The First Nordic Biomathematics Days

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ABSTRACTS

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Invited talks

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Numerical bifurcation analysis of physiologically structured population models via pseudospectral approximation

Joint work with Dimitri Breda, Mats Gyllenberg, Francesca Scarabel, Rossana Vermiglio and Babette de Wolff.

As structured population models lead to infinite dimensional dynamical systems, there exist no well-tested tools for their numerical bifurcation analysis. By way of polynomial approximation of the functions that describe the population state, one can reduce to a system of ODE for which such tools are readily available.

Deterministic (at the population level) physiologically structured population models can either be formulated as delay equations or as first order partial differential equations (often with the birth of new individuals described by a boundary condition).

The aim of this lecture is to explain for both formulations the main ideas of pseudospectral approximation and to demonstrate the potential of the approach by way of examples.

Susanne Ditlevsen
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The why and how of randomness

Randomness is ubiquitous in all biological systems. The nervous system is hugely affected by stochasticity, and noise and variability are fundamental of brain function. Information processing is faced with the challenge of acting in this unpredictable and random world, but even if cellular and molecular processes of life itself are noisy and variability in perception and behavior is observed for equal sensory inputs, the brain displays a remarkable precision, essential for survival. Is this ever-present noise a caprice of nature, which evolution has taught us to deal with the best we can? Or does stochasticity play a constructive role, increasing reliability and robustness, and the brain is a probabilistic device because this makes us more fit to survive? Is the noise beneficial or detrimental? Modeling with stochastic processes becomes more and more popular in neuroscience, not only because of the powerful mathematical tools from stochastic analysis, but also because of the increasing availability of measurements and data for dynamical processes, where randomness plays a major role.

In this talk I will discuss stochastic models of biological systems, and show some surprising and different dynamics not present in the deterministic models. The standard approach to deal with the noisy and highly variable data is to average over trials, to presumably get a more reliable output for further analysis. This might blur or entirely remove essential characteristics and mechanisms, which are fundamental for understanding the underlying function of the system under study. More advanced statistical methods and stochastic models are paramount to disentangle the finer mechanisms, because single trials carry information, which is not maintained in the average behavior.

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Populations - from few independently reproducing individuals to continuous and deterministic flows

When the density of populations grows, in pace with an environmental carrying capacity growth, general branching populations with interacting individuals and also in interplay with the environment, will stabilise towards a deterministic population flow, determined by an integral equation. The deviation between the original density and the limiting one, as the carrying capacity grows beyond all limits, will also converge to a diffusion process. This provides a firm basis in individual behaviour for ad hoc deterministic population models.

Oral presentations

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Formulating adaptive hypotheses in multivariate phylogenetic comparative methods

Joint work with G. Asimomitis, V. Mitov, M. PiwczyDski, T. Stadler.

Co-adaptation is key to understanding species evolution. Different traits have to function together so that the organism can work as a whole. Hence, all changes to environmental pressures have to be coordinated. Recently, we have developed R packages that are able to handle general, multivariate Gaussian processes realized over a phylogenetic tree. At the heart of the modelling framework is the so-called GLInv (Gaussian, mean depending linearly on the ancestral value and variance Invariant with respect to ancestral value) family of models. More formally a stochastic process evolving on a tree belongs to this family if * after branching the traits evolve independently * the distribution of the trait at time t, X(t), conditional on the ancestral value, X(s), at time s<t, is Gaussian with ** E[X(t) | X(s)] = w(s,t) + F(s,t)X(s) ** Var[X(t) | X(s)] = V(s,t), where neither w(s,t), F(s,t), nor V(s,t) can depend on X(.) but may be further parametrized. Using the likelihood computational engine PCMBase [2, available on CRAN] the PCMFit [3, publicly available on GitHub] package allows for inference of models belonging to the GLInv family and furthermore allows for finding points of shifts between evolutionary regimes n the tree. What is particularly novel is that it allows not only for shifts between a model's parameters but for switches between different types of models within then GLInv family (e.g. a shift from a Brownian motion (BM) to an Ornstein-Uhlenbeck (OU) process and vice versa). Interactions between traits can be understood as magnitudes and signs of off-diagonal entries of F(s,t) or V(s,t). What is particularly interesting is that in this family of models one may obtain changes in the direction of the relationship, i.e. the long and short term joint dynamics can be of a different nature. This is possible even if one simplifies the process to an OU one. Here, one is able to very finely understand the dynamics of the process and propose specific model parameterizations [PCMFit and current CRAN version of mvSLOUCH, 1, which is based on PCMBase]. In the talk I will discuss how one can setup different hypotheses concerning relationships between the traits in terms of model parameters and how one can view the long and short term evolutionary dynamics. The software's possibilities will be illustrated by considering the evolution of fruit in the Ferula genus.

