMATICAL MODELLING OF SELECTION BY A SEX-LIMITED FEMALE TRAIT: TO THE QUESTION OF LITTER SIZE POLYMORPHISM IN NATURAL POPULATIONS OF ARCTIC FOXES

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Sex-limited genes are present in both sexes of sexually reproducing species but expressed in only either sex and remain turned off in the other. These traits include animal productivity, such as milk production level and milk fattiness in cattle, egg production and egg size in chicken, and litter size in arctic foxes (2). Classic equations of mathematical population genetics are inappropriate for such genes because both parents define progeny genotypes, whereas fitness depends only on the mothers genotype. As a result, such a population is not in a HardyWeinberg equilibrium (figure). Therefore, one needs to develop an evolution model in equations for genotype frequencies instead of allele frequencies as in the classic theory of natural selection.

Our study proposed models of natural selection of the litter size trait, which is controlled by a sex-limited gene that is expressed only in females, to explain existing genetic variations in litter sizes in coastal, inland, and farmed arctic fox populations. We compared the possibilities of maintaining polymorphism in the framework of the classic theory of modeling with the case of selection by a sex-limited gene.

For now, whether a system of balanced genetic polymorphisms of litter size are maintained in natural populations remains an open question (2), because the populations of inland foxes might have fixed the dominant allele. Thus, one may suppose that the farmed foxes inherited the alleles for small and large litter size from coastal and inland populations, respectively. Alternatively, and more interestingly, they might inherit both alleles from the inland foxes providing that a system of balanced genetic polymorphism of litter size was maintained in the natural populations. However, the conditions for polymorphism maintenance in the classic model are restrictive for the range of values that characterizes the advantage of survival in small litters in years with low food supply.

Our study considering the inheritance type of this trait (i.e. sex-limited gene) allows to wide a range of the values resulted in the maintenance of polymorphism. Furthermore, it is known that the ability of fluctuations in selection to maintain genetic diversity is greatly increased when generations overlap. Generalization of the proposed model of natural selection on a population with two ages revealed that polymorphism can be maintained in an even wider range of parameter values. Thus, this study shows that selection by a sex-limited gene and overlapping generations increases the chances of maintaining polymorphism in inland populations of arctic foxes.

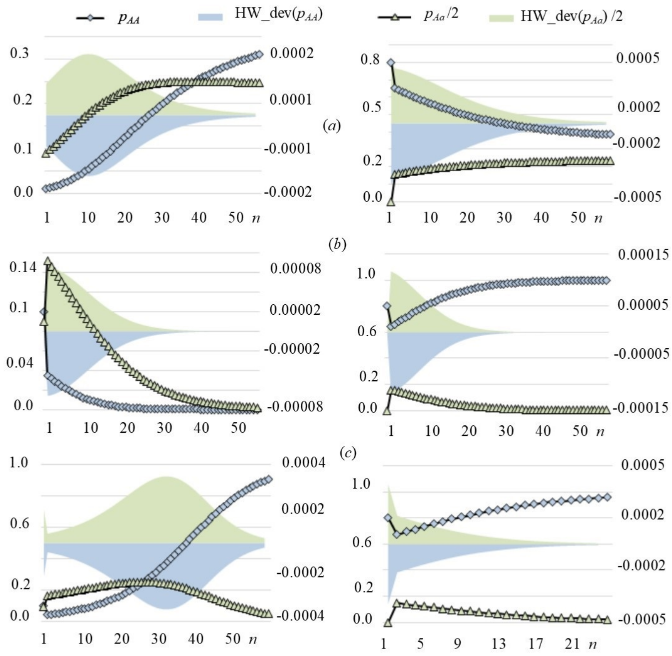

Figure 1: Dynamics of the frequencies of genotypes (p_{AA} and p_{Aa}, the left axis) and their deviations from HWE ($HW_{dev}(p_{AA})$ and $HW_{dev}(p_{Aa})$, the right axis) over generations under various types of selection.

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ADDITIVE MODELS - AN APPLICATION IN AGRICULTURE

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We estimate cumulants and derive prediction intervals in additive models.

We apply our results to real data in a grapevine experiment. We consider a model with two crossed factors: Clone, a random factor with two levels and Location, a fixed effects factor with three levels.

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RECONSTRUCTION AND ANALYSIS OF GENOME-SCALE METABOLIC MODEL OF *DAPHNIA PULEX*

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Daphnia pulex is the keystone organism of the environmental studies in aquatic ecosystems. The study on *D. pulex* genome was first published in February 2011 and contributed to numerous scientific researches (1). The developments in the experimental and computational methods have led to state-of-art technologies including *D. pulex* genome analysis, which provides a basis for genome-scale metabolic modeling and systems biology. The reconstructed metabolic model uses gene, protein and reaction associations, which are obtained from the gene annotation process (2). Since the experimental studies take so long and demand a high effort, our genome-scale metabolic model provides new information as a guide to experimental studies. In this study, all collected data such as reactions, genes, and enzymes are taken from KEGG and UniProt databases and lumped into the model to predict the flux rates (3; 4; 5). The metabolic model of *D. pulex* consists of 1051 reactions, 774 metabolites, and 697 genes. The current model can be used for elaborative understanding of cellular mechanisms and the effect of perturbations on *D. pulex* metabolism against environmental toxicants. *D. pulex* can be regarded as a model organism and hence the reconstructed genome-scale network can be further improved for context-specific investigation in the light of applied mathematics.

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MOLECULAR DOCKING OF BIVALENT APTAMERS AGAINST HUMAN TROPONIN I

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Cardiac troponin I (cTnI) is well known as a cardiac marker in ischaemic heart disease. In this study, bivalent aptamers (aptamers containing sites that are specific for different epitopes of a target protein) against cardiac troponin I were studied, using the molecular docking approach. Previously, the aptamers having the highest affinity and specificity for the cTnI (PDB ID: 4y99:C) were selected and the screening of aptamer pairs affine to various epitopes of the target was performed using the specially designed bioluminescent solid-phase assay. Different combinations of TnAp2, TnAp10, TnAp12, and TnAp8 with different lengths of linkers between them were tested. Nine aptamer pairs least competing for protein epitopes were selected for further analysis.

