

DYNAMICS, EQUATIONS AND APPLICATIONS

BOOK OF ABSTRACTS SESSION D42

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CONTENTS

Plenary lectures	7
Artur Avila , GENERIC CONSERVATIVE DYNAMICS	7
Alessio Figalli , ON THE REGULARITY OF STABLE SOLUTIONS TO SEMI- LINEAR ELLIPTIC PDES	7
Martin Hairer , Random loops	8
Stanislav Smirnov , 2D PERCOLATION REVISITED	8
Shing-Tung Yau , STABILITY AND NONLINEAR PDES IN MIRROR SYMMETRY	8
Maciej Zworski , FROM CLASSICAL TO QUANTUM AND BACK	9
 Public lecture	 11
Alessio Figalli , FROM OPTIMAL TRANSPORT TO SOAP BUBBLES AND CLOUDS: A PERSONAL JOURNEY	11
 Invited talks of part D4	 13
Weizhu Bao , MULTISCALE METHODS AND ANALYSIS FOR THE DIRAC EQUA- TION IN THE NONRELATIVISTIC LIMIT REGIME	13
Russel Caffisch , ACCELERATED SIMULATION FOR PLASMA KINETICS . . .	14
Albert Cohen , OPTIMAL SAMPLING AND RECONSTRUCTION IN HIGH DI- MENSION	15

Hugo Duminil-Copin , MARGINAL TRIVIALITY OF THE SCALING LIMITS OF CRITICAL ISING AND φ^4 MODELS IN 4D	15
László Erdős , FROM WIGNER-DYSON TO PEARCEY: UNIVERSAL EIGEN- VALUE STATISTICS OF RANDOM MATRICES	16
Eduard Feireisl , DISSIPATIVE SOLUTIONS TO THE COMPRESSIBLE EULER SYSTEM	16
Mats Gyllenberg , FINITE DIMENSIONAL STATE REPRESENTATION OF STRUC- TURED POPULATION MODELS	17
Clément Mouhot , QUANTITATIVE LINEAR STABILITY (HYPOCOERCIVITY) FOR CHARGED PARTICLES IN A CONFINING FIELD	18
Thaleia Zariphopoulou , STOCHASTIC MODELING AND OPTIMIZATION IN HUMAN-MACHINE INTERACTION SYSTEMS	18
Talks of session D42	21
Ellen Baake , A PROBABILISTIC VIEW ON THE DETERMINISTIC MUTATION- SELECTION EQUATION	21
Piotr Biler , GLOBAL EXISTENCE VS FINITE TIME BLOWUP IN KELLER- SEGEL MODEL OF CHEMOTAXIS	22
Barbara Boldin , ECO-EVOLUTIONARY CYCLES OF VIRULENCE UNDER SE- LECTIVE PREDATION	23
Tom Britton , EPIDEMICS IN STRUCTURED COMMUNITIES WITH SOCIAL DISTANCING	23
Andreas Deutsch , BIOLOGICAL LATTICE-GAS CELLULAR AUTOMATON MOD- ELS FOR THE ANALYSIS OF COLLECTIVE EFFECTS IN CANCER INVA- SION	24
Marie Doumic , ESTIMATING THE FRAGMENTATION CHARACTERISTICS IN GROWING AND DIVIDING POPULATIONS	25
William Fagan , IMPROVED FORAGING BY SWITCHING BETWEEN DIF- FUSION AND ADVECTION: BENEFITS FROM MOVEMENT THAT DE- PENDS ON SPATIAL CONTEXT	26
Jan Haskovec , RIGOROUS CONTINUUM LIMIT FOR THE DISCRETE NET- WORK FORMATION PROBLEM	27

Laura Kanzler , KINETIC MODELING OF COLONIES OF MYXOBACTERIA . .	28
Marek Kimmel , EXPECTED SITE FREQUENCY SPECTRA OF CELLS: COALESCENT VERSUS BIRTH-AND-DEATH-PROCESS APPROACH	29
Eva Kisdi , ADAPTIVE DYNAMICS OF PATHOGENS AND THEIR HOSTS . . .	30
Toshikazu Kuniya , GLOBAL BEHAVIOR OF A MULTI-GROUP SIR EPIDEMIC MODEL WITH AGE STRUCTURE AND ESTIMATION OF \mathcal{R}_0 FOR THE CHLAMYDIA EPIDEMIC IN JAPAN	30
Junling Ma , HOST CONTACT STRUCTURE IS IMPORTANT FOR THE RECURRENCE OF INFLUENZA A	31
Dietmar Ölz , MODELLING AND SIMULATION OF COLLECTIVE MIGRATION IN EPITHELIAL LAYERS	32
Joan Saldaña , EPIDEMIC OSCILLATIONS AND THE SPREAD OF AWARENESS	32
Christian Schmeiser , MATHEMATICAL MODELS OF ACTIN DRIVEN CELL MOTILITY	33
Kieran Sharkey , CAPTURING THE QUASI-STATIONARY DISTRIBUTION WITHIN A DETERMINISTIC FRAMEWORK FOR STOCHASTIC SIS DYNAMICS . .	35
Zuzanna Szymańska , MICROSCOPIC DESCRIPTION OF DNA THERMAL DENATURATION	36
Katarzyna Szymańska-Dębowska , CANARD SOLUTIONS IN EQUATIONS WITH BACKWARD BIFURCATIONS	36
Anja Voß-Böhme , MODEL-BASED INFERENCES ABOUT CELLULAR MECHANISMS OF TUMOR DEVELOPMENT FROM TISSUE-SCALE DATA	37
Hao Wang , ANIMAL MOVEMENT WITH SPATIAL MEMORY	38
Carsten Wiuf , ON THE STABILITY OF THE STEADY STATES IN THE N-SITE FUTILE CYCLE	39
Falko Ziebert , PHASE FIELD APPROACH TO SUBSTRATE-BASED CELL MOTILITY	40