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Trait Level Analysis of Multitrait Projection Matrices allows to implement kinship effects in evolutionary demography models

As most demographers, ecologists and geneticists know, kinship and demography strongly interact. Indeed, the dynamics of a population shapes its genealogy across generations, and this genealogy specifies relatedness between individuals at the population level down to the frequencies of kin within families. In turn, the presence and number of kin is of crucial importance for the vital rates and therefore the demography and many species in nature. Although pivotal, this framework - studying the coevolution of kinship and life history and that we call kinship demography - has seen little development since Goodman, Keyfitz and Pullum's pioneering 1974 paper [1] with regards to the influence of life history on kinship distribution and very rare efforts on the reciprocal effects of kin transfers on vital rates [2]. Here, we will discuss how matrix population models can help improve our understanding of the mechanisms of such a coevolution, in particular via the use of Multitrait Population projection Matrices and Trait Level Analysis [3], tools that allow to implement several categories within a projection matrix and to analyse their importance for the fitness and the dynamics of a population.

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Evolution of chronic viral infections and the effect of the population-level control

Joint work with Ethan Romero-Severson (LANL, USA).

We consider a population level model of the dynamics of a multiple strain infection. This research is motivated by a need for mathematical models that integrate within-host genetic diversity and genotypic (resp., phenotypic) evolution with epidemiological dynamics and consider the effects of joint 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 that can be both transmitted and possibly lost in later hosts. We consider both the epidemiological and evolutionary effects of both therapy for infected persons and chemo-prophylaxis-type measures for uninfected persons. We 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 R0 under different assumptions about the model structure and study how the endemic equilibrium state depends on the system's parameters. We also present a sensitivity analysis along the lines described in [1] and make a number of suggestions aimed at improving the intervention strategies design for combating the disease.

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Sami Lehtinen
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Coevolution of cannibalistic predators and timid prey: evolutionary cycling and branching

Joint work with Stefan Geritz (University of Helsinki).

We investigate the coevolution of cannibalistic predators and timid prey, which seek refuge upon detecting a predator. To understand how the species affect each other's evolution, we derived the ecological model from individual-level processes using ordinary differential equations. The ecological dynamics exhibit bistability between equilibrium and periodic attractors, which may disappear through catastrophic bifurcations. Using the critical function analysis of adaptive dynamics, we classify general trade-offs between cannibalism and prey capture that produce different evolutionary outcomes. The evolutionary analysis reveals several ways in which cannibalism emerges as a response to timidity of the prey. The long-term coevolution either attains a singularity, or becomes cyclic through two mechanisms: genetical cycles through Hopf bifurcation of the singularity, or ecogenetical cycles involving abrupt switching between ecological attractors. Further diversification of cannibalism occurs through evolutionary branching, which is predicted to be delayed when simultaneous prey evolution is necessary for the singularity's attainability. We conclude that predator-prey coevolution produces a variety of outcomes, including the emergence of new individual behaviour.

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Large and small worlds: learning and decision making in game theory for biology

Theories of rational decision making distinguish large and small worlds. The term small worlds denotes a modelling approach where individuals correctly represent probability distributions over states of the environment; it is a kind of philosophical Bayesianism. In contrast, in large worlds individuals have more limited representations, perhaps only guided by rewards; it is a criticism of Bayesianism. Learning theory in animal psychology is an example of a large-worlds approach. Game theory models of social interactions might use either of the approaches. There are however rather few thoroughgoing and successful small-worlds approaches to game-theory models of social interactions, with learning about social partners. The reason may be that it is hard to develop workable models in this way. There is also the question whether such models are biologically realistic. I argue that, in contrast, large-worlds models have several advantages. There is a spectrum of large-world modelling styles, from pure model-free reinforcement learning to assumptions about additional cognitive capacities of agents. These modelling styles can be combined with the study of evolution of learning and decision-making traits. Finally, large-worlds models might well be biologically realistic, and can successfully handle cooperation and conflict in social interactions.

