

NVTB School meeting 2023 abstract book

Keynote abstracts

Matrix population models for threatened species.

Hemerik L., Klok C., Ydenberg R.

Matrix population models can be of great use in conservation of threatened species. From these models, that are based on demographic data (survival and reproduction), we can infer the yearly population growth factor (λ , the dominant eigenvalue of the matrix). While some species reproduce year-round, many species have a specific breeding season, which needs to be considered in the model. This presentation shows how matrix models can shed light on the population dynamics and conservation status, using two case studies. The first case considers a seemingly declining population of small birds. This bird species migrates between the Arctic and the tropics. In the past, all birds migrated every year to the Arctic to breed, and back to the tropics to over-winter, but nowadays some birds skip a breeding season and over-summer in the tropics. Survival and reproduction are almost all known and a model can be developed. How can we use this model and infer the population trend? The second case shows how matrix models can be used to assess conservation status, even when demographic data are incomplete. IUCN criteria to assess the conservation status of animal species are the most authoritative and objective. While purely descriptive in nature, they can be translated into the relative size of the yearly growth factor. To facilitate assessment for species with incomplete demographic data, we extended an existing framework developed for modelling life cycles of species with a pre-adult stage of one year; in the current models we analyse life cycles with pre-adult stages (=juvenile and sub-adult together) longer than one year. We develop both Leslie-matrices and stage-structured matrices and compare these with respect to eigenvalues, and sensitivity / elasticity of underlying parameters. We illustrate this work with life history data and conservation status of marine mammal species.

Mode and frequency of transmission shape lifestyle strategies of mobile elements

van Dijk B., Arriens V., Bertels F.

Biology features many examples of nested replicators: entities living inside other entities. Mobile genetic elements (MGEs) are an example of this, with transposable elements (TEs) replicating inside chromosomes, or phages and plasmids replicating inside microbial cells. Determining what selection pressures act upon these lower-level entities can be challenging, as the interaction with its host has both short- and long-term effects and is highly dependent upon ecological context. In my presentation, I will discuss various models of TEs – arguably one of the simplest cases of a nested replicator – focusing on what determines evolution along the mutualism-parasitism continuum. I will illustrate how the evolutionary fate of these lower-level entities is largely determined by the mode and frequency of their transmission to new hosts. Frequent horizontal transmission favours parasitism and promotes TEs that rapidly amplify at the expense of their host. As horizontal transmission becomes more and more rare, TEs are shown to evolve a more temperate (commensal or mutualistic) lifestyle, either by replicating more slowly or by not replicating at all. Interestingly, I show that these results are not dependent on whether or not the TE carries a beneficial cargo gene, which is completely overridden by the selection pressure to amplify upon horizontal transmission. Based on this, we argue that the mutualism-parasitism continuum – i.e. the difference between selfish genetic elements (SGEs) and other mobile genetic elements (MGEs) – is not a matter of the direct fitness effects inferred upon the host, but primarily shaped by frequency of horizontal transmission. Finally, I will discuss how this pattern is not just true for mobile elements, but sets our baseline expectations for other forms of nested symbiosis, such as gut microbiomes and intracellular symbionts.

Long presentation abstracts

Introducing dynamic focal adhesions into a novel hybrid cellular Potts model with discrete fibrous extracellular matrix

Keijzer K.A.E., Tsingos E, Merks R.M.H.

The interaction between a cell and its microenvironment plays an important role in health and disease, including in tumor angiogenesis, metastasis and embryonic development. A key component of the microenvironment is the so called extracellular matrix (ECM). It consists of many small and large proteins that give mechanical support to cells and also offers a medium for cell-cell communication. Cells adhere to and sense the ECM via mechanosensitive contact points called focal adhesions (FA), which become stronger if more force is applied. We discuss the modelling of these mechanosensitive focal adhesions in a hybrid cellular Potts model with an explicit fibrous extracellular matrix. We extend the recently published work of [Tsingos et al, Biophysical Journal (2023)] which used static adhesions to model a contracting cell in ECMs of different stiffness. We then introduce ideas for inclusion of dynamic FAs developed in [Rens and Merks, iScience (2020)]. The inclusion of dynamic FA into the model with fibrous ECMs opens a new avenue. As a first step we show how cell spreading can be achieved because of the FAs. We then will discuss a selection of other examples: e.g., how focal adhesion dynamics can result in cell elongation and/or how ECM orientation, interconnectedness, and other aspects of ECM structure affect cell behavior.

