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MATHEMATISCHES FORSCHUNGSINSTITUT OBERWOLFACH

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Mathematische Modelle in der Biologie

20.10 - 26.10.1996

This was the seventh meeting on Theoretical and Mathematical Biology at Oberwolfach since 1975. It occured during an expanding phase in this field with many new research groups being initiated around the world. Forty scientists took part, with many interests, and from many backgrounds and countries. A large proportion were young scientists who had the opportunity the present their work in an informal atmosphere.

The meeting was organised by Wolfgang Alt (Bonn) and Odo Diekmann (Utrecht). The main topics discussed were cell physiology, population dynamics in an evolutionary perspective and interactions in space. The latter of these having a large overlap with the former two topics. Most of the talks were of an analytical or numerical nature. Of interest is to see the trend towards more computational models as computational power increases and computers become accepted in the field of Mathematical Biology. From a mathematical point of view there appeared a trend towards a merging of deterministic and stochastic concepts and models. There was also more emphasis on modelling complex systems from the microscopic to the meso- and macroscopic indicating a move away from more phenomenological modelling approaches.

Some of the topics covered which can be found in the proceeding abstracts are: spatially explicit models of ecological and evolutionary dynamics, deterministic and stochastic models of population and evolutionary dynamics, fitness landscapes and ESS's, immunology, epidemiology, recombination, adaptive dynamics, macroparasite interactions, coagulation, aggregation and fragmentation, random walks, Brownian motion and interacting particles, morphogenesis and wound healing, pattern formation, transmembrane signaling, dimer automata and microtubules and tumor formation.

The facilities at the institute were first rate and the staff friendly and helpful. The great food and beautiful surroundings made for an ideal setting for this conference.

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Fred Adler

Spatially-explicit models of local resource interaction: population dynamic and evolutionary consequences

Through a variety of approaches, modelers and empiricists have been studying the evolutionary consequences of local resource interaction. Individual-based models, lattice models, diffusion models, simulation models and experiments have all played a role in improving our understanding of the key factors in this area. I propose that a class of spatially-explicit individual-based models based on the dynamics of resources that are sufficiently flexible to address important issues, sufficiently realistic to be directly testable, and sufficient tractable to allow for derivation of population dynamic and evolutionary principles. In particular, these models have the potential to uncover the structure underlying basic scaling relations such as the -3/2 self-thinning law for plants and, more speculatively, the 3/4 metabolic scaling for animals, and cast new light on the evolution of interactions including exploitation and interference competition, facilitation, and cooperation.

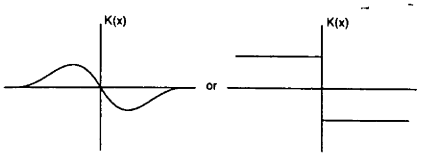
Wolfgang Alt

Modelling aggregation: working session

Heading for a class of simple continuum models helping to understand the transient dynamics of aggregation of individuals (e.g. epithelial cells in morphogenesis or wilderbeast forming a herd) we looked for an evolution equation describing both density dependent mobility, $\mu(u)$, as well as density induced drift, mean aggregate velocity vector $V = V[u]$, generally a functional of density $u = u(t, x)$:

$$\partial_t u \quad = \quad \nabla_x \cdot (\mu(u) \nabla_x \cdot u - uV)$$

With the simple assumption, $V[u] = Ku$, the slope of the integral $K(x)$ would induce aggregation. What is the role of the "diffusion term" $\mu(u)\nabla_x u$? For a motility that is reduced for high density it can lead to aggregation patterns with a plateau of maximal density.



However, even without diffusion, $\mu \equiv 0$, the hyperbolic equation is well-posed and has a behaviour similar to the Hopf-equation $\partial_t u + u \cdot u_x = 0$, for the integral $M(t, x) = \int_0^x u(t, x')dx'$, this leads to a formation of shocks, here Delta-Peak distributions in finite time.

In order to model cell or animal aggregates, in which also in regions of maximal density, $\mu = \mu_{\max}$ there occurs motion, e.g. due to further cell division enlarging the aggregate or to active motion, pushing the individuals within the dense "herd", we propose to treat systems of equations similar to those used in multi-phase flow models for composite materials, that take

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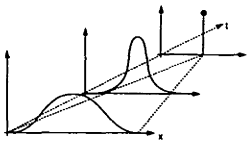

into account equations for the stresses within the compacted region.