PLENARY LECTURES

GENERIC CONSERVATIVE DYNAMICS

Artur Avila

Universität Zürich, Switzerland & IMPA, Brazil

ON THE REGULARITY OF STABLE SOLUTIONS TO SEMILINEAR ELLIPTIC PDES

Alessio Figalli

ETH Zürich, Switzerland

Stable solutions to semilinear elliptic PDEs appear in several problems. It is known since the 1970's that, in dimension $n > 9$, there exist singular stable solutions. In this talk I will describe a recent work with Cabré, Ros-Oton, and Serra, where we prove that stable solutions in dimension $n \leq 9$ are smooth. This answers also a famous open problem, posed by Brezis, concerning the regularity of extremal solutions to the Gelfand problem.

Random loops

Martin Hairer

Imperial College London, UK

2D PERCOLATION REVISITED

Stanislav Smirnov

University of Geneva, Switzerland & Skoltech, Russia

Joint work with **Mikhail Khristoforov**.

We will discuss the state of our understanding of 2D percolation, and will present a recent joint work with Mikhail Khristoforov, giving a new proof of its conformal invariance at criticality.

STABILITY AND NONLINEAR PDES IN MIRROR SYMMETRY

Shing-Tung Yau

Harvard University, USA

I shall give a talk about a joint work that I did with Tristan Collins on an important nonlinear system equation of Monge-Ampère type. It is motivated from the theory of Mirror symmetry in string theory. I shall also talk about its algebraic geometric meaning.

FROM CLASSICAL TO QUANTUM AND BACK

Maciej Zworski

University of California, Berkeley, USA

Microlocal analysis exploits mathematical manifestations of the classical/quantum (particle/wave) correspondence and has been a successful tool in spectral theory and partial differential equations. We can say that these two fields lie on the "quantum/wave side".

In the last few years microlocal methods have been applied to the study of classical dynamical problems, in particular of chaotic flows. That followed the introduction of specially tailored spaces by Blank-Keller-Liverani, Baladi-Tsujii and other dynamicists and their microlocal interpretation by Faure-Sjostrand and by Dyatlov and the speaker.

I will explain this microlocal/dynamical connection in the context of Ruelle resonances, decay of correlations and meromorphy of dynamical zeta functions. I will also present some recent advances, among them results by Dyatlov-Guillarmou (Smale's conjecture on meromorphy of zeta functions for Axiom A flows), Guillarmou-Lefeuvres (local determination of metrics by the length spectrum) and Dang-Rivière (Ruelle resonances and Witten Laplacian).

PUBLIC LECTURE

FROM OPTIMAL TRANSPORT TO SOAP BUBBLES AND CLOUDS: A PERSONAL JOURNEY

Alessio Figalli

ETH Zürich, Switzerland

In this talk I'll give a general overview, accessible also to non-specialists, of the optimal transport problem. Then I'll show some applications of this theory to soap bubbles (isoperimetric inequalities) and clouds (semigeostrophic equations), problems on which I worked over the last 10 years. Finally, I will conclude with a brief description of some results that I recently obtained on the study of ice melting into water.

INVITED TALKS OF PART D4

MULTISCALE METHODS AND ANALYSIS FOR THE DIRAC EQUATION IN THE NONRELATIVISTIC LIMIT REGIME

Weizhu Bao

National University of Singapore, Singapore

In this talk, I will review our recent works on numerical methods and analysis for solving the Dirac equation in the nonrelativistic limit regime, involving a small dimensionless parameter which is inversely proportional to the speed of light. In this regime, the solution is highly oscillating in time and the energy becomes unbounded and indefinite, which bring significant difficulty in analysis and heavy burden in numerical computation [4]. We begin with four frequently used finite difference time domain (FDTD) methods and the time splitting Fourier pseudospectral (TSFP) method and obtain their rigorous error estimates in the nonrelativistic limit regime by paying particularly attention to how error bounds depend explicitly on mesh size and time step as well as the small parameter [3]. Then we consider a numerical method by using spectral method for spatial derivatives combined with an exponential wave integrator (EWI) in the Gautschi-type for temporal derivatives to discretize the Dirac equation [3]. Rigorous error estimates show that the EWI spectral method has much better temporal resolution than the FDTD methods for the Dirac equation in the nonrelativistic limit regime [3]. We find that the time-splitting spectral method performs super-resolution in temporal discretization when the Dirac equation has no magnetic potential [5]. Based on a multiscale expansion of the solution, we present a multiscale time integrator Fourier pseudospectral (MTI-FP) method for the Dirac equation and establish its error bound which uniformly accurate in term of the small dimensionless parameter [1]. Numerical results demonstrate that our error estimates are sharp and optimal. Finally, these methods and results are then extended to the nonlinear Dirac

equation in the nonrelativistic limit regime [2]. This is a joint work with Yongyong Cai, Xiaowei Jia, Qinglin Tang and Jia Yin.