Eukaryotic complexity as a consequence of mitochondrial endosymbiosis

Von der Dunk, S.H.A., Snel, B., Hogeweg, P.

How the complex eukaryotic cell arose from its simpler prokaryotic ancestors remains an evolutionary enigma. Here we study the impact of the mitochondrial endosymbiosis in the context of gene regulatory networks, complementing energetic perspectives. The endosymbiotic state introduced several unique challenges to cells such as coordination of host and symbiont cell-cycles, and leakage between host and symbionts of transcription factors (regulatory interference) and stretches of DNA (resulting in gene transfer). These challenges likely impacted genome and network evolution in proto-eukaryotes and may explain various eukaryotic characteristics. We study a computational model where we force two simple cells that regulate their own cell-cycle into an obligate endosymbiosis. In most evolutionary replicates, the host and symbiont manage to adapt to the endosymbiotic setting by evolving some form of cell-cycle coordination. Strikingly, we find that regulatory interference, which is inherently harmful, drives the evolution of signaling between host and symbiont. In one replicate, through signaling, the host almost takes complete control of the symbiont cell-cycle, resulting in high fitness. Moreover, host control resembles the regulatory dominance of the nucleus over mitochondria that emerged during eukaryogenesis. In sum, this study reveals the informational challenges of endosymbiosis and how they are overcome by evolution, with important implications for eukaryogenesis.

Spontaneous regulation of non-coding sequences through border effect duplications neutrality bias

Beslon G., Foley M., Luiselli J., Banse P., Rouzaud-Cornabas J.

Despite a universal bias in favor of deletions, most bacterial genomes contain a significant fraction of non-coding sequences, raising the question of the conservation of these sequences. We used a combination of computational and mathematical tools to study the dynamics of non-coding sequences in the presence of various kinds of mutational events including substitutions, InDels and structural variants. Using Aevol - a simulation platform designed to study the evolution of genome structure - we studied the dynamics of non-coding sequences under the null hypothesis (no bias, perfect neutrality of non-coding sequences). While in this simple framework the amount of non-coding sequences should purely drift, it appeared to be tightly regulated and to be inversely proportional to the population size. Complementary analyses allowed us to identify a border-induced neutral bias in favor of segmental duplications over segmental deletions. This bias leads to a small but constant influx of non-coding sequences, with an order of magnitude of a few bases per generation. In the absence of selection, this bias leads to limitless non-coding sequences growth. However, the model also shows that selection for replicative robustness prevents the genome to grow above a certain threshold, which depends on selection strength, hence on population size. This suggests that the interplay of these two mechanisms regulates the amount of non-coding sequences in bacterial genomes.

Listeria motility increases the efficiency of epithelial invasion during intestinal infection

Wortel I. M. N., Kim S., Liu A. Y., Ibarra E. C., Miller M.J.

Many important human bacterial pathogens are motile, yet for many it remains unclear how this motility affects their ability to cause disease. Here, we sought to answer this question for *Listeria monocytogenes* (Lm), a food-borne bacterium causing severe gut infections that can lead to hospitalization or even death. After being ingested, Lm must engage specific "target cells" in the gut before it can cross the gut lining and cause infection. By imaging Lm interacting with mouse and human intestines, we found that Lm motility facilitates this process: motile Lm could more easily reach and move along the gut lining, allowing them to locate target cells faster than non-motile Lm. To further understand these dynamics, we built a cellular Potts model (CPM) of Lm gut infection, and explored how phagocytes might interfere with this process. Again, motile bacteria more efficiently located and invaded target cells, narrowing the window for phagocytes to capture them. But our simulations also challenge the commonly held view that phagocytes "hunt" bacteria, which move orders of magnitude faster. Instead, phagocytes in our simulations act like "fly paper" to capture bacteria. These findings provide new insights into the early dynamics of bacterial gut infections.

Ecological effects on the evolution of cefotaxime resistance in *Escherichia coli*

Wortel, M.T., Ruelens, P., de Visser, J.A.G.M.