Magnus Lindh
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Evolution of plant economics in a water limited environment

Plants rely on water for their photosynthesis. Water deficit initially leads to lower plant growth rate, later to hydraulic failure or carbon starvation, and ultimately to death. Plants have evolved many strategies to withstand long periods of drought, such as thick leaves, high wood density, early reproduction time, and deep roots. Our understanding of plant response to future climate depends critically on plant responses to drought. The expected increase in variation both in precipitation and temperature suggests that future models should include variability and not only mean values. Plants can be positioned in the plant economics spectrum depending on if their growth is fast or slow, where fast growth is associated with high mortality, and high water uptake. Functional trait changes associated with fast growth are for example a lower wood density and a lower leaf mass per area. Here we develop a minimal model based on a single trait related to growth rate, where plants are competing for space and water. We explore the importance of the trait and the soil water content on three functions describing birth rate, mortality and transpiration. We do this by compare the evolutionarily stable strategy (ESS), resulting from a competitive game between strategies defined by their trait value, with the two optimal strategies maximizing plant density or soil water content. We report the following findings: (1) When soil water only depends on plant density the trait minimizing soil water content is evolved. Increasingly fast growing plants evolve at an increasing background mortality. (2) With dynamic soil water a higher precipitation, or a lower evaporation, promotes the evolution of faster plants as well as higher plant densities and higher soil water content. (3) By comparing different model types we can conclude that a trait dependence on birth rate, mortality and transpiration is crucial to get an internal ESS between the strategy maximizing plant density and the strategy minimizing soil water content.

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Compression therapy as an inverse problem

Compression therapy has been utilized by clinicians long before Hippocrates for symptoms such as chronic leg ulcer, oedema, etc, but the art of application, i.e. bandaging is still mainly hidden in the dark. Maybe that will change soon. Could the future doctor for example even prescribe 20 mmHg on the saphenous vein and 30 mmHg on the proximal tibial vein for a patient? We will address this highly clinical question using an inverse problem and optimization in a FEM-environment to show that it is indeed, at least in principle, possible already today to achieve this specified treatment.

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A case study of the four-dimensional Leslie-Gower competition model

Joint work with Mats Gyllenberg and Jifa Jiang.

We study the Leslie-Gower model of four competing species. It is shown that, in certain circumstances, chaos can occur in the model, which can be generated by a cascade of quasiperiod doubling bifurcations starting from a supercritical Neimark-Sacker bifurcation. The chaotic attractor is contained in a three-dimensional invariant manifold, called the carrying simplex, which attracts all the nonzero orbits. The result also shows that the invasion attempts by an invader into a trimorphic population under the Leslie-Gower dynamics can lead to chaos.

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Mathematical model suggests competition between multiple clones as a unifying explanation for various phenomena in blood cancer

Joint work with Hans Hasselbalch (Zealand University)

The Cancitis model of the blood cancer, e.g. the Philadelphia negative myeloproliferative neoplasms (MPNs), has been developed and analyzed [1-4]. The MPNs have a low incidence but prevalence as lung cancer, since most MPN patients live with their MPNs for decades although with an increased morbidity burden due to a high risk of thrombosis and an increased propensity to develop autoimmune and chronic inflammatory diseases. Chronic inflammation is today considered to be a highly important pathogenetic factor for the development of MPNs both as a trigger and a driver of clonal evolution. The Cancitis model is based on known physiological mechanisms of human heterogeneous hematopoietic stem cells, their microenvironment, the mature blood cells, and the inflammatory response. The purpose of the models was to study the development of MPNs including the immunoediting mechanism. By geometric singular perturbation theory a model reduction is performed making the resulting reduced Cancitis model suitable to mathematical analysis. The reduction to two dimensions allows for a complete mathematical investigation of steady states and their stability. We provide conditions for a globally stable healthy state, MPN state or coexisting state with low number of cancerous cells. An approximate, closed form solution is derived. The model is validated against cytokine data and cell counts during treatment with interferon-2-alpha.