To predict the secondary structure of the selected bivalent aptamers the Mfold server was used (1). The tertiary structures of aptamers were obtained using the RNAComposer server (2). Low-resolution generic docking with the Global Range Molecular Matching methodology implemented in the GRAMM software was used to obtain protein-aptamer decoys (grid size 4,5 A, rotational step size 10) (3). The program performs an exhaustive 6-dimensional search through the relative shifts and rotations of the molecules, using only the atomic coordinates of the two molecules (information on the binding sites is not required). For each complex, the top 20000 possible structures were selected as decoys. Further, the Decoys As the Reference State potential (DARS-RNP) was used to assess obtained protein-RNA complexes and select a more native-like structure for each of them (4). Visualization of selected complexes as well as analysis of intermolecular bonds was carried out using Discovery Studio Visualizer (BIOVIA) (5).

As a result, reduced versions of TnAp8t (40 bp) and TnAp2t (27 bp) with 10 bp long linker between them demonstrated the highest number of molecular bonds with cTnI (22 bonds, 8 of them are electrostatic), while the same aptamer pair with 20 bp linker demonstrated the worst affinity with the protein (5 bonds). In addition to the TnAp8t-L10-TnAp2t pair, several pairs of aptamers were selected for further analysis: TnApt12t-TnAp2t, TnAp10-TnAp2t, and TnAp10-L19-TnAp2t forming 17, 16, and 11 bonds with cTnI, respectively.

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This poster was presented by T.A. Guseva.

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ROBUSTNESS AND FRAGILITY OF THE SUSCEPTIBLE-INFECTED-SUSCEPTIBLE EPIDEMIC CHAIN ON NETWORKS

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One of the most basic but still surprising model to investigate epidemic spreading in networks is the susceptible-infected-susceptible (SIS). Infected agents lying on the nodes of a network become spontaneously healed (susceptible) with rate μ and infect a susceptible contact with rate λ. There is a phase transition between a disease-free (absorbing) state and an active stationary phase, defining a epidemic threshold λ_c. This epidemic threshold is formally zero in the thermodynamical limit for random networks with a power-law (PL) degree distribution $P(k) \sim k^{-\gamma}$. However, real and computationally generated networks are finite, so the finite-size dependence is fundamental and usually done by mean-field approximations, such as the degree-based heterogeneous mean-field (HMF) and the individual-based quenched mean-field (QMF). The mutual activation of hubs is a mechanism that can explain the trigger of the epidemic, remaining active for a sufficient time to infect each other. In this work, the robustness of this activation mechanism is investigated by modifying slightly the standard SIS model while preserving its fundamental properties. The thresholds are the same for both HMF and QMF theories, while the mutual reinfection time of hubs predicts a finite threshold in the thermodynamical limit for $\gamma > 3$ in the modified versions. Statistically exact simulations on large synthetic networks corroborate this finite threshold. For $\gamma < 3$, the modified dynamics present a vanishing threshold in better agreement with HMF instead of QMF. Our results relight the discussion of the choice of suitable theoretical approaches and the conception of epidemic modeling to describe real systems.

Acknowledgements
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A HYBRID APPROACH TO STUDY CELLULAR DIFFERENTIATION PATTERNS

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During cellular differentiation, from an original group of identical cells, tissues develop “salt and pepper” patterns, in which adjacent cells reach different fates. A significant role in this pattern formation is played by lateral inhibition; precisely, transmembrane proteins Delta and Notch on different adjacent cells are involved in this process. However, it is not fully understood how global patterns are generated, in tissue, from local cellular interactions, without needing external agents contribution. There are several models which explore how this mechanism works, either with quantitative ODE or Turing like diffusion-reaction equations (1; 2). Here, our purpose is to introduce a hybrid approach for modeling this phenomenon. In particular, at the intracellular level, we will describe the problem in a continuous way, using ODE models, while for intercellular interactions we will take advantage of a parameter-free approach, adopting the logical formalism. The chosen hybrid strategy integrates different mathematical abstraction levels to describe distinct biological layers and their communications. Thus, it becomes crucial in dealing with problems for which we dont have a detailed knowledge of the processes involved. The hybrid approach herein employed allows us to combine the pros of different modeling techniques by overcoming the lack of quantitative information with a qualitative description that discretizes activation and inhibition processes, thus avoiding complexity.

Acknowledgements
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VIABILITY ANALYSIS OF A HOUSEHOLD WASTE MANAGEMENT MODEL

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The ecological consciousness has driven developed societies to explore alternatives to the growing need for energy and the consequent increase in waste production. The adjustment towards the valorization of waste and their transformation into energy, by various processes, of which anaerobic digestion is then necessary. However, so far the domain has not benefited much from a mathematical modeling approach. Our contribution consists of first building a model, where the dynamic is the evolution of both a waste stock and energy quantity, controlled by an investment strategy for the energy recovery from household waste. Afterward, applying constraints on the state of the model, and determine the biggest set of initial states where an investment and valorization sustainable policies could be made. The viability theory introduced by Aubin (1), is aligned with the conceptual framework we are looking for, thus, we sketch a viability kernel corresponding to the studies model, under the sustainable condition.

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CHAOS ANALYSIS AND EXPLICIT SERIES SOLUTIONS TO THE SEASONALLY FORCED SIR EPIDEMIC MODEL

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The dynamics of mathematical models describing the spread of an infection can display chaotic oscillations. In this work, we consider a generalization of the classical Susceptible-Infected-Recovered (SIR) epidemic model which accounts for seasonal effects. Combining numerical and analytic techniques, we gain new insights into the complex dynamics of a recurrent disease influenced by the seasonality.

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VeCTOR: VECTOR CLIMATE THREAT ONLINE RESOURCE

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The VeCTOR project aims to develop an online prognostic platform for climate-driven risk assessment of vector presence and vector-borne disease spread by exploiting the potential of the Copernicus Climate Change Service (C3S) infrastructure. Expansion of vector habitats and the distribution ranges of vector-borne pathogens such as malaria, dengue fever, and yellow fever is projected in the context of climate change. Intricate environmental dependency of vectors in light of an ever-changing environment requires an in-depth understanding of vector and disease dynamics for planning effective management strategies and minimising health impacts of future outbreaks.

Through this project, environment-driven spatiotemporal models of vector presence (1; 2) will be developed to enable daily, monthly, and annual risk prediction and the evaluation of vector control strategies for a growing list of disease vectors including mosquitoes and sand flies. Global surveillance data, collected as part of international collaborative initiatives such as VectorBase and VectorNet, and regional observations will be integrated, standardised, and exploited for improving predictive capacity and the range of applicability. The models will be curated and updated regularly through expert consultation and against the most recent observations.

By integrating climate datasets in essential tools for surveillance and forecast, the VeCTOR demo case aims to facilitate regional (Europe) and global climate-related risk anticipation at multiple temporal and spatial scales. The platform will serve and promote outreach to experts, decision- and policy-makers, and facilitate effective communication with the public.