Fitness landscapes map genotypes to fitness, visualizing possible evolutionary paths. These landscapes are studied both at the conceptual level and made explicit by measuring the fitness of nearby genotypes to create empirical fitness landscapes. Since the mapping of the genotype to fitness depends on the environment, approaches have included the environment (e.g. seascapes and deformability). These methods do assume a new genotype removes the old genotype. However, certain changes of the environment, such as the production of cross-feeding components or the removal of toxins from the environment, allow strains to coexist. Therefore, we introduce 'eco-fitness landscapes', which include ecological mechanisms of coexistence. We use an empirical fitness landscape of cefotaxime resistance in *E. coli* with a TEM1 gene coding for a beta-lactamase, which can break down the antibiotic. The breakdown decreases cefotaxime concentrations, which allow for growth of more susceptible strains. We measured properties affecting these dynamics, such as growth rates and antibiotic clearance rates, of eight different mutants, and show experimentally that coexistence is possible. Using this experimental data in a mathematical model we can create an empirical 'eco-fitness landscape' and predict how evolutionary trajectories are affected by coexistence. Including ecology in fitness landscapes may lead to more realistic predictions and a different view on the reachability of fitness optima.

Short presentation abstracts

Efficiently starting and preferentially filling a potato

van den Herik, B., ten Tusscher, K.

Yield of harvestable plant organs depends on photosynthetic output and the distribution of sucrose from source leaves across different sink organs. A recent study in potato demonstrated that the tuberigen StSP6A reduces activity of the StSWEET11 sucrose exporter in the phloem. While the study suggested that reducing phloem sucrose efflux enhances tuber yield, the physiological relevance and effect on phloem transport properties remained an open question. To answer these questions, we developed the first (multi-sink) mechanistic model for sucrose transport, specifically parameterized for potato plants. Starting with a single-sink model we demonstrated how the SP6A-StSWEET interaction contributes in a non-linear manner to phloem transport efficiency. Expanding to a two-sink model setup we investigated partitioning between sinks, showing that pathway properties determine sucrose partitioning. Additionally, we uncovered that xylem flow, through its hydraulic coupling to the phloem also affected sucrose partitioning. For potato tubers, it is the cumulative disadvantage compared to developing sink leaves that enables an undirected SP6A-mediated reduction of sucrose-efflux to preferentially benefit tuber resource partitioning. The targeted effect of SP6A on tuber yield thus arises as an emergent property of plant architecture and physiology. Combined with the tuber sink strength increase, this enables SP6A to significantly enhance tuber resource partitioning.

Behavioural plasticity in female mate choice causes sexual selection for costly male ornaments – no signal for male quality or mating benefit required

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

In various species, females choose mates based on a threshold preference function where they only accept males with a signal above an internal standard. This standard could be genetically fixed and determined at birth, but empirical evidence has shown that females in some species adjust their standard throughout their life based on the encountered signals. Here, we simulate the effects of an evolving standard, fixed or adjustable, on the evolution of a costly signal. The individual-based model has haploid males and females carrying genes for both a signal and standard. For the fixed standard, assuming costs for rejecting males results in selection for no standard in the females and consequently males produce no signal. If the female's standard is adjustable however, exaggerated costly signals are selected. This selection is driven by the plasticity of the female's mate choice. Each female randomly encounters males that differ in their signal, giving rise to variation in the standard within the female population. This variation gives a mating advantage for an exaggerated signal. Our findings suggest that for species with a fixed standard, maintaining this standard is rarely evolutionarily stable. In contrast, mate choice with an adjustable standard will select for exaggerated male signals. Such male ornaments can also evolve under the handicap principle, but our theory offers an alternative explanation where the ornament does not signal male quality or mating benefit.

2'-Fucosyllactose helps butyrate producers outgrow competitors in infant gut microbiota simulations

Versluis D.M., Schoemaker R., Looijesteijn E., Geurts J.M.W., Merks R.M.H.