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ACCELERATED SIMULATION FOR PLASMA KINETICS

Russel Caflisch

New York University, USA

Joint work with **Denis Silantyev** and **Bokai Yann**.

This presentation will discuss the kinetics of Coulomb collisions in plasmas, as described by the Landau-Fokker-Planck equation, and its numerical solution using a Direct Simulation Monte Carlo (DSMC) method. Acceleration of this method is achieved by coupling the particle method to a continuum fluid description. Efficiency of the resulting hybrid method is greatly increased by inclusion of particles with negative weights. This complicates the simulation, and introduces difficulties have plagued earlier efforts to use negatively weighted particles. This talk will describe significant progress that has been made in overcoming those difficulties.

OPTIMAL SAMPLING AND RECONSTRUCTION IN HIGH DIMENSION

Albert Cohen

Sorbonne Université, France

Motivated by non-intrusive approaches for high-dimensional parametric PDEs, we consider the general problem of approximating an unknown arbitrary function in any dimension from the data of point samples. The approximants are picked from given or adaptively chosen finite dimensional spaces. One principal objective is to obtain an approximation which performs as good as the best possible using a sampling budget that is linear in the dimension of the approximating space. We will show that this object if can is met by taking a random sample distributed according to a well chosen probability measure, and reconstructing by appropriate least-squares or pseudo-spectral methods.

MARGINAL TRIVIALITY OF THE SCALING LIMITS OF CRITICAL ISING AND φ^4 MODELS IN 4D

Hugo Duminil-Copin

IHÉS, France & University of Geneva, Switzerland

Joint work with **Michael Aizenman**.

The question of constructing a non-Gaussian field theory, i.e. a field with non-zero Ursell functions, is at the heart of Euclidean (quantum) field theory. While non-triviality results in $d < 4$ and triviality results in $d > 4$ were obtained in famous papers by Glimm, Jaffe, Aizenman, Frohlich and others, the crucial case of dimension 4 remained open. In this talk, we show that any continuum φ^4 theory constructed from Reflection Positive lattice φ^4 or Ising models is inevitably free in dimension 4. The proof is based on a delicate study of intersection properties of a non-Markovian random walk appearing in the random current representation of the model.

FROM WIGNER-DYSON TO PEARCEY: UNIVERSAL EIGENVALUE STATISTICS OF RANDOM MATRICES

László Erdős

Institute of Science and Technology, Austria

E. Wigner's revolutionary vision postulated that the local eigenvalue statistics of large random matrices are independent of the details of the matrix ensemble apart from its basic symmetry class. There have recently been a substantial development to prove Wigner's conjecture for larger and larger classes of matrix ensembles motivated by applications. They include matrices with entries with a general correlation structure and addition of deterministic matrices in a random relative basis. We also report on three types of universality, commonly known as the bulk, edge and cusp universality, referring to the behaviour of the density of states in the corresponding energy regime. While bulk and edge universalities have been subject to intensive research, the cusp universality has been studied only in very special cases before. Our recent work settles the question of this third and last type of universality in full generality.

DISSIPATIVE SOLUTIONS TO THE COMPRESSIBLE EULER SYSTEM

Eduard Feireisl

Czech Academy of Sciences, Czech Republic

Joint work with **Dominic Breit** and **Martina Hofmanová**.

We introduce the concept of (generalized) dissipative solutions to the compressible Euler system and review their basic properties:

- **Existence.** Dissipative solutions exist globally in time for any finite energy initial data.
- **Maximal dissipation, semigroup selection.** One can select a solution semigroup among dissipative solutions. The selected solution maximizes the energy dissipation (entropy production), see [1].

- **Weak-strong uniqueness.** A dissipative and a weak solution emanating from the same initial data coincide as soon as the weak solution belongs to certain Besov class and its velocity gradient satisfies a one sided Lipschitz condition, see [2].
- **Convergence of numerical schemes.** Cesaro averages produced by suitable numerical schemes converge strongly to a dissipative solution, see [3].

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FINITE DIMENSIONAL STATE REPRESENTATION OF STRUCTURED POPULATION MODELS

Mats Gyllenberg
University of Helsinki, Finland

Structured population models can be formulated as delay systems. We consider the question of when delay systems, which are intrinsically infinite dimensional, can be represented by finite dimensional systems. Specifically, we give conditions for when all the information about the solutions of the delay system can be obtained from the solutions of a finite system of ordinary differential equations. For linear autonomous systems and linear systems with time-dependent input we give necessary and sufficient conditions and in the nonlinear case we give sufficient conditions. The ideas and results are illustrated by models for infectious diseases and physiologically structured populations.

QUANTITATIVE LINEAR STABILITY (HYPOCOERCIVITY) FOR CHARGED PARTICLES IN A CONFINING FIELD

Clément Mouhot

University of Cambridge, UK

Joint work with **K. Carrapatoso, J. Dolbeault, F. Hérau, S. Mischler, and C. Schmeiser.**

We report on recent joint results in which we develop quantitative methods for proving the existence of a spectral gap and estimating the gap, for hypocoercive kinetic equations that combine the local conservation laws of fluid mechanics and a confining potential force. The proofs involve a cascade of correctors and global commutator estimates, as well as new quantitative inequalities of Korn type. The latter extend to the case of the whole space with a potential force the classical Korn inequality in a bounded domain of elasticity theory. These results are a step towards constructing global solutions near equilibrium to the full nonlinear Boltzmann equation for charged particles subject to a confining potential.