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THE DISTRIBUTION OF FUNGAL MITOCHONDRIAL *ATP* GENES IN AMINO ACIDS SPACE

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We studied the relations between triplet composition of the family of mitochondrial ATP synthase genes ($atp6$, $atp8$ and $atp9$) and their function. In total, 223 fungal mitochondrial genomes were used in this study. All gene sequences were extracted from the genomes in two versions: containing both exons and introns, and sequences without introns corresponding to their mRNA. Each gene sequence was transformed into triplet frequency dictionary, where the reading frame shift was equal either to $t = 1$ or $t = 3$.

In fact, the frequency dictionary of mRNA sequences with $t = 3$ matches with amino acid codons of an open reading frame, consequently it represents an amino acids frequency dictionary. Thereby, the distribution of the amino acid frequency representing points in 21-dimensional space (20 amino acids plus stop signal) was studied.

It was found that the points are separated into three clusters corresponding to those genes. The distribution in amino acids space was compared to the distribution in triplet space and appeared more accurate. Moreover, we separated the set of dictionaries by K-means into the classes for $K = 4$. Such kind of classification was rather unstable. Also, we checked the structuredness in 64-dimensional metric space on the set of points, which corresponds to each gene separately. It was found that species are spread among the clusters rather equally.

A comparative analysis of the clusters in the 21 and 64-dimensional metric space was carried out. As a result, we conclude that in case of analysis of all three genes ($atp6$, $atp8$ and $atp9$), the clusters distinguished by local density are clearly associated with the type of a gene, and in case of a single gene, a larger number of clusters is distinguished.

LIEBIG PRINCIPLE MANIFESTS IN STRATIFICATION OF CANCER PATIENTS VIA COMPLETE BLOOD COUNT

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Malignant neoplasms are among the key factors of mortality, worldwide. They are hard to detect and to cure, as a rule. We aimed to reveal and describe the relation between various cancer tumors (including localization and the type) and the data of complete blood count (CBC). The database comprise 974 entries of the patients suffering of various cancer diseases except the oncology of a blood system, itself. Due to inconsistency, the original database was trimmed to 867 entries where each patient was characterized with 21 CBC character. To begin with, we calculated correlations between the characters, and excluded from the analysis some of them comprising highly correlated couples; eight highly correlated couples have been found.

Next, we classified the data with K-means and elastic map technique. No essential classification with K-means (for $2 \leq K \leq 8$) has been found; on the contrary, elastic map technique reveals four distinct cluster. The clusters has no relation to sex, age, localization or diagnosis of a patient.

The clustering reveals two types of non-specific reaction of an organism on stress caused by the disease. The reaction manifests in the clustering of the patients into various groups differing in the typical figures of 14 CBC parameters. We traced the interlocation of the patients on elastic map, as some of those 14 parameters grow up from the minimal to the maximal figure. Each time the map was filled gradually, from the site specific for each parameter. On the contrary, four parameters (basophils, eosinophils, leucocytes abundance and relative content of immature granulocytes) yielded no specific reaction. The map filled randomly and almost homogeneously, for these parameters, as they grow up in value from minimal one to the maximal one.

Remarkable fact is that gradual filling observed for other 14 CBC parameters takes start from different sites of the map, for different parameters. This fact evidences for Liebig principle execution: the patients cluster according to the type of a non-specific reaction on the stress caused by cancer tumor, and the respond involves different resources into the action. This respond type is not directly related to a type of cancer or its localization.

This poster was presented by Michael Sadovsky.

MATHEMATICAL MODEL TO SIMULATE SPATIAL SPREAD OF INFECTIOUS DISEASES

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A multi-compartmental stochastic mathematical model is proposed to simulate the spread of diseases in animal populations. The dynamics of the disease will be simulated within and between properties. The spread between properties is carried out, at a short distance, considering the distance between infected and non-infected properties. Spreading over long distances will be carried out considering the structure of animal trade network.

INFERENCE OF UNSEEN GENETIC VARIANTS FROM LOCAL PRESENCE/ABSENCE INFORMATION

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In the last years, the development of new DNA sequencing technologies has provided researchers with a massive amount of data. However, extrapolating useful information and patterns from these data remains a huge challenge. In this context, statistical tools play a central role in giving insights into the genetic human profile and its mutational heterogeneity. The accumulation of DNA variants is recognized to fuel tumor occurrence, thus the need for developing methods to quantify mutation abundance and variability.

To this end, we propose a statistical framework to predict the number of mutations in a DNA sequence or in a whole tumor (global scale) starting from presence/absence information collected in certain samples (local scale). By mapping inference of unseen mutations into the unseen species problem in biodiversity, we could tackle genomic inference with tools from statistical ecology.

In details, we choose a Negative Binomial (NB) family of distributions to describe the probability for a mutation to occur in n samples. The choice of a NB family is due to the following properties that represent the key points of our method. First, NB distributions, for different ranges of parameters, can capture both exponential and power-law tails. Second, under the hypothesis of spatial homogeneity, random samplings of a NB can still be described via a NB. The latter property, named form invariance, results in a computable formula that bridges NB parameters at both local and global scales and that we use to determine an unbiased and consistent estimator of the mutation abundance.

We validate our framework on both DNA single-nucleotide polymorphism and synthetic spatial tumor growth datasets. We fit the empirical curves at local scale obtaining the local parameters for NB, and we use the form invariance property to retrieve global parameters. The results suggest the stability of the proposed method, displaying a positive correlation between the accuracy of prediction and the local scale size. Future perspectives may include this framework in the context of hybrid modelling. In this way, we could improve our predictions by coupling our approach with a dynamical representation of the tumor growth that tracks the mutation heterogeneity.

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INTERRELATED CHANGES IN GENETIC STRUCTURE AND DYNAMIC MODES OF POPULATION SIZE DUE TO EVOLUTION

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The population number dynamics is complexly connected with change in its genetic structure by cause-effect relations. Quantitative analysis of this interrelation is still an important fundamental problem. To study this problem we have developed a set of mathematical evolutionary models for population dynamics connecting both genetic and ecological approaches.

Analysis of these models shows, the evolutionary change of adaptive allele frequencies accompanied by an increase in the population average fitness can result in appearance of cyclic and chaotic modes of population dynamics. Increasing average fitness of ecologically limited populations proves to be in dissonance with stability of the population size growth. It obviously contradicts the intuitive concepts, the higher average fitness of population the more stability of the population.

Then we consider the more complex nonlinear models of structured population dynamics. The investigation shows, an increase in average individual fitness leads to appearance of chaotic attractors. Their structure and dimension vary with change in model parameter values (figure). In particular, increase in birth and survival rates results in complicating attractor and growth of its fractal dimension.

