Keynote abstracts

Computational approaches to analyze and predict mechano-regulated cardiovascular regeneration

Loerakker S.

Engineered cardiovascular tissues have the intrinsic ability to grow and adapt to changes in their hemodynamic environment. This fascinating adaptive capacity gives these tissues the potential to overcome the limitations of current cardiovascular replacements that are unable to accommodate changes in the recipient’s demands. For cardiovascular tissue engineering to be successful, however, we need to thoroughly understand the responsible growth and remodeling mechanisms of (engineered) cardiovascular tissues, and be able to steer tissue development towards establishing a physiological tissue organization that ensures long-term tissue functionality. In this talk, I will discuss how computational modeling, particularly when integrated with experimental research, can aid in addressing both challenges. I will give a conceptual overview of the computational models that we developed to analyze the growth and remodeling of cardiovascular tissues, with a primary focus on heart valves. Specifically, I will show how we used our models to understand postnatal human heart valve development and adaptation, to predict and steer the in vivo remodeling of tissue-engineered heart valves, and to understand the role of cell-cell communication in directing vascular adaptation.

Human cooperation by reciprocity

Egas C.J.M.

Explaining the evolution and maintenance of cooperation among unrelated individuals is one of the fundamental problems in biology and the social sciences. There is ample evidence that human cooperative behaviour towards other individuals is often conditioned on information about previous interactions. This information derives both from personal experience (direct reciprocity) and from experience of others (i.e. reputation; indirect reciprocity). Direct and indirect reciprocity have been studied separately, but humans often have access to both types of information. Here, I focus on two aspects that promote our understanding of cooperation by reciprocity. First, in many mathematical models reputation is considered as binary, being either good or bad. Intuitively, however, reputation feels more gradual and indeed some models and experiments address this intuition. It intuitively makes sense as well that individuals seldom become bad after one bad action and that it may take “bad” individuals some time to gain a good reputation. Using game-theoretic models I will show that allowing for gradation of reputations results in evolution of assessment rules that conform to this intuition. It appears advantageous to judge acts of possible cooperation in such a way that individuals have a high probability to become bad and a low probability to become good: Reputation “comes on foot and leaves on horseback”. Second, using game-theoretic experiments on indirect reciprocity I will argue that the current model frameworks fail to explain the diversity in consistent strategies human subjects display. Hence, future theoretical work should no longer focus on finding stable “ESS-type” strategies but on elucidating how coexistence of various strategies may maintain cooperation.
Long abstracts

Rethinking tipping points in spatial ecosystems

Banerjee S., Baudena M., Carter P., Bastiaansen R., Doelman A., Rietkerk M.

The theory of alternative stable states and tipping points has garnered a lot of attention in the last decades. It predicts potential critical transitions from one ecosystem state to a completely different state under increasing environmental stress. However, typically ecosystem models that predict tipping do not resolve space explicitly. As ecosystems are inherently spatial, it is important to understand the effects of incorporating spatial processes in models, and how those insights translate to the real world. Moreover, spatial ecosystem structures, such as vegetation patterns, are important in the prediction of ecosystem response in the face of environmental change. Models and observations from real savanna ecosystems and drylands have suggested that they may exhibit both tipping behavior as well as spatial pattern formation. Hence, in this talk, I will use humid savannas and drylands to illustrate several pattern formation phenomena that may arise when incorporating spatial dynamics in models that exhibit tipping without resolving space. I will argue that such mechanisms challenge the notion of large-scale critical transitions in response to global change and reveal a more resilient nature of spatial ecosystems.

Reverse engineering gene regulatory networks for proliferation and differentiation in the development of C. elegans