Recently, the model has been extended further to include several mutations making up a multiple clone competitive system, e.g. the JAK2, MPL and CALR mutations all associated with MPNs. Preliminary results by this generalized Canitis model indicates that such multi-clonal system may allow for oscillatory dynamics observed in the clinic. The model explains clinical observations such as sub-clones harboring up to hundreds mutations may emerge or outgrow; Relapse in AML treated patient has been attributed to the existence of various clones which may lie latently, i.e. as a small amount of cells, or be more pronounced. This phenomenon has recently been related to Clonal Hematopoiesis of Indeterminate Potential (CHIP) a state where multiple latent clones co-exist. Moreover, the generalized Cancitis model suggest an explanation for the unresolved clinical experiences that therapy may work well on a subpopulation (called good responders) having MPNs but not on others (denoted bad responders), while other may responds partially on the treatment (being in a coexistent equilibrium state).

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Evolution of dispersal in a spatially heterogeneous population with finite patch sizes

Joint work with Hisashi Ohtsuki and Joe Yuichiro Wakano.

Dispersal is one of the fundamental life-history strategies of organisms, so understanding the selective forces shaping the dispersal traits is important. In the Wright's island model, dispersal evolves due to kin selection even when dispersal is costly, and it has traditionally been assumed that the living conditions are the same everywhere. In order to study the effect of spatial heterogeneity, we extend the model so that patches foster different number of individuals and give different reproduction efficiency to individuals therein. We obtain an analytical expression for the fitness gradient, which shows that directional selection consists of three components: as in the homogeneous case, direct cost of dispersal selects against dispersal and kin selection promotes dispersal. The new component, spatial heterogeneity, more precisely the variance of so-called relative reproductive potential, tends to select against dispersal. We also obtain an expression for the second derivative of fitness, which can be used to determine whether there is disruptive selection: Unlike the homogeneous case, we found that divergence of traits through evolutionary branching is possible in the heterogeneous case. Our numerical explorations suggest that evolutionary branching is promoted more by differences in patch size than in reproduction efficiency. Based on our results, the existing spatial heterogeneity in the real world is a key determinant in dispersal evolution.

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Modelling Hematopoietic Stem Cells and their Interaction with the Bone Marrow Micro-Environment

Joint work with Thomas Stiehl (Heidelberg University), Morten Andersen (Roskilde University) and Johnny Ottesen (Roskilde University).

Blood cell formation (hematopoiesis) is a process maintained by the hematopietic stem cells (HSCs) from within the bone marrow. HSCs give rise to progenitors which in turn produce the vast amount of cells circulating in the blood. As HSCs are capable of self-renewal, a sustained production of cells is possible, without exhaustion of the HSCs pool. Mutations in the HSC genome give rise to a wide range of hematologic malignancies, such as acute myeloid leukemia (AML) or the myeloproliferative neoplasms (MPNs). As HSCs are difficult to investigate experimentally, mathematical modelling of HSC dynamics is a useful tool in the battle against blood cancers. We have developed a mechanism-based mathematical model of the HSCs and their interaction with the bone marrow micro-environment. Specifically, the model directly considers the reversible binding of HSCs to their specific niches, often omitted in other modelling works. By considering multiple HSC sub-populations, we have determined which properties confer growth advantages and defined a concept of HSC fitness. Our results imply that careful investigation of HSC properties can be used to understand different outcomes of bone marrow transplantation. Mathematical analysis reveals a separation of time-scales, allowing for a model reduction from a six-dimensional to a two-dimensional system of ODEs which captures the long-term behaviour of competition among wild-type and mutated HSCs. Combining the reduced model with a model of immune-system feedback in MPNs previously developed by the authors, we obtain a more accurate model of MPN development, with only a minor increase in model complexity. This allows for recreation of dynamics from data that could not previously be captured, as well as simulating the impact of process-parameters on cell dynamics during treatment. This shows great promise for future prediction of patient responses and design of optimal treatment schemes.