A reduced capacity for butyrate production by the early infant gut microbiota is associated with negative health effects, such as inflammation and the development of allergies. Here we develop new hypotheses on the effect of the prebiotic galacto-oligosaccharides (GOS) or 2'-fucosyllactose (2'-FL) on butyrate production by the infant gut microbiota using a multiscale, spatiotemporal mathematical model of the infant gut. The model simulates a community of cross-feeding gut bacteria at metabolic detail. It represents the gut microbiome as a grid of bacterial populations that exchange intermediary metabolites, using 20 different subspecies-specific metabolic networks taken from the AGORA database. The simulations predict that both GOS and 2'-FL promote the growth of *Bifidobacterium*, whereas butyrate producing bacteria are only consistently abundant in the presence of propane-1,2-diol, a product of 2'-FL metabolism. The results suggest that in absence of prebiotics or in presence of only GOS, bacterial species, including *Cutibacterium acnes* and *Bacteroides vulgatus*, outcompete butyrate producers by feeding on intermediary metabolites. In presence of 2'-FL, however, production of propane-1,2-diol specifically supports butyrate producers.

Elephant poaching: a family tragedy

Croll J.C.

In some species, individuals live in close proximity to their family for most of their lives. Interactions between family members, as well as the composition of social kin groups, can strongly influence individual life histories. Certain types of kin can for example enhance the survival or fertility of family members through cooperation and social learning, while others may lower vital rates through competition. Understanding the impact of changes in kin structure on the population dynamics is crucial for the conservation and management of populations in which individuals have strong family bonds. The African elephant is an example of a species in which family groups are important for individual survival and reproduction. A herd of African elephants consists of closely related females and their offspring and is led by an old matriarch. Ivory poaching of African elephants has been found to disrupt the composition of family groups due to additional mortality of specific age classes. It is frequently argued that this disruption of family groups amplifies the effects of poaching on the dynamics of African elephant populations. To address the feedback between individual vital rates and kin structure, I use a matrix model for kin structure as an intermediate step in calculating population growth rates. With this approach I will demonstrate how various interactions between kin could affect the consequences of poaching for family groups and populations of African elephants.

Spontaneously formed topological structures build dynamic spatial patterns in biological cellular automata

Koopmans L. , Youk H.

By communicating through secreting and sensing signaling molecules, cells are capable of regulating their gene-expression states without the existence of an external morphogen gradient. This mechanism gives cell populations the ability to self-organize into ordered, dynamic spatial patterns. These patterns are of special interest as they can propagate information over space. In this research, a cellular automaton was used to model such cell populations with the ability to form traveling waves. We discovered that the formation process of traveling waves is governed by the creation, movement, and annihilation of topological structures, referred to as vortices.

The Fundamental Diagram of T Cell Crowding Exhibits Regions that Correspond to Different Cell Behaviors

Wouters L.L.

T cells play an important part in the immune response. They are often in continuous movement searching for foreign antigens in dense lymph nodes or cooperatively attacking infected cells at infection sites, and thus have to be able to move efficiently within large crowds of T cells. We have studied the characteristics of T cell behavior during crowding by modeling T cells with an Act-CPM model in a crowd-inducing microchannel. Their crowd behavior was investigated in a fundamental diagram (FD) where the cells' speed was plotted against their density. The FD is usually used to separate systems into individual and social crowds, where their speed is respectively limited or not affected by the density. While the T cells were expected to exhibit a similar relationship as social crowds, the FD is more complex and can be separated into three regions that correspond to a different behavior and speed distribution: single cells with a speed distribution that is dependent on the motility type at low densities, cells moving while touching other cells in a train formation with a non-zero unimodal speed distribution at intermediate densities, and collisions with low speeds at high densities. Instead of a smooth relationship between speed and density, these collisions create an abrupt decrease in speed. Different motility types of the cells do not affect this overall pattern, but do affect the proportion of cells at intermediate and high densities, suggesting a change in crowd behavior.

Dynamic Modelling and Optimization of Intercrop Systems

de Jong, M.N., Devia, C.A., Giordano, G., Anten, N.P.R.