Ovide Arino

Density dependence in egg to larva recruitment in a fish population

This talk addresses the issue of explaining the low recruitment rate of eggs into the juvenile stage in a population of fish. Several possible causes are briefly discussed. A model is proposed based on the competition of larvae and a threshold to be reached by the larvae in order to go to the juvenile stage. This work has been done in collaboration with M. L. Hibd (University of Marrakes) R. Bravo de la Passa (University of Alcala de Henars). It is part of the research programme on the Sole of the bay of Biscay undertaken in collaboration with ECOHAL, a laboratory at the marine institute IFREMER (Nantes, France).

Ellen Baake

Exactly solved sequence space models

Mutation-selection models in sequence space have not been solved exactly except in trivial cases. To remedy the situation, we first show that the parallel mutation-selection model is equivalent to an Ising quantum chain. Three explicit examples with representative fitness landscapes are then discussed and exactly solved with methods from statistical mechanics.

Nicola Bellomo

Modelling population dynamics with kinetic interaction and competition

Two recent papers [2,3] have developed a cellular (kinetic) theory for the analysis of the competition between tumor and immune system cells in the early stage of tumor onset. This competition will eventually result in the depletion of the tumor or in its growth. The analysis was referred to a stage called the *free cells regime*, that is such that the interactions, and therefore competition or cooperation, occur at a cellular level between pairs of individuals. Mathematical aspects developed by various authors, e.g. [1], as documented in [2].

Although the original motivation of the above cited papers was strongly related to modelling tumor dynamics, it is recognized that the models proposed in [2,3] can be reasonably generalized to several fields of biological and social sciences. The mathematical structure of these models is similar to the one of the nonlinear kinetic theory and, in particular, to the Boltzmann equation. Indeed, the evolution equation is an integro-differential equation with quadratic type nonlinearity in the integral term.

The aim of this research line is to provide a sufficiently complete analysis: modelling, qualitative and quantitative analysis, related to above mentioned class of models. The modelling should provide a general framework that includes, as particular cases, the models proposed in [2,3]. The general framework is the one of mathematical methods in modelling and related

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qualitative analysis for population dynamics.

[1] Arlotti, L. and Bellomo, N., On a new model of population dynamics with stochastic interaction, *Transp. Theory Statist. Phys.* **24**, (1995), 431-443.

[2] Bellomo, N., Forni, G. and Preziosi, L., On the kinetic (cellular) theory for the competition between tumors and host-immune system, *J. Biol. Systems* **4**, (1996), (in press).

[3] Bellomo, N., Preziosi, L., and Forni, G., Tumors immune system interactions: The kinetic cellular theory, in *Modelling Tumor Immune System Dynamics*, Adam, J. and Bellomo, N. (eds.), (1996), Birkhäuser.

Maarten Boerlijst, Sebastian Bonhoeffer and Martin Nowak

Viral quasi-species and recombination

Virus populations are complex ensembles of distinct but related genomes (so called quasi-species). Mathematical descriptions of viral quasi-species focus on point mutations as the major source of variation. However, retroviruses (and many other viruses) are able to recombine their genomes. We study a mathematical model of viral quasi-species dynamics which incorporates both point mutation and recombination. We show that for low mutation rates recombination can reduce the diversity of the quasi-species and enhance overall fitness. For high mutation rates, however, recombination can push the quasi-species over the error threshold, and thereby cause a loss of all genetic information. Finally, recombination introduces bistability to the quasi-species; if the frequency of an advantageous mutant is below a certain threshold, it will not be selected.

James Cushing

Nonlinear dynamics in insect populations: from equilibria to chaos, from mathematical models to laboratory experiments