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Mathematical models of social-ecological systems

Joint work with Jamila L. Haider, Steven J. Lade and Maja Schluter.

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 growth (representing stock or resource) or disease dynamics, but the social aspect presents significant challenge for modelling. Great diversity of human activities and ways people affect and respond to changes in the ecosystem require tailored approach and careful choice of systems variables. Economic activities such as agricultural production or fishing, evolution of social norms and their influence on individual behavior and opinion dynamics are examples of social aspect that need to be included in the models. The aim of the talk is to present social-ecological research as a field that could provide challenges for mathematical modeling and benefit from it. We illustrate social-ecological modeling on the example of poverty traps, which are defined as undesired self-reinforcing mechanisms that keep individuals or community 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 level and interactions between these two levels. Using nonlinear systems of ODEs and numerical methods for their analysis, we investigate how within and cross-level interactions shape long term behavior and stability of the multilevel system and connect our results to some open questions in sustainability science.

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The succession of ecological divergence and reproductive isolation in adaptive radiations

Joint work with Mikael Pontarp and Per Lundberg (Lund University).

Adaptive radiation, the rapid generation of many species, is an important source of biodiversity and a major constituent of the tree of life. Despite substantial progress, there is still no general theory of the processes and mechanisms of radiations of entire clades, nor a full understanding why some of them are more speciose than others. Here we use a versatile but detailed model of diversification through adaptive radiation, tracking the evolution from a single ancestral species to a fully diversified clade. In our model, evolving clades exploit all ecological opportunities long before reproductive isolation is completed for any of the incipient species. The generation of bona fide biological species, if ever completely attained, happens relatively late during the cladogenesis and is preceded by recurring hybridization events. This decoupling of ecological diversification and reproductive isolation shows that adaptive radiations are not necessarily a sequence of well-defined and isolated speciation events. The single speciation perspective is insufficient for an accurate understanding because an adaptive radiation is the joint evolution of an entire ecological community. Our results also have important implications for how we interpret phylogenetic data and the prevalence of sexual selection as an important reproductive barrier between recently radiated species.

Claus Rueffler
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Evolutionary diversification driven by competition for resources - does organismal complexity matter?

Joint work with Paula Vasconcelos (Uppsala University).

Consumers generally experience trade-offs in their ability to find, handle and digest different resources, an observation with great significance for our understanding of the evolution and maintenance of biological diversity. To explore the conditions under which to expect the evolution of specialist or generalist species theoreticians rely on a few main workhorses such as various variants of Lotka-Volterra models and models of heterogeneous patches connected by migration. What most of these models have in common is that competition between alternative consumer phenotypes is mediated by a single quantitative trait (think beak size). The broad picture that emerges from these studies is as follows: A generalist evolves if it can utilize different resources or habitats relatively well (weak trade-off), while evolutionary diversification resulting in coexisting specialists occurs if the generalist, despite being able to utilize a broad set of resources, has a relatively low efficiency for each of them (strong trade-off).((The focus on a single evolving quantitative trait has its origin in the desire of theoreticians to study mathematically tractable models and does not reflect biological reality. Instead, in any empirical system the interaction between consumers and their prey will be determined by many jointly evolving traits. Here, I describe our recent work based on the Rosenzweig-MacArthur-model with two resources in which we allow for the joint evolution of up to three consumer traits that mediate interactions with the resources. We show that under joint evolution of two or more foraging traits the boundary between trade-offs resulting in resource specialists and resource generalists is shifted toward weaker trade-off curvatures. In particular, weak trade-offs can result in evolutionary branching leading to the evolution of two coexisting resource specialists while the evolution of a single resource generalist requires particularly weak trade-offs. These findings are explained by performance benefits due to epistatic trait interactions enjoyed by phenotypes that are specialized in more than one trait for the same resource. In my presentation, I pay particular attention to the conceptual complexities that arise when studying evolution in multivariate trait spaces.