The study shows, all types of dynamic modes could consequentially occur during evolution of a limited population affected by density-independent natural selection increasing average fitness of populations according to the Fishers fundamental theorem of natural selection. We called the simultaneous action of density-independent selection and density-dependent non-selective ecological limiting factors as F-selection. The paradox of F-selection is that F-selection is density-independent, but leads to cyclic and chaotic modes of population dynamics, which creates conditions for density-dependent selection, like r- and K-selection.

To illustrate our theoretical results we use a specific example of existing genetic diversity by litter size in various (natural and artificial) arctic fox (*Alopex lagopus*) populations.We compared the possibilities of maintaining polymorphism in the framework of the classic theory of natural selection by an autosomic gene with the case of selection by a sex-limited gene, that is expressed only in females.

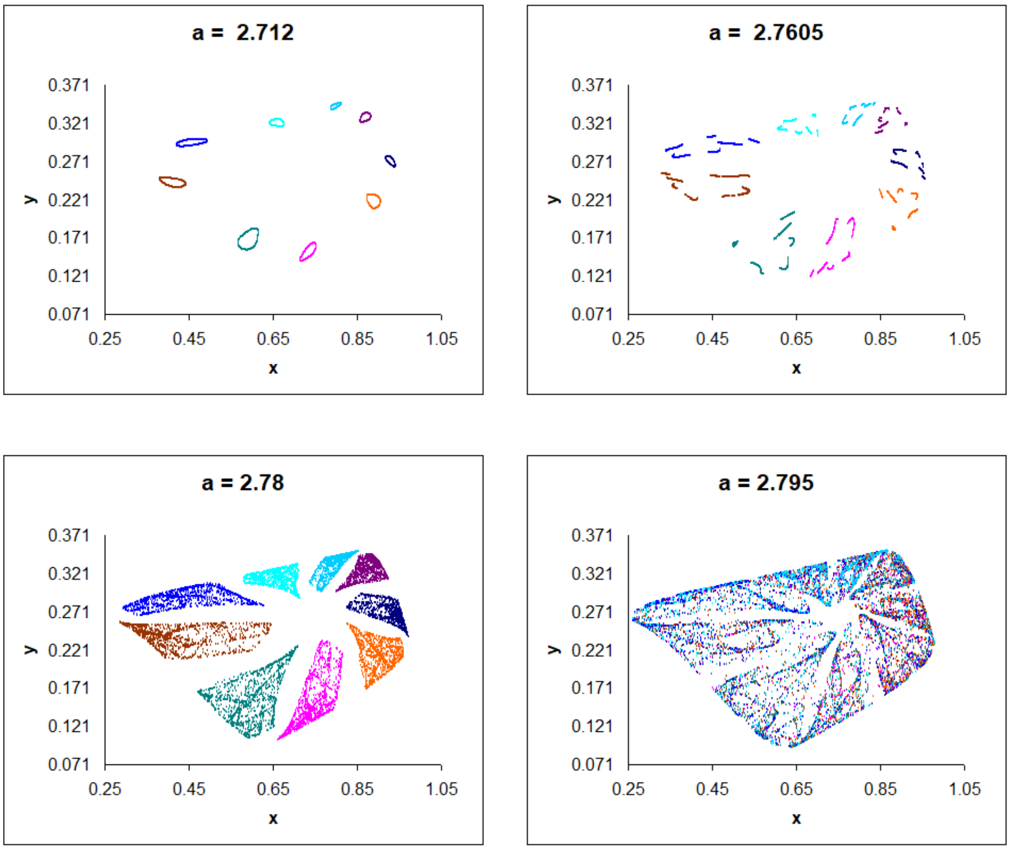

Figure 1: Attractor changes with growing birth rates (a). Here x and y are relative numbers of juvenile and reproductive group of population correspondingly.

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POPULATION DYNAMICS AND FORAGING BEHAVIOR IN A PREDATOR-PREY SYSTEM WITH FAST BEHAVIORAL DYNAMICS

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Classical biological models, (3), (1), consider the bifurcations occuring in a natural system with increasing nutrient concentration. These models assume constant behavior for animal individuals, to simplify the models as discussed in (3). In recent years there has been considerable interest in expanding the modelling to encompass the effect of dynamic behavior on foraging behavior and risk aversion, (4).

We model the interaction of predator and prey populations with adaptive behavior. The interactions and growth terms are given by type II functional responses. We model a situation where the predators and prey can choose how much time to spend foraging, eg. time spent in the upper layers of the ocean as in (7) or (6). The adaptive behavior is added by finding the instantaneous inner Nash equilibrium of this game. This builds on the work for type I responses in (5).

Adaptive behavior changes the biological system in a fundamental fashion, heavily dampening, and often even removing, oscillations in a Rosenzweig-MacArthur system and making the system more resilient to nutrient shocks. As a result of this, the topological nature of a seasonally driven system is altered, with seasonality only forcing a moving steady-state. In addition, a system with adaptive behavior has the ability to sustain a greater population of both prey and predators in comparison to one with static behavior. This is illustrated in the figure above for predators.

Summarizing, we find that a predator prey-system with adaptive behavior have largely non-oscillatory population dynamics with changing resource availability in contrast to a system with static behavior, expanding on the classical results of (1).

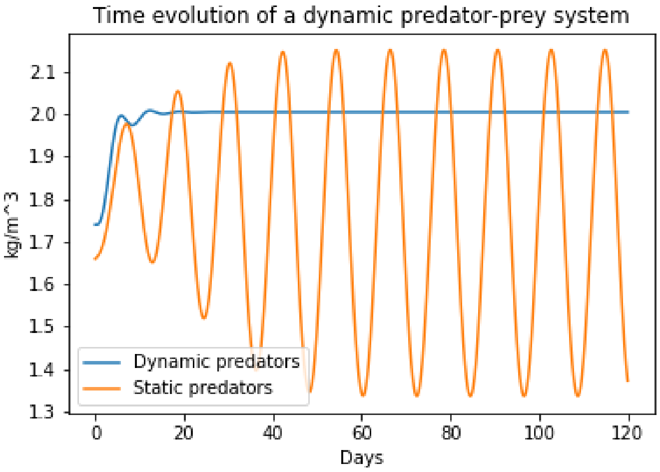

Figure 1: Population dynamics with adaptive vs. static behavior

Using our model we can also reproduce the results of (2) on the effect of nutrient concentration on the activity of planktonic grazers: In a model with only grazers and resources, we find that on short time-scales the activity level falls drastically when increasing the nutrient concentration.