STOCHASTIC MODELING AND OPTIMIZATION IN HUMAN-MACHINE INTERACTION SYSTEMS

Thaleia Zariphopoulou

University of Texas at Austin, USA

Joint work with **Agostino Capponi and Svein Olefsen.**

I will introduce a family of human-machine interaction (HMI) models in optimal asset allocation, risk management and portfolio choice (robo-advising). Modeling difficulties stem from the limited ability to quantify the human's risk preferences and describe their evolution, but also from the fact that the stochastic environment, in which the machine optimizes, itself adapts to real-time incoming information that is exogenous to the human. Furthermore, the human's risk preferences and the machine's states may evolve at different scales. This interaction creates an

adaptive cooperative game with asymmetric and incomplete information exchange between the two parties.

As a result, challenging questions arise on, among others, how frequently the two parties should communicate, what information can the machine accurately detect, infer and predict, how the human reacts to exogenous events and what are the effects on the machine's actions, how to improve the inter-linked reliability between the human and the machine, and others.

Such HMI models give rise to new, non-standard optimization problems that include well-posed and ill-posed sub-problems, and combine adaptive stochastic control, stochastic differential games, optimal stopping, multi-scales and learning.

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TALKS OF SESSION D42

A PROBABILISTIC VIEW ON THE DETERMINISTIC MUTATION-SELECTION EQUATION

Ellen Baake

Universität Bielefeld, Germany

Joint work with **Fernando Cordero and Sebastian Hummel**.

We reconsider the prototype version of the mutation-selection differential equation of population genetics. It describes the dynamics of the type composition of an infinite-size population of individuals with two possible types that undergo selection and recurrent mutation. We develop the genealogical point of view to this equation by tracing back the lines of descent of individuals from the population at some (forward) time t . We revisit the ancestral selection graph, which is the standard tool to trace back ancestral lines in populations under selection. Based on this, we introduce the killed ancestral selection graph, which yields the type of a random individual, based on the individual's potential ancestry and the mutations that define the individual's type. The result is a *stochastic representation of the solution of the (deterministic) differential equation*, which is formulated in terms of a duality theorem. This way, the well-known stationary behaviour of the differential equation (and its transcritical bifurcation) translates into the asymptotic behaviour of a (killed) birth-death process.

References

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GLOBAL EXISTENCE VS FINITE TIME BLOWUP IN KELLER–SEGEL MODEL OF CHEMOTAXIS

Piotr Biler

University of Wrocław, Poland

Joint work with **Grzegorz Karch** and **Jacek Zienkiewicz**.

We consider the parabolic-elliptic model for the chemotaxis with fractional (anomalous) diffusion ($\alpha \in (0, 2)$) in several space dimensions ($d \geq 3$)

$$(1) \quad \begin{aligned} u_t + (-\Delta)^{\alpha/2} u + \nabla \cdot (u \nabla v) &= 0, & x \in \mathbb{R}^d, \ t > 0, \\ \Delta v + u &= 0, & x \in \mathbb{R}^d, \ t > 0, \\ u(x, 0) = u_0(x) &\geq 0, & x \in \mathbb{R}^d. \end{aligned}$$

Global-in-time solutions are constructed under (nearly) optimal assumptions on the size of radial initial data. Moreover, criteria for blowup of radial solutions in terms of suitable Morrey spaces norms are derived.

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ECO-EVOLUTIONARY CYCLES OF VIRULENCE UNDER SELECTIVE PREDATION

Barbara Boldin

University of Primorska, Slovenia

Joint work with **Eva Kisdi** and **Stefan A.H. Geritz**.

In nature, diseased animals do not die peacefully on their deathbeds. Rather, they are often more likely to fall victim to predators, who selectively prey upon the weak. Such disease-induced selective predation brings about changes in prey populations, which may in turn alter the evolutionary dynamics of pathogens. The resulting eco-evolutionary system may exhibit rich dynamics with multiple attractors and limit cycles. We introduce a novel technique to provide a constructive proof that the system can exhibit stable limit cycles under realistic assumptions about model ingredients and perform a detailed bifurcation analysis for a concrete example of a predator-prey-pathogen system.

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EPIDEMICS IN STRUCTURED COMMUNITIES WITH SOCIAL DISTANCING

Tom Britton

Stockholm University, Sweden

Joint work with **Frank Ball**, **KaYin Leung**, and **Dave Sirl**.

Consider a large community, structured as a network, in which an epidemic spreads. Infectious individuals spread the disease to each of their susceptible neighbors, independently, at rate λ , and each infectious individual recovers and becomes immune at rate γ . The social distancing is modeled by each susceptible who has an infectious neighbor rewires away from this individual to a randomly chosen individual at rate ω . Our main result is surprising and says: the rewiring is rational from an individual perspective since it reduces the risk of being infected, but at the same time it may be harmful for the community at large in that the outbreak may get bigger compared to no rewiring ($\omega = 0$).