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Predictive survival analysis of human gut microbiome

Joint work with Ville Laitinen (velait@utu.fi), Teemu Niiranen (tejuni@utu.fi) and Leo Lahti (leo.lahti@utu.fi)

Large-scale population cohort studies of the human microbiome are becoming common and present a novel context for statistical machine learning methods for survival analysis. Such studies provide unique opportunity assess which microbiome features are associated with various survival outcomes, such as mortality risk. However, predictive analysis of a time-to-event endpoint variable with the gut microbiome variation as measured by metagenomic sequencing is complicated by the special characteristics and limitations of the sequencing and taxonomic profiling process. The issues that need to be accounted for include the need for normalization of the taxonomic reads, larger underlying variation than seen in otherwise similar RNASeq analysis, restriction of taxonomic species composition information to simplex, and several choices of plausible informative ecological features. In this presentation I discuss these topical challenges to survival analysis posed by microbial metagenomics, and how the existing survival analysis methods (namely, Cox proportional hazards regression with feature selection and regularization) could be adjusted in order to address the particular characteristics of contemporary microbiome profiling studies.

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Gaussian processes in population growth models

Joint work with Marcelo Hartmann, Geoffrey Hosack and Rich Hillary.

Gaussian processes (GPs) are flexible and versatile nonparametric models that have received increasing interest in ecological applications. Traditionally they are used to model spatial and termporal random effects but they are increasingly often applied to other applications as well. In this talk I will present a case study on semiparametric and temporally varying population growth models. We show how temporally varying Ricker population growth models can be formulated under hierarchical GP models and extended to the multispecies setting by incorporating cross-covariances among species. We also show how recently proposed semiparametric approach for population growth modeling can be formulated in the same formalism. As a case study, we examine the productivity of three Pacific salmon populations and compare the alternative Ricker population growth functions using models' posterior probabilities. Our results show substantial temporal variation in maximum reproductive rates and reveal temporal dependence among the species with direct management implications. However, our results do not support semiparametric population growth functions but show that they may lead to ecologically unrealistic results.

Posters

Anni Halkola
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Modelling the killer T-cell and cancer cell subpopulation competition under immuno- and chemotherapies

Joint work with Kalle Parvinen, Satu Mustjoki and Tero Aittokallio.

Each patient's cancer has a unique molecular makeup, often comprised of distinct cancer cell sub-populations. Improved understanding of dynamic processes and evolutionary competition between the cancer cell populations is critical for making treatment more effective and personalized. It has been shown that immunotherapy, in particular, inhibition of programmed cell death protein 1 (PD-1), increases the survival of patients with melanoma. However, some of the questions in immunotherapy concern the timing of treatment and benefits of combination therapy. In the present work, we introduce a model for the dynamics of active killer T-cells and cancer cell subpopulations. Rather than using the approach that defines the cancer cell populations based on their genetic makeup alone, we consider also other, non-genetic differences that make the cell populations sensitive or resistant to a therapy. We show how mathematical modelling of population dynamics and treatment responses provides insights into effects of mono- or combination therapies, as well as into treatment sensitivity and resistance in virtual melanoma patients. Using the model, we make predictions of possible outcomes of the various treatment strategies and provide hypotheses regarding, for example, therapeutic efficacy and side-effects. It is shown that for immunotherapy, for instance, starting with a denser treatment schedule enables one to change to a sparser schedule later. Furthermore, combination of targeted and immunotherapy results in a better treatment effect, compared to mono-immunotherapy, and with a patient-tailored combination a stable chronic disease might be reached. Similar results are seen when comparing combination of cytotoxic and immunotherapy to cytotoxic mono-therapy.

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On the generality of the diploid male vortex in parasitoid wasps with single-locus complementary sex determination

Joint work with Prof. Veijo Kaitala (University of Helsinki).