Gene regulatory networks in development integrate spatio-temporal signals to generate the right number of cells with the right fates at the right time and place. The C. elegans invariant cell-lineages allow the study of this process almost without inter-individual variation. Here, we focus on the postembryonic M lineage (PEML) in hermaphrodites, which originates from a single progenitor and initially gives rise to 18 cells with three distinct cell types – body wall muscles, coelomocytes, and sex myoblasts; the latter proliferate at later stages to contribute smooth muscle cells to the worm’s reproductive organs. Prior work has identified PEML’s key symmetry breaking cues: along the anterior-posterior (A-P) axis, a non-canonical Wnt-dependent asymmetric re-distribution of β-catenins and the TCF transcription factor among daughter cells; along the dorso-ventral axis, a ventrally restricted activation of the Notch pathway.
A back-of-the-envelope calculation reveals graded Wnt activation levels along the A-P axis. Counterintuitively, symmetry breaking in fate specification does not occur in the most anterior/posterior cells, with the highest signal-to-noise ratio, but in cells with intermediate Wnt activation levels. Is this consistent with PEML’s systematic reproducibility? Can the Wnt pathway be entirely responsible for fate specification along the A-P axis?
To address these questions, we model differentiation and proliferation in the PEML using nonlinear differential equations. Resulting models tend to lose A-P asymmetries generated in prior cell divisions, confirming the need for finely tuned parameters to recapitulate wildtype
fate specification. Alternatively, we propose two models that overcome these issues by relying on either an additional A-P spatial cue or a temporal symmetry break and evaluate their properties and plausibility. Overall, our study highlights how a quantitative examination of mechanistic ideas can identify gaps in the state-of-the-art.

**Human milk oligosaccharide decreases microbial mucin consumption by stimulating bacteria that do not share extracellular resources in infant gut simulations**

**Versluis D.M., Wijtkamp C., Looijesteijn L., Geurts J.M.W., Merks R.M.H.**

Intestinal mucin acts as a barrier protecting the infant gut wall against diseases such as colitis and rotavirus. In vitro experiments have shown that the gut microbiota of breastfed infants consumes less mucin than the microbiota of non-breastfed infants, but the mechanisms are incompletely understood. The main difference between human milk and most infant formulas is the presence of human milk oligosaccharides (HMOs) in human milk. We hypothesize that HMOs protect mucin by favoring non-mucin consuming bacteria in the microbiota. To understand the underlying mechanisms we used a computational modeling approach that describes the metabolism and ecology of the infant gut microbiota. We show that extracellular digestion of the HMO 2'-fucosyllactose by the mucin-consumer *Bifidobacterium bifidum* makes this species vulnerable to competitors. The digestion products become 'public goods', and can be consumed by *Bacteroides vulgatus* instead of *B. bifidum*. Our model predicts that the non-mucin consuming *Bifidobacterium longum* can then become dominant, despite growing less efficiently on HMOs than *B. bifidum* in monocultures, because *B. longum* does not produce public goods. We conclude that the theory of public goods in microbial ecology may be key to understanding the effects of HMOs on the mucin-consuming potential of the developing infant gut microbiota.

**The spatial agent-based model OHDEAR : Effects of predation and disturbance on forager groups**

**van Weerden J.F. , Verbrugge R., Komdeur J.**

Group living is of benefit to foraging individuals by improving their survival, through passive risk dilution by sheer numbers and through increasingly more active processes, ranging from cue transmission to alarm calling. Focusing on the lower end of this range: An involuntary visual cue can be given by a fleeing action, and lead to cue transmission of information within a group. This model is a bottom-up model of foragers as agents with embodiment in a simple environment, where only assumptions about basic competences for living are made, valid for a wide group of species.

We use an agent-based and spatially explicit model to investigate the effect of disturbance by predators (always fleeing is the appropriate reaction) and, to make the model more realistic, added harmless passers-by, that now cause false fleeing. We set out to investigate whether adaptive behaviour could improve outcomes: We investigated whether two very common subconscious behaviours can mitigate the detrimental effects of false fleeing. The first is “experience gain”, an experiential change, the second is “fear updating”, an emotional change.
To implement these behaviours we needed to: 1) define better the anti-predator behaviour chain: “detection, recognition, and response”. 2) how to deal with the combined probabilities of the detection- and recognition sigmoids. We added three fear levels: one each for predator and pass-by and one for the environment, as base for response when detection without recognition occurred. 3) the initial levels for these behaviours had to be defined. These modelling decisions are shown to be very important. HIREC situations with new predators or with newly released groups can be mapped to these initial settings: does the forager group meet a familiar predator type or a novel one for instance, giving insight into what is most important for forager groups.

Zania A., von der Dunk S.H.A., Hogeweg P.