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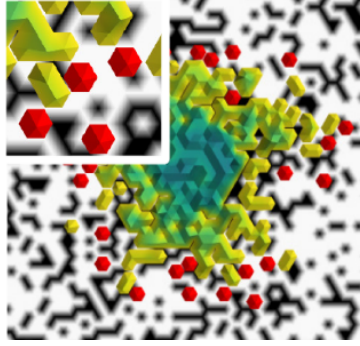
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BIOLOGICAL LATTICE-GAS CELLULAR AUTOMATON MODELS FOR THE ANALYSIS OF COLLECTIVE EFFECTS IN CANCER INVASION

Andreas Deutsch

Technische Universität Dresden, Germany

Cancer invasion may be viewed as collective phenomenon emerging from the interplay of individual biological cells with their environment. Cell-based mathematical models can be used to decipher the rules of interaction. In these models cells are regarded as separate movable units. Here, we introduce an integrative modelling approach based on mesoscopic biological lattice-gas cellular automata (BIO-LGCA) to analyse collective effects in cancer invasion. This approach is rule- and cell-based, computationally efficient, and integrates statistical and biophysical models for different levels of biological knowledge. In particular, we provide BIO-LGCA models to analyse mechanisms of invasion in glioma and breast cancer cell lines.



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ESTIMATING THE FRAGMENTATION CHARACTERISTICS IN GROWING AND DIVIDING POPULATIONS

Marie Doumic

CNRS & Sorbonne Université, France

Joint work with **Miguel Escobedo**, **Magali Tournus** and **Wei-Feng Xue**.

Growing and dividing populations may be described either by stochastic branching processes or by integro-differential equations, both related by the fact that the integro-differential equation may be seen as the Kolmogorov equation of the branching process. Denoting $u(t, x)$ the concentration of individuals of size x at time t , a typical growth-fragmentation equation may be written as

$$\frac{\partial}{\partial t}u(t, x) + \frac{\partial}{\partial t}(g(x)u(t, x)) + B(x)u(t, x) = \int_0^1 B\left(\frac{x}{z}\right)u\left(t, \frac{x}{z}\right)\frac{dk_0(z)}{z},$$

where $g(x)$ is the growth rate, $B(x)$ the division rate, and k_0 is called the (self-similar) fragmentation kernel, which characterizes the probability for a dividing particle of size $\frac{x}{z}$ to give rise to an offspring of size x . During the last decade, using the asymptotic behaviour of this equation or of the related stochastic process to estimate the division rate ($B(x)$ in the equation) of a population has led to many interesting questions and results, in mathematics as well as in biology. In this talk, I will review some of them, and focus on the question of estimating the fragmentation kernel k_0 , which revealed a much more ill-posed problem than estimating the division rate $B(x)$. We then applied our methods to fragmenting protein fibrils, following the experiments done by W.F. Xue's laboratory in the university of Kent.

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IMPROVED FORAGING BY SWITCHING BETWEEN DIFFUSION AND ADVECTION: BENEFITS FROM MOVEMENT THAT DEPENDS ON SPATIAL CONTEXT

William Fagan

University of Maryland, College Park, USA

Joint work with **Tyler Hoffman, Daisy Dahiya, Eliezer Gurarie, Robert Stephen Cantrell, and Chris Cosner.**

Animals use different modes of movement at different times, in different locations, and on different scales. Incorporating such context-dependence in mathematical models represents a substantial increase in complexity, but creates an opportunity to more fully integrate key

biological features. Here we consider the spatial dynamics of a population of foragers with two subunits. In one subunit, foragers move via diffusion (random search) whereas in the other, foragers move via advection (gradient-following search). Foragers switch back and forth between the subunits as functions of their spatial context (i.e., depending on whether they are inside or outside of a patch, or depending on whether or not they can detect a gradient in resource density). We consider a one dimensional binary landscape of resource patches and non-habitat and gauge success in terms of how well the mobile foragers overlap with the distribution of resources. Actively switching between dispersal modes can sometimes greatly enhance this spatial overlap relative to the spatial overlap possible when foragers merely blend advection and diffusion modes at all times. Switching between movement modes is most beneficial when an organism's gradient-following abilities are weak compared to its overall capacity for movement, but switching can actually be quite detrimental for organisms that can rapidly follow resource gradients. An organism's perceptual range plays a critical role in determining the conditions under which switching movement modes benefits versus disadvantages foragers as they seek out resources.

RIGOROUS CONTINUUM LIMIT FOR THE DISCRETE NETWORK FORMATION PROBLEM

Jan Haskovec

KAUST, Saudi Arabia

Motivated by recent papers describing the formation of biological transport networks we study a discrete model proposed by Hu and Cai consisting of an energy consumption function constrained by a linear system on a graph. For the spatially two-dimensional rectangular setting we prove the rigorous continuum limit of the constrained energy functional as the number of nodes of the underlying graph tends to infinity and the edge lengths shrink to zero uniformly. The proof is based on reformulating the discrete energy functional as a sequence of integral functionals and proving their Γ -convergence towards a continuum energy functional.