Most parasitoid wasps have complementary sex determination (CSD), which produces sterile or inviable males when homozygous at sex determining loci. Zayed and Packer (2005) have theoretically shown that small populations have elevated risks of extinction due to positive feedback between inbreeding and small population size, referred to as the diploid male vortex. Consistent with limited empirical support, a few modeling papers have suggested that diploid male vortices may not be as common as indicated by Zayed and Packer because balancing selection at sex determining loci tends to maintain high allelic diversity and because immigrants can introduce locally new alleles in spatially structured populations. However, the generality of the conclusion is yet uncertain, as these models were either developed for a particular system or based on models atypical for host-parasitoid interactions. The objective of our paper is to attest the conclusion in several well-studied host-parasitoid models. We derived analytical expressions of the conditions for a diploid male vortex in a single population. Then, we developed stochastic individual-based versions of the models and tested the effects of various behaviors, diploid male fertility, temporal fluctuation in host populations, and spatial population structure on the likelihood of a diploid male vortex. We found that a small increase in dispersal probability, diploid male fertility, and female discrimination against diploid males as a mate and a small decrease in primary sex ratio can alleviate the risk of a diploid male vortex, even when host populations fluctuate with high amplitudes and synchronously. However, populations become more prone to extinction when the temporal dynamics of host abundance are autocorrelated. We conclude that spatially connected parasitoid populations may be more robust to a diploid male vortex than anticipated by Zayed and Packer. However, if future climate change induces more temporally autocorrelated host abundance, the likelihood of a diploid male vortex could increase substantially.

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Non-parameteric modeling of state shifts in microbial communities

Contemporary research in microbial ecology has focused on cross-sectional data sets, whereas the longitudinal behavior of these complex ecosystems is still not very well understood. Despite the increasing availability of dense and long time series, our understanding on the temporal aspects such as stability, resilience and the existence and switches between alternative stable states in microbial communities remains limited, partially due to the shortage of targeted statistical tools that can take into account the specific properties of microbiome profiling data. Due to the immense complexity of naturally occurring microbial communities, constructing robust mechanistic models has proven to be challenging, and there is a demand for new methods that can infer essential aspects of microbial ecosystem dynamics when knowledge of the underlying mechanics is limited. We show how stochastic non-parametric models can characterize key aspects of microbiome dynamics based on few modeling assumptions, thus providing flexible means to quantify stability, resilience, and state shifts under varying conditions. Furthermore, we show how the analysis of limited time series data can be supported by broader cross-sectional data collections by combining elements from the Bayesian framework and non-linear stochastic differential equations. Our experiments with simulated and real microbiome profiling data sets demonstrate how non-parametric methods can provide robust means to quantify essential aspects of stability, resilience, and state switches in microbial communities even when the underlying data generating processes are unknown. The information obtained via such models can inform future experimentation on the manipulation and restoration of microbial ecosystem states.

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Learning by sequentially making model more complex: Case study with the seasonal flu in Finland

How complex the model for analysing reality (i.e. doing Science) should be? If model is too simple, it would miss important features of the researched object. If the model is too complex, the results would be obscured. But what if we could use a spectrum of models of varying complexity? In this project, I'm analysing the burden of seasonal influenza in Finland using registry data. I'm starting by fitting a simple SIR model, and then sequentially making the model more complex (e.g. introducing vaccination or age groups). I will present the results, and will argue that this approach give us better understanding than using a single model.

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Concentration and cell-size homeostasis: lessons from the piecewise deterministic Markov processes (PDMP)

Growth of a cell and its subsequent division into daughters is a fundamental aspect of all cellular living systems. During these processes, how do individual cells correct size aberrations so that they do not grow abnormally large or small? How do cells ensure that the concentration of essential gene products are maintained at desired levels, in spite of dynamic/stochastic changes in cell size during growth and division? Both these questions have fascinated researchers for over a century. We review how advances in singe-cell technologies and measurements are providing unique insights into these questions across organisms from prokaryotes to human cells. More specifically, diverse strategies based on timing of cell-cycle events, regulating growth, and number of daughters are employed to maintain cell size homeostasis. Interestingly, size homeostasis often results in size optimality proliferation of individual cells in a population is maximized at an optimal cell size. We further discuss how size-dependent expression or gene-replication timing can buffer concentration of a gene product from cell-to-cell size variations within a population. Finally, we speculate on an intriguing hypothesis that specific size control strategies may have evolved as a consequence of gene-product concentration homeostasis.