Sexual reproduction and the evolution of endosymbiosis

Sexual reproduction is a trait shared in all eukaryotes, and was present in the last eukaryotic common ancestor. Current eukaryotes mostly inherit mitochondria from one parent, but the mechanisms that ensure this vary hugely in different species, and the ancestral trait is unknown. It is unknown when sex appeared in relation to the acquirement of mitochondria and its role in the evolution of endosymbiosis. In this project, a multilevel, individual based model of endosymbiosis (von der Dunk et al., 2023) is used to study the role sex in the co-evolution of host and symbiont genomes. Evolutionary simulations were performed on populations of cells that live on a 2D grid, each cell consisting of one host and one or more symbionts. When there is sexual reproduction, the symbionts are inherited from 2 parent cells. Our results indicate that sex poses threats, due to the emergence of selfish symbionts that can drive populations to extinction. However, resolution of this conflict is possible, and can drive the evolution of signaling and allow the host to control the symbiont’s cell cycle. In fact in most cases the populations that do survive outperform the asexual populations that evolve under the same conditions.

Alber M.

Combined multi-scale modeling and experimental study of regulation mechanisms of shape formation during tissue development

The regulation and maintenance of an organ’s shape and structure is a major outstanding question in developmental biology. The Drosophila wing imaginal disc serves as a powerful system for elucidating design principles of the shape formation in epithelial morphogenesis. Yet, even simple epithelial systems such as the wing disc, are extremely complex. A tissue’s shape and structure emerge from the integration of many biochemical and biophysical interactions between proteins, subcellular components, and cell-cell and cell- extracellular matrix (ECM) interactions. Results obtained using iterative approach combining multi-scale mathematical and computational modelling and quantitative experimental approach will be used in this talk to discuss direct and indirect roles of subcellular mechanical forces, nuclear positioning, cell growth and division and interaction with ECM in shaping the major axis of the wing pouch during the larval stage in fruit flies, which serves as a prototypical system for investigating epithelial morphogenesis. The research findings demonstrate that subcellular mechanical forces can effectively generate the curved tissue profile, while extracellular
matrix is necessary for preserving the bent shape even in the absence of subcellular mechanical forces once the shape is generated [1]. The developed integrated multi-scale modelling environment can be readily extended to generate, and test hypothesized novel mechanisms of developmental dynamics of other systems, including organoids that consist of several cellular and extracellular matrix layers.

Short abstracts

**Numerical insights into collective cell motion during gastrulation**

**Keta Y.-E., Henkes S.**

Vertex models are powerful computational tools which represent cell tissues as two-dimensional polygonal tilings, and enable to use methods from statistical physics in order to describe emerging collective behaviour from microscopic interactions. We first show how cell-cell junction activity, which dominate in the early embryonic development, leads to a form of collective motion which cannot be described by the widespread description of cell tissues as collections of self-propelled objects. We then employ these tools to model epithelial tissue spreading. In particular we demonstrate how, combined with data extracted from the experimental growth of zebrafish embryos, these provide further insights in the role of keratin in epiboly.

**Exploring Synthetic Cell Division: Modeling Lipid Bilayer Membrane Dynamics**

**Sillano P.**

Cell division is a fundamental process in life and also one of the major challenges in synthetic biology. While numerous nature-inspired mechanisms have been proposed, our understanding remains limited.

My aim is to model synthetic cell division in silico, with a focus on understanding the physics of lipid bilayer membranes during the process. In silico experiments can deal with spatio-temporal scales inaccessible to wet lab techniques and they can be used to test the validity of theoretical models.

By employing coarse-grained molecular dynamics simulations, I capture essential physical properties such as surface tension, bending rigidity, and thermal fluctuations response. I successfully reproduced membrane reshaping under various conditions, including osmotic shock and protein-induced curvature change.

Future research will involve modeling Dynamin as a single-protein machinery to perform cell division, in collaboration with experimentalists.