KINETIC MODELING OF COLONIES OF MYXOBACTERIA

Laura Kanzler

Universität Wien, Austria

Joint work with **Sabine Hittmeir, Gerhard Kitzler, Angelika Manhart, Christian Schmeiser, and Joachim Schöberl.**

Myxobacteria are rod-shaped, social bacteria that are able to move on flat surfaces by 'gliding' and form a fascinating example of how simple cell-cell interaction rules can lead to *emergent, collective behavior*. Observed movement patterns of individual bacteria in such a colony include straight runs with approximately constant velocity, alignment interactions and velocity reversals [1], [2], [3]. Experimental evidence shows that above mentioned behavior is a consequence of direct cell-contact interaction rather than diffusion of chemical signals, which indicates the suitability of kinetic modeling.

In this talk a new *kinetic model of Boltzmann-type* for such colonies of myxobacteria will be introduced and investigated. For the spatially homogeneous case an existence and uniqueness result will be shown, as well as exponential decay to an equilibrium for the Maxwellian collision operator. The methods used for the analysis combine several tools from kinetic theory, entropy methods as well as optimal transport. The talk will be concluded with numerical simulations confirming the analytical results.

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EXPECTED SITE FREQUENCY SPECTRA OF CELLS: COALESCENT VERSUS BIRTH-AND-DEATH-PROCESS APPROACH

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Joint work with **Khanh Dinh, Roman Jaksik, Amaury Lambert, and Simon Tavaré.**

Recent years have produced a large amount of work on inference about cancer evolution from mutations identified in cancer samples. Much of the modeling work has been based on classical models of population genetics, generalized to accommodate time-varying cell population size [1]. Reverse-time, genealogical, views of such models, commonly known as coalescent theory, have been used to infer aspects of the past of growing populations [2]. Another approach is to use branching processes, the simplest scenario being the linear birth-death process (lbdp), a binary fission Markov age-dependent branching process. A genealogical view of such models is also available [3]. As will be seen in the sequel, the two approaches lead to similar but not identical results.

Inference from evolutionary models of DNA often exploits summary statistics of the sequence data, a common one being the so-called Site Frequency Spectrum. In a sequencing experiment with a known number of sequences, we can estimate for each site at which a novel somatic mutation has arisen, the number of cells that carry that mutation. These numbers are then grouped into sites which have the same number of copies of the mutant. Consider genealogy of a sample of $n = 20$ cells that includes 13 mutational events out of which 7 mutations are present in a single cell, 3 are present in 3 cells, 2 are present in 6, and 1 mutation is present in 17 cells. If we denote the number of mutations present in k cells by η_k , $\eta_1 = 7$, $\eta_3 = 3$, $\eta_6 = 2$, and $\eta_{17} = 1$, with all other η_k equal to 0. The vector η is called the Site Frequency Spectrum (SFS). It can be computed from the statistics of mutations in a sample of cells, in which DNA has been sequenced.

We examine how the SFS based on birth-death processes differ from those based on the coalescent model. This may stem from the different sampling mechanisms in the two approaches. However, we also show that despite this, they can be made quantitatively comparable at least for the range of parameters typical for tumor cell populations. We also touch upon the "singleton estimation problem" and the "self-renewal fraction versus proliferation rate" controversy.

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ADAPTIVE DYNAMICS OF PATHOGENS AND THEIR HOSTS

Eva Kisdi

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This talk will review how pathogens evolve to exploit their hosts, and how hosts in turn evolve under selective pressure from their pathogens. Special attention is paid to nonlinear feedbacks, which are responsible for a wide range of dynamical phenomena including the evolution of diversity and the emergence of evolutionary cycles via Hopf bifurcations. I discuss whether pathogens can evolve so virulent that they drive their hosts extinct, and whether hosts can escape their pathogens by evolving such that the pathogen is no longer viable.

GLOBAL BEHAVIOR OF A MULTI-GROUP SIR EPIDEMIC MODEL WITH AGE STRUCTURE AND ESTIMATION OF \mathcal{R} , FOR THE CHLAMYDIA EPIDEMIC IN JAPAN

Toshikazu Kuniya

Kobe University, Japan

In this talk, we study the global behavior of a multi-group SIR epidemic model with age structure. Under the assumptions that the disease transmission coefficient is independent of the age of infective individuals and the sum of the mortality and the recovery rate is constant, the model can be rewritten into a multi-group SIR model with age-dependent susceptibility. We then define the basic reproduction number \mathcal{R}_i by the spectral radius of the next generation matrix and show that \mathcal{R}_i completely determines the global behavior of the model: if $\mathcal{R}_i < \infty$, then the disease-free equilibrium is globally attractive, whereas if $\mathcal{R}_i > \infty$, then the endemic equilibrium is globally attractive. In the application, we estimate \mathcal{R}_i for the chlamydia epidemic in Japan in 2015 by comparing four special cases of our model: a homogeneous model, an age-independent two-sex model, an age-dependent one-sex model and an age-dependent two-sex model. In conclusion, we see that \mathcal{R}_i is in the range 1.0148-1.0535, the age structure has more influence on the estimation result than the two-sex structure and disregarding the age structure could lead to the underestimation of \mathcal{R}_i .

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HOST CONTACT STRUCTURE IS IMPORTANT FOR THE RECURRENCE OF INFLUENZA A

Junling Ma

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Joint work with **Juan M. Jaramillo**, **Pauline van den Driessche**, **Sanling Yuan**.