Building on this, we analyze the inter-trophic flux in the tri-trophic model we have developed on long and short time-scales.

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MODELING THE DYNAMICS OF SPATIOTEMPORAL PATTERN FORMATION OF MALIGANT GLIOMAS AND IMMUNE SYSTEM INTERACTION

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We report a mathematical model which depicts the spatiotemporal dynamics of malignant gliomas, macrophages, cytotoxic T-lymphocytes, immuno-suppressive factor TGF- and immuno-stimulatory cytokine IFN- through a system of five coupled reaction-diffusion equations (2). We perform local stability analysis of the biologically based mathematical model for the growth of glioma populations and their environment. A sensitivity analysis is conducted by using Partial rank correlation coefficient (PRCC) (2) technique to determine how the gliomas-immune model output is affected by changes in a specific parameter disregarding the uncertainty over the rest of the parameters. The presented stability analysis of the model system demonstrates that the temporally stable positive interior steady state remains stable under the small inhomogeneous spatiotemporal perturbations. We conduct some numerical simulations in one and twodimensions. The irregular spatiotemporal dynamics of gliomas, macrophages and cytotoxic T-lymphocytes are discussed extensively. The numerical simulations indicate that the cell distributions are quasi-stationary with time and inhomogeneous in space. The heterogeneous dynamics of the model system have both biological and mathematical connotation and the concepts of gliomas dormant phenomenon.

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NON-LINEAR STATISTICS (ELASTIC MAP) IMPLEMENTATION TO DETECT PARKINSONS DISEASE vs. ESSENTIAL TREMOR

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Parkinsons disease and essential tremor are quite difficult to distinguish through custom diagnostics. Both pathologies manifest in tremor. Unlike essential tremor, Parkinsons disease may be detected through olfactory dysfunction, quite before any motor manifestation. There are some fine differences in tremor pattern observed for Parkinsons disease patients, in comparison to those with essential tremor. Currently, there are several technical tools to measure mechanical features of tremor. Besides, olfactory dysfunction may also be used as diagnostic feature, for such patients.

We analyzed the records of tremor obtained from patients with Parkinsons disease and essential tremor; the patients did not differ statistically in age, in these two groups, with unbiased sex representation. For both patient groups, kinetic features of tremor have been measured and recorded. Also, the olfactory function was measured, using standard protocol of Sniffins stick test. Finally, each patient in the record is characterized with 332 variables.

It was found that custom statistics is able to distinguish patients with essential tremor from those with Parkinsons disease when compared over a tight set of variables; greater majority of data does not yield any reliable separation. Reciprocally, any linear (e. g. K-means) clustering technique failed to resolve the patients with essential tremor, and those with Parkinsons disease. On the contrary, non-linear statistics, that is elastic map technique, was the powerful tool to cluster the patients. Clustering developed by elastic map reliable differentiate patients with Parkinsons disease from the patients with essential tremor. It should be stressed that reliable clustering is observed over the subset of kinetic records comprising those with the distribution pattern close to the normal one; elimination of all other variables improved clustering. Moreover, a combination of these selected kinetic data and olfactory function measurements also improved the clustering.

Comparative analysis of olfactory function data obtained both from sick patients and healthy people reveals almost no difference between them. This controversy was hypothesized to result from the peculiarities of the current Sniffins test one subtest. To resolve the problem, we proposed the new version of the protocol, and tested it over the healthy people. The new version stipulates randomization of testing of various smell agent concentrations, instead of a regular one proposed by the standard protocol. Implementation of the new version significantly improved the test feasibility.

This poster was presented by Michael Sadovsky.

ASSEMBLY OF THE MITOCHONDRIAL GENOME OF SIBERIAN CEDAR (*PINUS SIBIRICA*)

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Most plants have two types of organelles with their own genome: mitochondria and chloroplasts. It is well known that mitochondrial genome is inherited over the maternal lines and is rather complex. Currently, mitochondrial genomes have been published only for four gymnosperms.

Isolation of intact mitochondria was carried out at the Laboratory of Plant Genetic Engineering, SIFiBR SO RAN. In the forest genomics laboratory of Siberian Federal University, the mitochondrial sequences of *Pinus sibirica* were obtained. Sequencing was performed on the IlluminaHiSeq 2000 platform. The contigs were assembled using the CLC BIO. 879595 scaffolds with a total length of 283.4 Mb were obtained.

Mitochondrial scaffolds were selected by aligning the genomic assembly with BLAST against a base of 3489 (143.5 Mb) complete and partial sequences of mitochondrial genomes of seed plants. As a result, 97 scaffolds with a total length of 3.1 Mb were selected.

Protein-coding genes were searched using BLAST in the Genomic Workbench CLC software by aligning the assembly against well-annotated cycad and ginkgo genomes, tRNA genes were detected using tRNA-scan and Aragorn, rRNA genes were detected using RNAmmer. 40 protein-coding genes were found located in 7 scaffolds, also 18 tRNA genes and 2 rRNA genes were found. The total length of the repeats was 0.2 Mb, which is 6.2% of the total assembly length using RepeatModeler, TEclass.

To compare with, the total assembly length for *Picea glauca* (1) is 5.9 Mb, *Pinus taeda* (2) is 1.2 Mb, *Picea abies* (3) is 4.3 Mb. We believe the difference in the size of the mitochondrial genome results both from the difference in sizes of the non-coding regions, and the number of genes.

This poster was presented by Michael Sadovsky.

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EPIDEMIOLOGICAL MODELS USING FRACTIONAL CALCULUS

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The Fractional Calculus, or non-integer order Calculus, has attracted attention due to its range of applications in problems of scientific and technological interest, because it generalizes traditional integration and differentiation techniques and introduces nonlocality as the intrinsic property of its operators. Then, the fractional derivatives are very useful to describe physical systems and for biological problems, especially due to the memory property, that allow the recovery of the behaviour of the function in moments before the time slot which it is analysed (1).

In this work, the concepts of Fractional Calculus are used for the construction of the epidemiological models that describe two recent outbreaks: cholera and plague, which were considered extinct diseases, but returned with overwhelming power, due to poor health and hygiene conditions of the countries affected. For such cases, we applied the respective model to describe recent epidemics and to predict the dynamics of each one of these diseases.

Since 2017, Yemen has been suffering with the largest cholera outbreak documented, which has infected more than 1.5 million people and left about 2500 dead (2). Given this scenario, we built a model which describes the dynamics of the disease, including the vaccination of the population, and using data from the numbers of infected and dead population, we could obtain the epidemiological parameters that describe the behaviour of cholera for this case and this model can be useful to predict the other cholera outbreaks (3).