**Consequences of alternative stable states for short-term model-based control of cyanobacterial blooms**

**Jacobs B., van Voorn G., van Heijster P., Hengeveld G.M.**
Cyanobacteria (or “blue algae”) are photosynthetic bacteria that may produce toxic compounds and are notorious for their ability to form sudden intense blooms. We explore potential management strategies for short-term mitigation efforts of cyanobacterial blooms informed by process-based dynamic models. We focus on the case where blooms are linked to the existence of alternative stable states, such that, under the same conditions but depending on the past, a lake may be dominated either by cyanobacteria, causing a harmful algal bloom, or by green algae and macrophytes in a clear water state. Changing conditions may cause the favourable clear water state to disappear through a tipping point, causing the lake to switch rapidly to the turbid cyanobacteria state. At the same time, it may take considerable effort to undo this tipping and return to the favourable state. We identify four different strategies for bloom mitigation in this scenario: Doing nothing, reacting to a bloom, resetting the lake at a later point, and preventing the bloom. We found that these strategies have different cost profiles. The optimal strategy depends on many factors, including the relative costs of blooms and interventions, the time during which the environment favours a bloom and the bifurcation structure that determines where in parameter space blooms appear and disappear. In general, low bloom costs and short bloom times favour not intervening, while high bloom costs favour prevention. In between, waiting for more favourable conditions before resetting to a clear state may be preferable, especially for long bloom times, where constant intervention becomes expensive. In conclusion, the presence of alternative stable states with bifurcations in a lake provides interesting opportunities for the short-term model-based mitigation of cyanobacterial blooms, which lake managers could use to their benefit.

**Pattern formation in Mechanochemical models**

*Nesenberend D.N.*

It is well known that chemical as well as mechanical cues play an important role in morphogenesis. To study this interaction, we derive and analyse a so-called mechanochemical model, which describes a biological surface (e.g. a cell membrane or a tissue surface) that is evolving over time, driven by the morphogen concentration and the surface curvature [1]. We study the one-dimensional version of this model, where the surface is described as a curve. There is a chemical diffusing on the curve that is locally inducing its curvature. The curve is constrained by its fixed global length, inducing an inhibiting effect. Numerical simulations show many interesting patterns developing over time. We use an analytic tool called Geometric Singular Perturbation Theory to understand these numerical simulations [2]. We show the existence of particular periodic patterns, highlighting the importance of pattern selection by the geometric constraints of the curve.

The mechanochemical model has an interesting link with experimental work on Septin, a membrane binding, curvature-inducing molecule. Incubated in particular conditions, Septin can induce the formation of golf ball patterns on lipid vesicles [3]. Septin plays an important role in many processes, like cell division and cell motility. Understanding the pattern formation process visible in vitro can help unravel Septin's biological mechanism.
A universal bias in the genotype-phenotype map of RNA

Von der Dunk, S.H.A., Martin, N.S., Dingle, K. and Louis, A.A.

The architecture of genotype-phenotype maps is crucial for understanding the evolutionary process. Recent studies have increasingly shown that developmental biases in the genotype-phenotype map, i.e. some phenotypes being more accessible by mutation than others, may be at least as important as adaptive processes for predicting evolutionary outcomes and explaining major evolutionary trends. In particular, studies have revealed a bias towards simplicity: complex phenotypes are encoded by fewer genotypes than simple phenotypes and therefore they are less likely to appear through random mutation.

For the RNA sequence-to-structure map, a classical example of a genotype-phenotype map, simplicity bias has been shown only for short sequences up to length L=126 using approximate estimates of neutrality [1] or coarse-graining of the secondary structure [2]. Here, we studied the complexity of real and randomly sampled RNA structures without coarse-graining and at biologically more relevant lengths (L=100 to L=1000) to investigate a potential bias towards simplicity.

We find that the real RNA structures are much simpler than randomly sampled RNA structures but very similar to structures found among randomly sampled RNA sequences, in agreement with simplicity bias. At first glance, bacterial and eukaryotic RNAs appear to have slightly different mean complexity, which could implicate a specific role for selection in these two domains. Yet, we find that compositional differences of bacterial and eukaryotic RNA sequences explain most of the differences in structural complexity, suggesting that non-adaptive forces such as mutational biases underlie phenotypic complexity.


Phosphorylation impacts the dynamical behaviour of the SARS-CoV-2 nucleocapsid protein

Loonen S., Šoštarić N., Bauer M.