An important characteristic of influenza A is its ability to escape host immunity through antigenic drift. Individuals infected by a strain of influenza A during an epidemic have decreased immunity (estimated to be 12-25

MODELLING AND SIMULATION OF COLLECTIVE MIGRATION IN EPITHELIAL LAYERS

Dietmar Ölz

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Joint work with **Z. Neufeld, A. Czirok, and H. Khatae.**

The mechanochemical coupling between the cells aligned in epithelial layers impacts characteristic features of their collective migration. I will introduce a 1D model for collective cell migration in epithelial sheets in which the cytoskeletons of adjacent cells are coupled both, mechanically and through mechanochemical feedback. The travelling wave analysis of the mathematical model can be made explicit predicting a polarization wave and associated wave speed which we can be observed in experiments. Finally I will also talk about recent results based on particle simulations of collective cell migration.

EPIDEMIC OSCILLATIONS AND THE SPREAD OF AWARENESS

Joan Saldaña

University of Girona, Spain

In this talk we consider an epidemic model with a preventive behavioural response triggered by the risk perception of infection among individuals. The analysis of models combining disease and behaviour dynamics has mostly focused on the impact of the latter on the initial growth of an outbreak (computation of R_0) and the existence of endemic equilibria (see, for instance, [2, 3, 5] for mean-field models). Here we ask whether the interplay between behaviour and disease spreading is always able to prevent periodic re-emergence of a communicable disease when awareness decays over time.

In a recent work [4], it was shown that oscillations are ruled out in Susceptible-Aware-Infectious-Susceptible deterministic models with a single compartment of alerted hosts and no demographics, but they can occur when one considers two distinct compartments of aware hosts who differ

in their willingness to alert other susceptible hosts. Progressive levels of awareness in epidemic modelling were considered in [1], whereas the introduction of an additional compartment of active alerted hosts in an SIS model (without awareness decay) was made in [6].

In a deterministic context, such epidemic flare-ups translate into solutions of ODE models showing sustained oscillations which approach zero when there is a high enough fraction of alerted individuals in the population (see [4]). The question we will address here is how robust these oscillations are when we move away from such a deterministic framework and consider stochastic simulations of the epidemic dynamics.

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MATHEMATICAL MODELS OF ACTIN DRIVEN CELL MOTILITY

Christian Schmeiser

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Joint work with **Aaron Brunk, Stefanie Hirsch, Gaspard Jankowiak, Angelika Manhart, Dietmar Oelz, Diane Peurichard, Nikolaos Sfakianakis, and Christoph Winkler.**

Actin is one of the most important proteins occurring in practically all eukaryotic cells. It has the ability to polymerize and to form microfilaments, an essential part of the cytoskeleton. Among other functions, actin filaments contribute to the motility of crawling cells. In particular, a network of actin filaments supports the lamellipodium, a motility organelle of many cell types. The lamellipodium is a flat cell protrusion, and a first theoretical explanation of its flatness has been provided in [6]. Based on this flatness, a two-dimensional anisotropic two-phase continuum model, the *Filament Based Lamellipodium Model*, has been formulated and analyzed in [5] and then extended and used for simulations in [3] and [7]. The qualitative behaviour of submodels has been analyzed in [1] and in [4].

Recently, polymerization driven cortical flow has been modelled as an alternative mechanism for cell motility in [2]. The model is able to explain experimental results on adhesion-free motility in artificial micro-channels with structured walls.

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CAPTURING THE QUASI-STATIONARY DISTRIBUTION WITHIN A DETERMINISTIC FRAMEWORK FOR STOCHASTIC SIS DYNAMICS

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Joint work with **Christopher Overton and Robert Wilkinson** .

The stochastic susceptible-infectious-susceptible (SIS) model represents an important class of epidemic dynamics, and is thought to represent processes such as the spread of sexually transmitted diseases and computer viruses. A feature of this model is the existence of a single absorbing state, corresponding to the disease free state, to which the system will always converge for finite population sizes and finite infection transmission parameters.

There has been a long history of deterministic representations of the SIS model. Relating these models to the stochastic dynamics frequently makes use of mean-field assumptions, which are derived from the infinite population limit [1]. These models provide useful theoretical insight but do not feature the absorbing state, and therefore it is hard to link the insights back to the stochastic model.

In this work we develop novel methods to account for the absorbing state of the stochastic model within a deterministic framework. We do this by obtaining a deterministic approximation to the quasi-stationary distribution (QSD) of the model; i.e. the long-term steady-state behaviour conditional on not having reached the absorbing state [2, 3]. In particular, we build a system of population level equations, which when solved provide an accurate and efficient approximate to the QSD of the Markovian network-based SIS model for a large range of networks and parameter sets.

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MICROSCOPIC DESCRIPTION OF DNA THERMAL DENATURATION

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Joint work with **Mateusz Dębowski** and **Mirosław Lachowicz**.

We propose a microscopic model describing the process of DNA thermal denaturation. The process consists of the splitting of DNA base pairs resulting in the separation of two complementary DNA strands. In contrast to the previous modelling attempts we take into account the states of all base pairs of DNA which in fact imposes the microscopic nature of the approach. The model is a linear integro-differential non-autonomous equation describing the dynamics of probability density which characterizes the distances between the bases within individual base pairs. We take into account not only the strength of double and triple hydrogen bonds between the complementary bases but also the stacking interactions between neighborhood base pairs. We show basic mathematical properties of the model and present numerical simulations that reproduce the sigmoid shape of DNA melting curves and reveal the appearance of experimentally observed denaturation bubbles.