This talk will describe an on-going interdisciplinary effort designed to demonstrate the importance of nonlinear phenomena in population biology by means of nonlinear mathematical models in conjunction with long term, controlled and replicated, laboratory experiments and extensive statistical tests of parameter estimation (with confidence intervals) and model validation. The laboratory animals used are species of flour beetles (Tribolium). A discrete stage structured model is derived that reflects the life cycle history of the beetle and the dominant nonlinear mechanism driving their dynamics (namely, intra-stage cannibalism). A stochastic version of the model provides the means to connect data with the model. A historical set of data was used to obtain parameter estimates and theoretical predictions of beetle dynamics when selected parameters are changed [1]. Bifurcation theory provides the means by which to organize the experimental design and protocols. A series of replicated experiments were carried out for one year to demonstrate that the model predicted bifurcations can be produced in the laboratory [2]. Based on the success of these results, another series of experiments has been conducted over the last two years that is designed demonstrate that further types of attractors predicted by the deterministic model, including chaos and strange attractors, are obtainable in the laboratory cultures. This project not only provides a thoroughly validated documentation of nonlinear dynamics and bifurcation theory in population dynamics, but provides the first rigorously validated case of chaos in a biological population. Other nonlinear phenomena are also been studied by the model and the same interdisciplinary effort, including the ability of transient phenomena caused by saddle nodes to predict differences in routes that orbits take to attractors

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and thereby, stochastically, to account for observed differences in data from replicated cultures; and the ability of the model to predict an unusual phenomenon observed by Jillson [3] that the total population biomass can increase when the environmental resource is periodically fluctuated.

[1] Dennis, B., Desharnais, R.A., Cushing, J.M. and Costantino, R.F., Nonlinear demographic dynamics: mathematical, models, statistical methods, and biological experiments, Ecological Monographs 65 (3), (1995), 261-281.

[2] Costantino, R.F., Cushing, J.M., Dennis, B. and Desharnais, R.A., Experimentally induced transitions in the dynamics behaviour of insect populations, Nature 375, (1995), 227-230.

[3] Jillson, D., Insect populations respond to fluctuating environments, Nature 288, (1980), 699-700.

Andreas Deutsch

On the Origin of Swarms by Means of Orientation-Induced Pattern Formation

It is typical of life cycles in many microorganisms that a phase of individually moving cells (dispersal) is followed by a state of cooperative gliding (aggregation and/or swarming) - examples are abundant among slime moulds (e.g. *Dictyostelium discoideum*) or myxobacteria. How can such transition to social pattern formation be initiated?

Clearly, some sort of interaction is necessary as a precondition for aggregation. Traditionally, models have been studied which are based on substances ("attractants") produced by the cells and diffusing within the surrounding medium. We use a different approach solely based on cells having a natural axis of orientation, moving according to this direction and reorienting due to the orientation distribution of neighbouring cells (the "degree of dependence" being tuned by a sensitivity parameter). The model is formulated as a stochastic cellular automaton ("lattice-gas").

Simulations show a phase transition if the sensitivity parameter supersedes a critical value - beyond the threshold formation of oriented patches is observed. We demonstrate that the critical value obtained in simulations can be confirmed by linear stability analysis of the underlying Boltzmann equation (neglecting correlations, "Stoßzahlansatz"). This analysis further suggests possible scenarios of swarm pattern initialization by subtle increase of sensitivity or cell density if these changes occur within the critical region.

Ulf Dieckmann

The dynamical theory of coevolution: a unifying perspective

A unifying framework is presented for describing the phenotypic coevolutionary dynamics of a general ecological community. We start from an individual-based approach allowing for the interaction of an arbitrary number of species. The adaptive dynamics of species' trait values is derived from the underlying population dynamics within the community; in consequence, the evolutionary process is driven by ecological change.

We present a hierarchy of four dynamical models for the investigation of coevolutionary systems. The necessity of stochastic treatment is demonstrated and deterministic approximations are derived where appropriate. The mathematical framework advanced here to our knowledge is the first one to combine the individual-based, stochastic perspective with a fully dynamical analysis of the phenotypic coevolutionary process.

Deductions are given to derive various well-known equations from the literature of (co)evolu-

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tionary modelling as special cases of our approach. In particular, equations central to the fields of evolutionary game theory, adaptive dynamics, replicator dynamics and reaction-diffusion systems are recovered. In consequence, the different domains of validity for these models are delineated and several ad-hoc assumptions can be removed.

Odo Diekmann

An invasible yet unbeatable strategy: working session

In discussions about adaptive dynamics the following rather special yet illuminating example shows that invasibility may not tell the whole story:

$$\begin{aligned} x(t) &= cx(t-3)g(x(t-3)+y(t-4)) \\ y(t) &= c\gamma y(t-4)g(x(t-3)+y(t-4)) \end{aligned}$$

This example "describes" a semelparous population, like Pacific Salmon, in which two subpopulations compete in the nursery. One reproduces after three years, the other after 4 years. If $\gamma < 1$, the last is out-competed in steady state. But it may invade successfully in a two cycle since it can synchronise to the good years. But by a phase shift the resident 3-type may strike back and ultimately out-compete the 4-type.