The nucleocapsid protein (N-protein) of SARS-CoV-2 is involved both in synthesis of viral RNA molecules, as well as in packaging of the 30 kb genomic RNA element of the virus. How the N-protein is able to switch between these two operating modes remains poorly

understood. One proposed switching mechanism between the non-specific regulation of transcription and translation, and the specific packaging of viral genomic RNA molecules, is the degree of phosphorylation of the protein. Early in the infection, host kinases heavily phosphorylate N-protein, after which the degree of phosphorylation in the N-protein pool gradually diminishes over the course of an infection. N-protein has several intrinsically disordered domains, and thus its full-length 3D structure has not been experimentally resolved. In addition, the impact of phosphorylation on the structure has also not been established. To better understand what the N-protein structure may look like, and what the impact of phosphorylation is on this structure, we employ the atomistic molecular dynamics software suite GROMACS, and assess the dynamic behaviour of both phosphorylated and unphosphorylated versions of the N-protein homodimer. We show that the introduction of phosphorylation yields a more dynamic and open protein structure. Furthermore, we introduce several types of RNA into the simulation, and show that there is a qualitative difference in the mode of RNA binding between a phosphorylated and an unphosphorylated version of N-protein. Our results corroborate the hypothesis that the degree of phosphorylation leads to a conformational switch of the protein, where in one mode it acts as a replication regulator, and in the other mode it acts as a genome packager.

**Mechanistic remodeling of waning immunity and reinfection by COVID-19 in Manaus**

van Meenen, R.J.P.

Modeling COVID-19 reinfections has been a focus of recent research, particularly concerning the dynamics of sequential severe waves of infections and deaths. Despite numerous proposed models successfully simulating a severe wave followed by a milder one, accurately representing the dynamics of two severe waves, as observed in Manaus, has remained challenging.

Manaus faced one of the world's worst infection and death rates in 2020, the first year of the pandemic. An initial seroprevalence study suggested that 76% of the population had been infected after the first wave, which should have resulted in herd-immunity. These findings made it difficult to explain the resurgence of COVID-19 deaths by late 2020 that resulted in an even more devastating second wave. Many different epidemiological models were proposed to explain these two waves, however these models disagree with each other and with experimental data.

In this study, we present a novel approach using a data-driven deterministic SIRWD-model to study the dynamics of both waves in Manaus. Our model incorporates a novel mechanistic relationship between the waning of immunity and reinfection, greatly improving the fitting to observed in-hospital deaths and seroprevalence data. We introduce a second susceptible class representing waned recovered individuals, who are protected against severe outcomes, but remain susceptible to reinfection by the Gamma P.1 variant, contributing to its spread.

This improved model provides a comprehensive understanding of the factors driving the deadlier second wave, highlighting the role of waning immunity prior to reinfections occurring with the emergence of the Gamma P.1 variant.

**Transition to sexual dimorphism in mirror-image flowers: insights from adaptive dynamics**

Enantiostyly is a type of floral asymmetry in which the styles of flower are either deflected to the left or right side of the floral axis (mirror-image flowers). Phylogenetic evidence indicates that in several monocotyledonous lineages, dimorphic enantiostyly (all flowers of a plant have the same style orientation) has evolved from monomorphic enantiostyly (flowers within a plant have both stylar orientations). Here, we use a modelling approach based on adaptive dynamics to investigate the ecological driving forces behind the transition from monomorphism to dimorphism in the sexual system of enantiostylosous plants. Our results indicate that, depending on the balance between inbreeding depression following geitonogamy, pollination efficiency, size of the daily floral display, and plant density, dimorphism can evolve from an initial, monomorphic population. We use population genetics simulations to show that the observed evolutionary transitions are possible assuming a plausible genetic architecture.

Sexual selection driven by direct benefits leads to the erosion of direct benefits

Riederer J.M., Cordeschi G., Weissing F.J.

Most sexual selection models assume that the evolution of female choosiness is driven by indirect (genetic) benefits, such as the production of more viable offspring or more attractive sons. There is ample empirical evidence that female choosiness can also provide direct (non-genetic) benefits, including access to good territories or paternal care. Yet, theoretical models of direct-benefits sexual selection are scarce. Here, we explore such a model using individual-based evolutionary simulations. In the model, males differ in the amount of resources at their disposal. Males can allocate resources into parental care (a direct benefit) or into ornamentation. Females can choose mates based on their ornamentation. The simulations reveal that female choosiness for ornamented males readily evolves, which in turn drives males to allocate more resources to ornamentation. At the individual level, females benefit from choosiness, since ornamentation is positively related to the amount of paternal care received. However, at the population level, coevolution between male ornamentation and female preferences leads to (almost complete) erosion of direct benefits. We also discuss intricacies of the co-evolutionary dynamics, such as transient polymorphisms in both male and female strategies, reversals in the direction of evolution, and population extinction (‘evolutionary suicide’) driven by direct-benefit sexual selection.