In 2017, Madagascar health authorities reported more than 2500 cases of the human plague, with a total of 221 deaths (4). In 2019, many people in China have been diagnosed with the plague. Even though the epidemiology of this case is not stated, China has a population very susceptible to the spread of this kind of epidemic (5). Typically, plague transmission models consider only fleas and its rodent hosts as the main vector of plague transmission, but some authors propose a model that considers the transmission between humans and the case where the flea bites directly the human, in addition to plague transmission using the mouse as host and the flea as a vector (6). Based on this model, we built the fractional approach for the system of equations and analyse the consequences of this choice.

For each of the studied cases a model composed by fractional differential equations was proposed and, using data provided by the World Health Organization, we were able to estimate the parameters and perform numerical simulations for each of them. The use of fractional derivatives allows a more detailed resolution of the system of equations and thus obtaining a system capable of describing the behaviour of each one of its equations, especially for the equation that describes the infected population. Thus, we conclude that non-integer derivatives allow us to model memory effects and it results in a more powerful approach to describe the dynamics of these diseases analysed.

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IDEAL FLUIDS OF OPTIMAL FORAGERS

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Diel vertical migration is considered as one of the largest daily movements of marine species where animals remain in deep, dark water during daylight hours to avoid visual predation and migrate to upper levels at dusk to feed. The migration of each organism can be rationalized as a trade-off between growth and survival with strategies as spatial distributions of the populations. The dynamics driving vertical migration has broad implications for fluxes through the food-web predator-pray interactions and how biomass is transported from lower to higher trophic levels (1; 4); for vertical transport of carbon from upper to deeper layers (i.e. the so-called ”biological carbon pump”) with implications for global climate study (2).

Here, we present the idea for expressing diel vertical migration as a ”vertical game” in terms of partial differential equations and show preliminary results of analysis of these equations. In the model setup we consider a population of animals distributed over the water column, and assume that each player (an animal) in this game moves optimally, seeking regions which offer high growth rates and small mortality, penalizing formation of regions with high density of the population. Recent results either doesn’t take into account cost of movement (4) or doesn’t resolve time continuously (1). Here, we formulate the problem in continuous time and incorporate costs on excessive movements in our model. We show that the Nash equilibrium for this mean field game (3) is characterized by partial differential equations, which govern the distributions and migration velocities of animals. The derived system of PDEs has similarities to equations that appear in the fluid dynamics, specifically the Euler equations for compressible inviscid fluids. We show that if the environment is constant, the ideal free distribution emerges as an equilibrium. This equilibrium is hyperbolic, so that solutions can both converge to and depart from the ideal free distribution. We also present a discussion on computational approaches for solving this game theoretical model. We solve derived partial differential equations using spectral methods and present initial numerical results.

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MODELING TUMOR CELL GROWTH INCLUDING NUTRIENT DEPENDENT AUTOPHAGY

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In *in vitro* experiments with tumor cells (1) it could be observed that lack of nutrients does not only lead to starvation in the long term, but can also enhance temporary growth if the nutrient stress is sufficient. To describe this effect, a basic system of ordinary differential equations (ODEs) is presented, which describes cell proliferation according to the available nutrients and the induction of cell necrosis and autophagy due to nutrient deprivation. Autophagy is a regulated intracellular mechanism to recycle or remove components of the cell, which are unnecessary or dysfunctional. It is a natural process i.a. to maintain proper cell function but it can also be promoted, e.g. by various stressors. In the case of nutrient deprivation, this mechanism provides the cell with energy to ensure survival and proliferation and in cancer cells this process might be upregulated (2). In general, the balance between apoptosis and autophagy is important, when considering tumor development.

The unknown parameters of the model are estimated by using Bayesian inversion methods. The corresponding data sets for the parameter calibration are time resolved measurements of populations of liver cancer cells, which are provided with varying amounts of nutrients in an avascular environment. The presented ODE model serves as a basis for modeling and quantifying effects of mechanical properties of the extracellular matrix on the growth of tumor cells.

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DELAY INDUCED MULTIPLE STABILITY SWITCH AND CHAOS IN A PREDATOR-PREY MODEL WITH FEAR EFFECT

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We propose a delayed predator-prey model with fear in the prey population. We consider that the growth rate of the prey population is suppressed due to the fear of predators. It is also considered that there is a time lag between the time of perceiving predator signals through chemical and/or vocal cues and the changes in life-history and behavioral responses in the prey population. We study boundedness, persistence, local and global behaviour of the delayed system. Moreover, the Hopf-bifurcation analysis around the interior equilibrium with respect to the delay parameter is established. The stability and direction of Hopf-bifurcation are also studied. It is observed that fear induce delay has both stabilizing and destabilizing effects depending on the magnitude of the delay parameter. We observe that for the gradual increase of the magnitude of delay, the system dynamics switches multiple times between stable focus and limit cycle oscillations. However, for a higher value of the delay parameter, the system ultimately enters into the chaotic regime. The delay system also exhibits node-cycle bi-stability behavior between the interior equilibrium point and stable limit cycle. Numerical simulations are also performed to validate analytical findings.

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SOCIAL AND INDIVIDUAL COST OF VACCINATION FOR IMPERFECT VACCINATION

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It is known that imperfect vaccination decreases the rate of infection, but, as side effect, increases the average age at infection. In this work we consider an age-structured population with imperfect vaccination. Our aim is to compare the social and individual costs of such a vaccination, assuming that disease costs are age dependent. We determine the parameter region for which vaccination has positive social impact. Further, we study the Nash equilibria corresponding to the individual optimum. We further describe different actions where both the society and individuals goals are attained.

MODELLING THE EFFECT OF IMMUNOTHERAPIES ON HUMAN CASTRATION-RESISTANT PROSTATE CANCER

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We analyse the potential effect of immunotherapies on castration-resistant form of prostate cancer (PCa). In particular, we examine the potential effect of the dendritic vaccine *sipuleucel-T*, the only currently available immunotherapy option for advanced PCa (3), and of *ipilimumab*, a drug targeting the Cytotoxic T-Lymphocyte Antigen 4 (CTLA4), exposed on the CTLs membrane, currently under Phase II clinical trial. The model, builiding on the one by Rutter and Kuang (1), includes different types of immune cells and interactions and is parameterised on available data.