Régis Ferriere and Oscar DeFeo

Adaptive dynamics: three routes to dimorphism

A crucial issue in the study of adaptive dynamics is the transition from a monomorphic state to a dimorphic state. Consider the case of a resident strategy X that can be invaded by new strategies Y. For different Y's, the outcome of the competitive process may yield either a new monomorphic state (Y takes over X) or a dimorphic state (X and Y coexist). How does either outcome relate to the reverse invasion, or the lack thereof, of type Y by type X? We offer an answer based on the bifurcation analysis of possible routes to dimorphism of a simple, yet general model of life-history evolution. We find that across a transcritical point, the transition exactly matches the sign change of the invasion exponent of X. Along with an attractor crisis, the transition may take place although the invasion exponent of X is still negative. In fact, the eventual transition is completely indeterminate in this case, due to the fractal structure of the basin of the dimorphic attractor. Finally, one may follow a fold-Hopf bifurcation route to dimorphism. Then a positive invasion exponent for X is not sufficient to ensure transition to dimorphism: in the population density phase space, the Y invariant manifold connects with itself by a heteroclinic loop, which entails that Y is invasible, yet unbeatable.

Eckhard Finke

Deterministic and stochastic models for dynamics of population growth and genetic structure

Estimations of the extinction risk of small populations are based on investigations of the population dynamics. However this dynamic is influenced also by the internal genetic structure of the endangered species. Thus we explore a stochastic model, which coupled models from population genetics and the population ecology.

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In small populations the genetic structure is determined essentially through the mating system (particularly through the degree of inbreeding or out-breeding). In the developed model a parameter a has been introduced, which describes a certain realization of the mating system. For $a > 1$ one receives inbreeding, for $a < 1$ out-breeding and for the borderline case $a = 1$ random mating.

The simulation of different genetic structures (selection coefficient) with different mating systems shows strong differences in:

- extinction risk,
- conservation or loss of genetic variability,
- influence of spatial structures.

The interpretation of the results as well as the deterministic analysis of the model yield references for the protection of endangered species.

Marino Gatto

Optimal body size and allometric relationships in macroparasites

Host parasite density dependent models together with allometric relationships between various demographic parasites and the size of both parasites and their mammalian host are employed to investigate the problem of evolutionary optimal body sizes in parasites. One starts with the general macroparasite model of the form:

$$\begin{aligned} \frac{dH}{dt} &= \eta H\left(1-\frac{H}{K}\right)-\alpha P \\ \frac{dP}{dt} &= \frac{\lambda P H}{H_0+H}-(\mu+\alpha+b)P-\alpha\frac{k+1}{k}\frac{P^2}{H} \end{aligned}$$

where H and P are host and parasite densities, η and K are the intrinsic rate of increase and the carrying capacity of hosts, λ the fertility of parasites, μ the intrinsic mortality of parasites, b the host mortality, α the parasite induced mortality, H_0 a semi-saturation constant which depends on the contact rate in an inverse fashion, k a parameter describing the clumping of parasites inside their hosts.

Let Ω be the body size of parasites and W the body size of hosts. From extensive investigation of different assemblages of mammals and intestinal nematodes it is possible to derive the following allometric relationships: $K \sim W^{-0.7}$, $\eta \sim W^{-0.27}$, $b \sim W^{-0.26}$, $\mu \sim \Omega^{-0.25}$, $\lambda \sim \Omega^{0.5}$, $\alpha \sim (\Omega/W)^2$. Three evolutionary criteria are used:

- Maximum rate of spread of parasites in a parasite free population of K hosts,
- Non-invasibility of a host-parasite complex by a parasite with a different body size,
- Maximum adaptability to a range of different environmental conditions.

All the criteria point out that there exists a linear correlation between host and parasite body size on a log-log scale. For realistic values of the parameters the slope is approximately 0.8 as shown in the following figure. This result qualitatively matches existing data.