Four causes of nursery function degradation and their consequences for declining marine juvenile species

Sterl, X.M., Ten Brink, J.A., Van Leeuwen, A.

Many ecologically and economically valuable fish species inhabit shallow coastal habitats as juveniles before migrating offshore as adults. However, in recent decades, fish densities in many of these coastal habitats have decreased dramatically. The exact causes of these declines remain unknown. We investigated four scenarios that may explain the decline of fish densities in nursery habitats: decreased food availability in the nursery, increased mortality in the nursery, increased mortality in the adult habitat, and decreased connectivity from the adult habitat to the nursery. We simulated these scenarios using a physiologically
structured population model, which takes the entire life cycle of individual fish into account. Our model includes three habitats, namely a focal nursery, an adult habitat, and alternative nursery areas. Our results show that each of the four scenarios can indeed lead to the disappearance of fish populations from nursery areas. However, we also find that the exact consequences for the size distribution and individual growth are different for each scenario. Specifically, decreased food availability in the focal nursery leads to slow juvenile growth, whereas increased mortality in the focal nursery leads to fast juvenile growth. Moreover, we demonstrate that high-quality alternative nurseries can act as a population refuge and can even prevent population extinction when the focal nursery is heavily disturbed. These findings highlight the importance of protecting coastal nursery grounds for fish population conservation.

The evolution of sensitive periods beyond early ontogeny: Bridging theory and data

Walasek N., Panchanathan K, Frankenhuis W.E.

Sensitive periods, during which experiences have a large impact on phenotypic development, are most common early in ontogeny, yet they also occur during later ontogenetic stages, including adolescence. At present, however, we know little about why natural selection favors sensitive periods for some traits early in ontogeny and for others later in ontogeny. This article synthesizes recent mathematical models and empirical studies that explore sensitive periods beyond early ontogeny. Across formal models, we observe two general patterns. First, sensitive periods emerge beyond early ontogeny when an organism’s uncertainty about the environment-phenotype fit increases at later developmental stages. Second, sensitive periods also emerge beyond early ontogeny when cues at later stages reduce this uncertainty more than earlier cues do. In the empirical literature, we observe that traits showing sensitive periods beyond early ontogeny tend to be social traits, particularly among mammals. Connecting theory to data, we hypothesize that mammals have evolved to expect highly reliable information from peers in adolescence to reduce uncertainty about the current and future social environment (e.g. social dominance, mate value). Finally, we highlight current gaps in our understanding, describe how different ways of quantifying sensitive periods influenced observed patterns, and suggest future directions for strengthening bridges between empirical and theoretical studies of sensitive periods. Ultimately, we hope our synthesis will contribute towards an integrative science of sensitive periods across the biological and the social sciences.

The evolution of parental care qualitatively depends on how reproduction is affected by density dependence

Boog, D.A., Egas, M., Ploeger, A., van Veelen, M.

In various sexually reproducing species, the parents may provide care for their offspring. This parental care reduces the offspring mortality, but also limits the parent’s mating opportunities. This conflict of interest has led to the evolution of various different distributions of care, which can be roughly categorized into either biparental or uniparental care. An important question is understanding what determines which distribution of care evolves. Our previous work showed that in an agent-based model, the risk of your partner dying before finishing parental care selects for biparental care. However, a similar agent-based model
found selection for uniparental care instead. To examine what causes this difference in evolutionary outcome, we scrutinized the differences in assumptions between the two models. In both agent-based "time-in time-out" models, haploid males and females search for a partner in the mating pool (time-in) to reproduce. After mating, the parents move to the parenting pool (time-out) to care for their offspring. The distribution of care that evolves is determined by how the reproduction process is affected by population density. Density-dependent birth rate resulted in the evolution of biparental care, whereas density-dependent offspring mortality selected for uniparental care. With the density-dependent birth rate, an individual produced only a few offspring during their life, but each offspring had a low mortality. The density-dependent offspring mortality meant that individuals produced more offspring during their life, but each offspring had a higher mortality. This directly affects the benefit and cost of parental care, resulting in a different evolutionary outcome in the conflict of interest between the parents. The result has important implications for the evolution of parental care: the ultimate distribution of care depends on what is the limiting resource for the offspring.