Our results show that the vaccine has only a very limited effect on PCa, while repeated treatments with *ipilimumab* appear potentially capable of controlling and even eradicating an androgen-independent prostate cancer. From a mathematical analysis of a simplified model, it seems likely that, under continuous administration of *ipilimumab*, the system lies in a bistable situation where both the tumor-eradication equilibrium and a high-tumor equilibrium are attractive. The schedule of periodic treatments could then determine the outcome, and mathematical models could help determine an optimal schedule.

While the results appear promising, a caveat is that the anti-CTLA4 effect of the drug has been estimated from the patients that most benefited from the therapy (2), and thus may be over-optimistic.

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SIGNAL FIDELITY AND ROBUSTNESS IN *ESCHERICHIA COLI* PHOSPHATE RESPONSE WITH SYNTHETIC PROMOTERS

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Escherichia coli regulates inorganic phosphate (P_i) uptake in order to survive under varying environmental conditions. The sensory machinery consists of a two-component system (TCS), an histidine kinase and a response regulator that relays the signal to the genetic components. Achieving a quantitative understanding of the biochemical mechanism in TCS has implications in biotechnology applications. This way, targeted genetic modification on organisms can be applied in order to enhance their natural capacity for certain tasks and to fine-tune their behaviour.

Building on previous work, here we give a detailed mathematical analysis of various models of *E. coli* response mechanism for P_i intake. Our analysis is done in relation to signal fidelity in response to external P_i concentration with two contributions.

As the first contribution, we propose a spectrum of models with varying levels of detail. Choosing a more refined model over a simpler one provides advantages in terms of a higher detail in biochemical resolution. In contrast, a simpler model can be instrumental by abstracting away from many system parameters, and this way can guide an analysis with a focus on the dominant model trends. Starting from the most detailed model proposed in (1), we present a spectrum of reduced models that agree with the biological notions in the literature. These models contain a smaller number of reactions and parameters in their chemical reaction network representations. Moreover, they are in qualitative agreement with the more detailed model in terms of their steady state dynamics.

As the second contribution, we analyse the input-output robustness to variations in the concentrations of the system components. We study the system's equilibria and their relation to protein total concentrations. Input-output robustness is a favourable feature for the systems that provide a response signal to an incoming stimulus. The output level of a TCS response to an input signal is generally sensitive to changes in the protein concentrations, which often vary from cell to cell. Therefore, robustness of the input-output relation enables to finely tune the systems response to the external stimulus.

Starting from the two-component system proposed in (2), we modify its chemical reactions network until we get one of the reduced models we propose. Each step of this process is identified by a model, which is analysed in terms of its input-output relation (see Figure 12). Moreover, by bifurcation analysis, we study the steady state behaviour, which can vary in response to changes in the parameter values. Finally, we analyse the noise in the biochemical machinery in the phosphate economy of *E. coli*. The biochemical process of gene expression is a source of significant intrinsic noise that can imply a loss of coherence in the output signal. We quantify the effect of different synthetic promoter designs on signal robustness in conditions of different external P_i concentration regimes. The results with our reduced model confirm the observations in (3). That is, an increased promoter binding rate is associated to a moderate decrease in the output fluctuation, while increased promoter unbinding rate comes with an appreciable increase in output fluctuations.

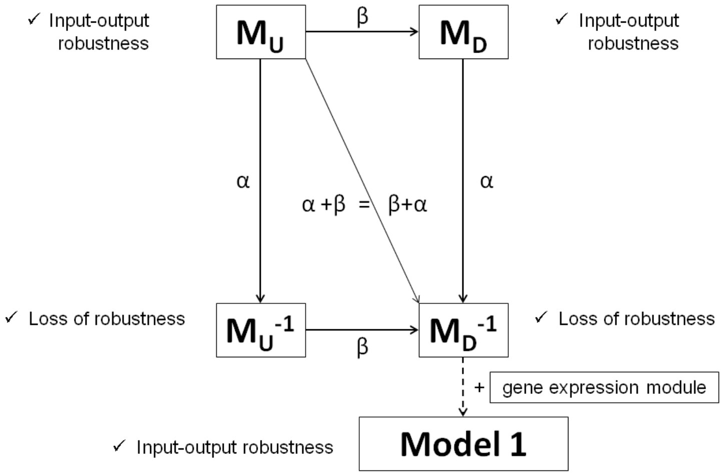

Figure 1: The construction scheme of the analyzed models. The solid arrows indicate going from one model to another through the addition of one reaction. The symbol -1 represents the addition of phosphorylated histidine kinase dephosphorylation (α), whereas the letter D identifies the addition of phosphorylated response regulator dimerization and the reverse reaction (β). The dashed arrow represents the transition from model M_D^{-1} to a larger one, Model 1, by adding the gene expression module.

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COMPARTMENTAL-MULTI-PATCH MODELING AND SIMULATION OF ZIKA-VIRUS SPREAD

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The Zika Virus is a mosquito borne flavivirus which was found to cause Gullian-Barré syndrome. In addition the disease is transmitted directly from infected human to susceptibles. To model the disease spread we make certain assumptions on the parameters and divide the area of interest into multiple patches. The main idea of multi-patch modeling is to incorporate the fact that a population of a region is diverse, be it humans or mosquitoes. By this multi-patch approach we are also able to consider the evolution of the disease due to human mobility. The basis is an SIR-UV model in every patch. We analyze the model with respect to the non-negativity of the feasible region, behaviour of reproduction number with different choices of parameters, existence of equilibria and stability. By a heuristic limit procedure we obtain a system of PDEs which involves a cross diffusion between the compartments. For the latter finite elements and finite differences will be used for numerical simulations.

HETEROGENEOUS FOREST FIRE MODEL WITH ENLARGED NEIGHBOURHOODS AND FORBIDDEN SITES

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The concept of self-organized criticality (SOC) is related to the ability of a dynamical system to evolve towards a critical phase spontaneously and which signature is the scale invariance of its observables. The forest fire model proposed by Drossel and Schawbl (1) in 1992, regards an homogeneous population of trees and its fire-size distributions suggest typical SOC behaviors. On literature it is reported that wildland fires whose frequency-area histograms are either power-law distributions or other heavy-tailed distributions. In 2011, Camelo-Neto and Coutinho (2) proposed a CA model in which two distinct populations of trees are considered: one consisting of trees with low flammability (with a parameter R of resistance to ignite) and the other composed by high flammability (susceptible trees).

The current work (3) is carried out using cellular automata models and some ingredients have been added either to amplify or restrict the fire spreading. On one hand, the number of neighbors interaction was increased allowing the fire front to reach further and, on the other hand, random forbidden site were added to the lattice which does not interact with the fire and are no allowed to sprout trees, in that way constraining the propagation. So far, results have showed that observable distributions present two distinct behaviours, qualitatively agreeing with the wildland fire reports. The next step is to understand which are the critical parameters to shift from on phase to the other and develop scalable algorithms that would reduce finite-size effects.