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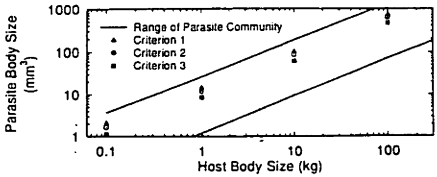

Danny Grunbaum

Describing movements of populations resulting from individual based biased random walks

Taxis, area-restricted search, and other forms of biased random walks are important elements of cell migration in immune responses, wound healing, and morphogenesis; they also are the basis of many foraging, dispersal, and reproductive behaviors in micro-organisms and in higher animals. Mathematical models which relate population-level advective and diffusive fluxes to observations of individual behavior are important tools in understanding and predicting these processes. Typically, these models assume that individual behavior is governed by Markov processes, and result in advection-diffusion equations with variable coefficients. The usefulness of this approach to biologists has been limited in part by overly simplistic individual behaviors assumed in existing models. In particular, previous models have drastic and unrealistic limitations on individuals' physiological or cognitive "memory". I present derivations of advection-diffusion equations for more general and realistic individual behaviors, in which individuals possess state variables that can encode both their memory of recent conditions and also complex internal state dynamics. The analysis is based on an eigenmode expansion of Boltzmann-type integral equations in velocity and state variables, and takes advantage of a difference in time- and space-scales between individual responses and environmental variations. A perturbation expansion results in a general advection-diffusion equation that may be solved analytically or numerically to investigate the effects of various behaviors and substrate distributions. I show how the results of these equations can be cast in terms of measurable and biologically relevant parameters. and can give useful insights in ecological, evolutionary, and medical applications.

Shay Gueron

Steady-state group size distributions of discrete coagulation fragmentation processes and their applications to animal grouping

The talk deals with discrete coagulation-fragmentation processes. We consider a fixed size population in which groups coagulate and fragment at different rates, and look for the resulting stationary group size distribution. We define the problem is defined as an ergodic, discrete time, homogeneous Markov process where the states space is the set of all partitions of the population size. We show how to translate given coagulation and fragmentation rates into a transition matrix. Computing the eigenvector of this transition matrix gives the stationary probability distribution on the states space, from which we obtain the desired stationary group size distribution. Practical use of this direct method is limited to relatively small populations because the dimensions of the transition matrix grow exponentially with the population size. We overcome this restriction by developing a Monte Carlo simulation method, whose complexity per step grows only linearly with the population size.

The coagulation-fragmentation problem appears in different contexts such as polymer kinetics, and the related models use integral equations or infinite sets of differential equations. These are based implicitly on a heuristically motivated approximation and are reasonable only

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for large populations. We derive here a new set of discrete coagulation-fragmentation equations for the stationary group size distribution, and solve them by applying the same approximation while pointing out explicitly where it is made. We explain why this approach is inaccurate for small populations and demonstrate by examples that when the coagulation-fragmentation rates limit stable groups to be small with respect to the total population, it becomes is a fairly good approximation. We relate the discrete problem to the analogous continuous model by comparing our results for large populations to the steady state solutions of the coagulation-fragmentation integral equation. The agreement between these independent results is a step towards justifying the continuous formulation for large populations.

While the proof for the general case remains open, we study the special case of a pair formation dynamics, and prove that the solution of the coagulation-fragmentation equations converges to the exact solution when the population size grows to infinity. Finally, we use the discrete model to study animal grouping and show that modal group size distributions can emerge autonomously from "monotonic" coagulation/fragmentation rates if the population is large enough.

Mats Gyllenberg

Structured metapopulation models

The greatest threat to the survival of species worldwide is loss of suitable habitat. Presently, continual fragmentation, deterioration and destruction of habitats are going on. The appropriate framework for treating the consequences of changes in habitat structure is that of metapopulation dynamics.

The classical model of Levins, who coined the term "metapopulation" is based on several simplifying assumptions, for instance:

1. Spatial arrangement of habitat patches is ignored,
2. All patches are assumed to be identical (of the same size and quality)
3. Local dynamics, in particular the effect of migration upon local dynamics, is ignored.

In this talk I outline several different modelling approaches by which one can relax some or all of the above assumptions. The common feature of these approaches is that one starts by modelling mechanisms at the local level, then lifts the model to the metapopulation level and finally studies phenomena at the metapopulation level. Both continuous-time and discrete-time as well as deterministic and stochastic models are treated. It is shown that these structured models generally have quite a different qualitative behaviour than unstructured models. These differences can be crucial in applications to conservation biology.