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CANARD SOLUTIONS IN EQUATIONS WITH BACKWARD BIFURCATIONS

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Joint work with **Jacek Banasiak** and **Milaine Seuneu Tchamga**.

We consider a singularly perturbed initial value problem in the case of intersecting quasi stationary manifolds. The main results are concerned with the asymptotic behavior of solutions as the small parameter tends to zero.

Our results are related to the Tikhonov approach. The main condition for the validity of the Tikhonov theorem is that the quasi steady states be isolated and attractive. In applications, however, we often encounter the situation when two or more quasi steady states intersect. It involves the so called *exchange of stabilities*: the branches of the quasi steady states change from being attractive to being repelling (or conversely) across the intersection. The assumptions of the Tikhonov theorem fail to hold in the neighbourhood of the intersection but it is natural to expect that any solution that passes close to it follows the attractive branches of the quasi steady states on either side of the intersection. However, in many cases an unexpected behaviour of the solution is observed - it follows the attracting part of a quasi steady state and, having passed the intersection, it continues along the now repelling branch of the former quasi steady state for some prescribed time and only then jumps to the attracting part of the other quasi steady state. Such a behaviour we call the *delayed switch of stability*. We shall focus on the so called *backward bifurcation*, in which two of three quasi steady states intersect and exchange stabilities at the intersection.

As an application, we consider two predator-prey models: the Rosenzweig-MacArthur model and the Leslie-Gowers/Holling model. In both these cases the quasi-steady manifolds intersect and a backward bifurcation occurs along their intersection. We give a proof of the existence of canards and provide an exact value of time at which the stability switch occurs.

MODEL-BASED INFERENCES ABOUT CELLULAR MECHANISMS OF TUMOR DEVELOPMENT FROM TISSUE-SCALE DATA

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Cancer development is widely understood as a multistep process in which cells increase in malignancy through progressive genotypic and phenotypic alterations. Although there is an increasing knowledge about the biology of the involved cellular processes in vitro, the transfer of the results to in-vivo situations remains a challenge. This is due to the fact that the early phase of tumor development, which initially involves only a small number of cells, is hardly

observable while the cellular basis of tissue-scale observations is difficult to decipher. Cell-based mathematical models provide a valuable tool to investigate in which way tissue-scale observables depend on cellular mechanisms and intercellular interaction. Here, we analyze the population dynamics of spatial and non-spatial Markov models which describe genetic and phenotypic cell changes and use these findings to calibrate the models by tissue-scale data. This allows to generate quantitative predictions about tumor initiation, progression and regression behavior.

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ANIMAL MOVEMENT WITH SPATIAL MEMORY

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Joint work with **Junping Shi, Chuncheng Wang, Qingyan Shi, Yongli Song, and Xiangping Yan.**

Animals often self-organize into territorial structure from movements and interactions of individual animals. Memory is one of the cognitive processes that may affect the movement and navigation of the animals. I will review several mathematical approaches to animal spatial movements, and then introduce our recent work via a modified Fick's law to model and simulate the memory-based movement. Results on bifurcation and pattern formation will be shown for these non-standard reaction-diffusion models.

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ON THE STABILITY OF THE STEADY STATES IN THE N-SITE FUTILE CYCLE

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Joint work with **Elisenda Feliu** and **Alan Rendall**.

The multiple or n -site futile cycle is a biological process that resides in the cell. Specifically, it is a phosphorylation system in which a molecular substrate might be phosphorylated sequentially n times by means of an enzymatic mechanism. The system has been studied mathematically using reaction network theory and ordinary differential equations. In its standard form it has $3n + 3$ variables (concentrations of species) and $6n$ parameters. It is known that the system might have at least as many as $2\lfloor \frac{n}{2} \rfloor + 1$ steady states (where $\lfloor x \rfloor$ is the integer part of x) for particular choices of parameters. Furthermore, for the simple futile cycle ($n = 1$) there is only one steady state which is globally stable. For the dual futile cycle ($n = 2$) the stability of the steady states has been determined in the following sense: There exist parameter values for which the dual futile cycle admits two asymptotically stable and one unstable steady state. For general n , evidence that the possible number of asymptotically stable steady states increases with n has been given, which has led to the conjecture that parameter values can be chosen such that $\lfloor \frac{n}{2} \rfloor + 1$ out of $2\lfloor \frac{n}{2} \rfloor + 1$ steady states are asymptotically stable and the remaining steady states are unstable.

We prove this conjecture here by first reducing the system to a smaller one, for which we find a choice of parameter values that give rise to a unique steady state with multiplicity $2\lfloor \frac{n}{2} \rfloor + 1$. Using arguments from geometric singular perturbation theory, and a detailed analysis of the centre manifold of this steady state, we achieve the desired result.

PHASE FIELD APPROACH TO SUBSTRATE-BASED CELL MOTILITY

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I will give an introduction to the substrate-based crawling motility of eukaryotic cells and survey our recent advances in its modeling. A modular approach, based on the phase field method to track the deformable and moving cells [1], allows us to describe, e.g., cell movement on structured substrates with modulated adhesion or stiffness [2], collective cell migration [3], as well as motion in 3D confinement [4]. I will also discuss the example of cellular shape waves [5], where the computational approach allows for additional insight via semi-analytic methods (employing asymptotic reduction and multiple scales).

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