Intercropping is the agricultural practice of growing crops in a mixed culture, instead of in a monoculture. Intercropping can improve yield and reduce the need for chemical inputs by (1) reducing interspecific competition w.r.t. intraspecific competition, and (2) introducing facilitative interactions, for instance by soil enrichment. Research on intercropping is dominated by empirical studies, supported by detailed simulation-oriented modelling. In our work, we build simple dynamical systems to model interactive plant growth in an intercropping system, based on well-established ecological models, such as the competitive Lotka-Volterra equations. The state variables represent plant biomass, with fixed population densities, corresponding to single-generation agricultural settings. We present spatially-explicit, individual-based models where each plant is affected by neighboring plants, as well as associated mean-field models where each variable represents the average biomass per plant species, and is affected by density-dependent intra-and-interspecific interactions. For some patterns, the individual-based models can be converted to mean-field models by summing the ecological interactions across an infinite field. Other patterns can only be approximated by mean-field models using numerical methods. Mean-field models can in turn directly be used for optimal control, for instance to find the optimal species densities that maximize a weighted yield objective.

Irregular boundary between in silico sinoatrial and atrial cells affects propagation

de Jong M.A., Merks R.M.H.

The sinoatrial node is the primary pacemaker of the human heartbeat. Even though this node is only a few millimeters across, it manages to activate the rest of the atrium. The leading hypothesis for this phenomenon is that the sinoatrial node is electrically insulated from the rest of the heart, except for some sinoatrial conduction pathways. We have modeled the sinoatrial node with a hybrid Cellular Potts model, combined with a reaction-diffusion model for the electrophysiology. A tissue of pacemaker cells is connected with a tissue of atrial cells through a narrow isthmus, mimicking a conduction pathway. Due to this configuration, as small number of pacemaker size has to activate a relatively large number of atrial cells. Hence, a specialized boundary between the two cell types is necessary to achieve robust propagation. Two leading hypotheses are the presence of transitional cell types and interdigitation. Interdigitation is expressed by the presence of finger-like protrusions of the pacemaker cells into the atrial tissue. We have focused on the latter hypothesis and found that an intermediate level of interdigitation can indeed improve the robustness of the system. Furthermore, a wider isthmus width also improves robustness, whereas the mosaic model, a mix of pacemaker and atrial cells near the boundary, reduces robustness. In future work, we aim to extend our model to also include transitional cells.

Modeling plant root tropism interactions

Jordan O., Garcia Gomez M., ten Tusscher K.

In plants, a tropism is the specific movement or growth in response to environmental stimuli. One of the oldest documented examples of tropisms is gravitropism. This is the downward growth of roots along the axis of gravity. Halotropism, the growth of roots away from a salt gradient, is a relatively novel tropism that was only recently properly described. Both of these tropisms work by creating a spatial asymmetry of the growth hormone auxin in the root tip, causing asymmetric cell growth that bends the roots towards a certain direction. The goal of my research project is to investigate how these two tropisms interact with each other when they are competing and both want to send the root in opposite directions. This is a difficult question as both tropisms seem to rely on very similar mechanisms to establish and maintain their auxin asymmetry. To investigate this interaction I am using a computational model of an Arabidopsis root tip. This model is able to simulate the passive and active transport of auxin between and within cells of the root. My goal is to expand this relatively simple model with new conditions and dynamics such that it is able to simulate a possible mechanism that can explain the still poorly understood interactions between gravitropism and halotropism.

Modeling the interplay between structural variations and substitutions generates saltational evolutionary dynamics.

Banse P., Trujilo L., Beslon G.

Evolution often occurs by bursts that are difficult to explain in the classical view of evolution centered on substitutions. Recent results in microbial evolution, for example in the Long Term Evolution Experiment, suggest that these bursts can be caused by structural variants (SVs). Using computational simulations, we establish a clear link between the fixation of SVs and the apparition of key innovations and propose a theoretical framework to explain how bursty dynamics arise from the interplay between SVs and substitutions. As a matter of fact, the number of possible mutations and the distribution of their fitness effect is very different between SVs and substitutions. SVs have a larger impact on the genome, and are significantly more often deleterious. It is thus expected, for similar mutation rates, to witness more frequently the fixation of substitutions than SVs. However, there are many more possible SVs (for example cubic for interspersed duplications, versus linear for substitutions). Hence, the possibilities of favorable substitutions are exhausted faster, leading to stasis periods until a lucky SV appears, initiating a new burst. We show that dynamics of burst and stasis occur in this simple evolutionary models, shedding a new light on saltational evolution.