**Entropy production rate of microbes with a metabolic shift can decrease with growth rate**

Droste M. J., Planqué R., Bruggeman F. J.

Thermodynamics considers life, and particularly a population of growing microbes, as an open out-of-equilibrium system that exchanges energy and matter with its surroundings. Through conversions these can be exploited by the cell to maintain its internal processes, thereby growing, and preserving its structure and function. During these processes, Gibbs free energy is dissipated while entropy is produced. Earlier results suggest that entropy production rate (EPR) is an important quantity to predict behaviour of microbes. Here, we ask under which conditions the EPR of steady-state microbial growth rises with the growth rate, which is a key property of the population.

In steady-state chemical reaction networks, both the reaction rates and EPR increase when the thermodynamic driving force of the network increases. We show that this follows from a positive flux-force relationship, provided that the net conversion of substrates into products remains fixed. This result is generalized to microorganisms with a fixed conversion cultivated in a chemostat. This experimental setup allows for calculation of the EPR through a thermodynamic black-box description of microbial growth. Some microbes show a metabolic shift as function of their growth rate, which changes the net conversion of their metabolic network. For instance, some (completely) degrade glucose into carbon dioxide and water at slow growth, while they degrade it partially at fast growth (e.g. forming acetate or ethanol). Since partial degradation involves the extraction of less free energy from glucose, fast growth can be accompanied by a lower thermodynamic driving force. This may result in a reduced EPR as function of growth rate. We analyse this situation using chemostat models of yeast, which we parameterised with experimental data. We also derive a quantitative criterion that can be used to predict the EPR of shifts in metabolic strategies across microbial species.
Plants and mycorrhizal fungi trading: when is a deal a deal? An explicit-resource model with variable trade investment

van Schijndel, L.L.M., Siero E., Doekes H.M.

Mycorrhizal fungi, which can trade nutrients for plant carbon, are often called a promising alternative to solve the overuse of fertilisers in agriculture. However, we do not understand well under which conditions trade actually occurs when multiple actors are involved, and what the cost/benefit ratio to the crop is. Wyatt et al. (Evolution, 2014) modelled this for multiple plants and fungi trading, and found a network-wide exchange rate. However, their model requires each organism to give a fixed amount of resources in trade, and assumes every plant could trade with every fungus. Yet in a crop field, many plants and fungi are too far away to trade, leading to more fragmented trading networks. We want to know whether we still expect a global exchange rate in such a sparse network. Moreover, single-connected organisms would be exploited by their partners because of the fixed spending requirement. Hence, we ask if the global exchange rate result still holds when plants and fungi can also hoard resources instead of trade them. Therefore, we are developing a model where a plant and a fungus can freely choose the amount of resources they give in trade. Joint evolutionary optimisation of these amounts results in an optimal exchange rate for each pair of traders. In the future, we want to extend this model to multiple plants and fungi and test whether we find a global exchange rate, and whether this depends on the network structure.

Family matters: linking kin interactions to population growth

Croll J. C., Caswell H.

In many species, individuals are embedded in a network of kin with whom they interact. The interactions among kin may affect the survival and fertility rates, and thus the life history of individuals. This causes feedback between individual life histories, the kin network and the dynamics of the population. The tight social bonds within family groups of African elephants result in strong interactions between kin. For example, the presence of the mother and the age of the matriarch increase the survival of juveniles, and the presence of a sister increases the fecundity of young females. This suggests that factors disturbing the family structure of African elephants, such as poaching, could strongly impact the growth rate of the population. We describe a model that calculates the kin network of an individual while incorporating the feedback between the network and the life history of the individual. We link this model to the population growth rate and demonstrate that interactions between family members amplify the negative effects of poaching on the family structure and growth rate of African elephant populations. This suggests that changes in the family structure of social animals can be very important in the response of populations to disturbance.