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MATHEMATICAL MODELING ON THYROID CANCER TREATMENT USING ODE WITH ALLEE EFFECT

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The continuous increase in the number of papillary thyroid cancer (PTC) cases is a global trend (1). The most commonly used treatments for extinction of these tumors are thyroid gland removal surgery and therapeutic application of radioactive iodine I-131 (RAI) (2). Interleukin 6 (IL-6) is studied in PTCs due to the presence of high concentrations of this cytokine in malignant tumors (3). Models of ordinary differential equations (ODE) are common in the study of cancer biology, in which various types and subtypes of malignancies are addressed (4). In this work we propose an Allee effect ODE model to study PTC treatment with RAI, the following variables are assumed: the activity of RAI, the number of tumor cells during treatment, and IL-6 and thyrogobulin concentrations. The aim of the study is to evaluate different therapeutic doses of RAI in treatment considering a positive influence of IL-6 on tumor proliferation. Results obtained through numerical simulations and linear stability analysis indicate minimal doses of RAI capable of causing tumor extinction when certain immune system-related biological conditions or other factors are considered. Furthermore, the scenarios obtained show that small doses, even leading to tumor extinction, allow delays in the total elimination of malignant cells.

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TIME-VARYING EPIDEMIC TRANSMISSION IN HETEROGENEOUS NETWORKS

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Classic epidemiological models are generally based on two assumptions: first, the mass-mixing, which means all the individuals have a uniform contact pattern, and second, that the parameters - such as the transmission rate - are constant in time. Of course, while these assumptions may simplify the analysis, it can be useful to formulate models with a more realistic approach. Simple models could be refined, starting from two observations.

First of all, a person would transmit or contract the disease from their own neighbourhood of individuals which they have contact relationships with. Moreover, spreading also depends of connections between individuals. Therefore, it is reasonable to replace the assumption of the mass-mixing with heterogeneous networks, that specify who is connected to whom and in which way (1). In this context, each person is a node and the degree k of a node is defined as the number of neighbourhood of an individual.

Regarding the second assumption, an other consideration that we make is about the parameters. A more reasonable approach should take into account seasonality of the disease; the basic idea is taking parameters which depends on a switching signal. In particular, the most common approach is consider a time-varying transmission rate (2). For simplicity, it has been considered the transmission rate as a piece-wise constant function, subject to a switching rule.

I will talk about SIS, SIR, SIRS and SEIR models with network contact patterns and time-varying transmission rates. The behaviour of these models is analysed, discussing the existence of the endemic equilibrium and developing stability criteria using the method of Lyapunov functions.

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CO-CIRCULATION OF INFECTIOUS DISEASES AND HEALTH OPINIONS

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Risk-taking and health-protective behaviour in the context of infectious diseases depend on social norms and beliefs, but are also influenced by epidemic spread. On the other hand, social norms/health opinion distribution may affect course of an outbreak. We investigate the impact of changing health protective behaviour due to social influence and risk of acquiring infection on epidemic dynamics.

We propose an ODE model that captures concurrent dynamics of two health-related opinions and infection spread. The model accounts for effects of various social behavior features, such as varying contact intensities and assortative mixing. We model an opinion switching rate with Holling type III functional response that depends on the density of individuals holding an opinion. The switching rate can be modified by disease prevalence. Infection was modeled using a Susceptible-Infected-Susceptible (SIS) or a Susceptible-Infected-Removed (SIR) model. Local and global stability analysis yielded possible stable opinion distributions in a disease-free population. We computed the basic reproduction number for different opinion distributions and used bifurcation analysis to investigate how mixing patterns that simultaneously shape both opinion distribution and disease spread, impact the opinion and epidemic dynamics.

In a disease-free population, multi-stability between an equilibrium of coexisting opinions and equilibria where one of the two opinions is dominant may occur. The course of an epidemic depends on the distribution of opinions at the onset of the epidemic. During an epidemic outbreak, behaviors can be modified further. Subsequently, the outbreak can cause a shift of the whole population to the health protective opinion, which will dominate even after the outbreak has ended. Re-

duction of contact rates will affect both opinion and infection propagation and as such may cause elimination of health-protective opinion and subsequently cause increase in prevalence, rather than decrease. For certain behavior combinations, sustained oscillations may arise causing epidemic waves. These cycles can be interpreted as a process where, as individuals adopt a health-protective opinion, prevalence declines and subsequently, with pressure to switch to the health-protective opinion reduced, some individuals revert to their risk-taking behaviour. This outcome aligns with results by He et al. (1) which indicated that behavior adaptation is one of key factors in explanation of appearance of several waves of incidence during 1918 influenza pandemic in England and Wales.

Our findings indicate that, depending on different socialization paradigms, various types of interventions may yield different qualitative and quantitative outcomes, not all of which would be beneficial for population health.

This poster was presented by Emil Iftekhar.

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MATHEMATICAL MODELLING OF MOSQUITO DISPERSAL

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The presence of invasive mosquitoes in Italy, in particular Aedes albopictus, has a significant impact on public health. Indeed, this species can transmit several pathogens, including chikungunya virus, whose largest outbreak in Europe occurred in Lazio region (Central Italy) in 2017. Currently, health risk estimate for mosquito-borne pathogens is limited by the difficulty to predict the spatial and temporal spread of vectors at a small scale.

To address this problem, we treated Ae. albopictus dispersal as a diffusion process, which can be represented by a partial differential equation, and exploited data obtained in three Mark-Release Recapture (MRR) experiments carried out in Padua (northern Italy). In particular, we modelled this process using the heat equation, whose analytical solution is already known, taking also explicitly into account mosquitoes mortality, which was estimated based on data collected under semi-field conditions simultaneously to MRR experiments. Several theoretical functions (e.g. exponential, Gompertz and Weibull functions, as well as a regression model) were tested, obtaining an estimated average daily mortality, computed over a time window of two weeks, of 2% in the first experiment and 1% in the second and third experiment. We compared the different functions both by the mean square error and a likelihood test.

The only unknown parameter of the equation, i.e. the diffusion coefficient, was estimated through a Markov Chain Monte Carlo procedure by fitting the model to the observed mark-release recapture data. The solution turns out to be a normal bivariate distribution that represents the probability of mosquito location at different time steps. Our findings could help to better define the area to be treated by emergency insecticide treatments in the case of notification of any Ae. albopictus-borne pathogen infection.

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