Karl-Peter Hadeler

Epidemic spread by correlated random walks

Models for reactions and motion of particles usually assume the form of reaction diffusion equations. Here the underlying process is Brownian motion. Like the heat equation, these show the unwanted effect of infinitely fast propagation. More realistic models for motion in space are correlated random walks and - in higher space dimensions - systems of Boltzmann type.

The standard SIR model for an epidemic has been combined with correlated random walks. Then the models for the spread of epidemics in space become hyperbolic systems of partial differential equations. Reaction diffusion systems for epidemic spread can be seen as limiting

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cases for large speeds and frequent turns. Various features connecting the contact and the motion processes can be incorporated into these models.

For the case where only infectives move (the "Rabies problem") [1] and the limiting case of slow infectious [2] the problem of existence of traveling front solutions has been discussed in detail.

[1] Hadeler, K.P., Traveling epidemic waves and correlated random walks, in: *Differential Equations and Applications to Biology and Industry*, Martelli M. et al. (eds.) 145-156, World Scientific, Singapore (1996).

[2] Hadeler, K.P., Spatial epidemic spread by correlated random walk, with slow infectives. To appear in *Proceedings of the Dundee Conference on Ordinary and Partial Differential Equations* (1996).

Andreas Herz

Simplicity and complexity in population dynamics

Nicholson's laboratory experiments with isolated insect populations demonstrate that resource limitations can cause intrinsic oscillations in the size of a biological population. The experimental data show fluctuations with a pronounced periodic signature and oscillation periods that are surprisingly robust under variations of the experimental conditions.

Based on an analysis of a age-structured population model, a theoretical explanation for these phenomena is presented. In the model it is assumed that the probability to survive to age a and then reproduce does not depend on the population size. The "potential fecundity" thus defined is described by some kernel $F(a)$. The competition for resources is modeled by a nonlinear function g which describes the relation between the number $x(t)$ of eggs laid at time t and the entire potentially reproductive population at that time, $\int F(a)x(t-a)da$. Together, these assumptions result in the nonlinear Volterra integral equation $x(t) = g[\int F(a)x(t-a)da]$.

Under certain conditions, this model allows for a precise prediction of the oscillation period without any parameter estimates from time-dependent experimental data. The analysis is based on a Lyapunov functional for monotone nonlinearities g and kernels $F(a)$ that are symmetric around some a_{mean}. For humped nonlinearities, numerical simulations show period-doubling bifurcations together with strict locking of the period between the bifurcations.

In the limit of a vanishing spread of the reproductive age, where $F(a)$ becomes a delta function $\delta(a - a_{\text{mean}})$, the model reduces to the well-known logistic map. A comparison between the present model, the logistic map, and models using delay-differential equations with a single maturation delay highlights the relation between dynamical phenomena exhibited by these different approaches, their biological validity, and, more generally, the limits of simplified population models.

Thomas Hillen

Qualitative Analysis of semi-linear Cattaneo Equations

The linear Cattaneo equation appears in heat transport theory to describe heat wave propagation with finite speed. It also can be seen as a generalization of a correlated random walk. If the system admits non conservative forces (or reactions) then a nonlinear Cattaneo system is obtained:

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$$
\begin{aligned}
u_t + \nabla v &= f(u), \\
\tau v_t + D\nabla u + v &= 0,
\end{aligned}
$$

where $u(t,x) \in R$ and $v(t,x) \in R^n$ are functions of time $t \geq 0$ and space $x \in \Omega \subset R^n$. In the heat transport interpretation u is the temperature and v is the heat flow. If the system describes random motion of particles then u is the particle density and v the particle flow.

We consider asymptotic behavior of solutions of the nonlinear Cattaneo system. Following Brayton and Miranker a Lyapunov function is defined which shows global existence of solutions and that the set of all stationary solutions forms a global attractor.

Georgy Karev

Structural models of biological community dynamics and the ergodic theorems

Theory of structural models is the most adequate tool for constructing mathematical models that links effects at individual, population and community levels. These models may be used for studying of population and community dynamics in evolutionary perspective. This talk contains the results describing asymptotic behaviour of the general autonomic age-state model with n types of individuals described by several structural variables; existence, uniqueness, stability and exact form of limit distributions, estimate of convergence speed, method of calculating the age structure and "regulating functionals" of limit distributions; besides that, methods of researching of two classes of nonlinear community models; separate and Gurtin-McKamy type models are proposed. The main results may be applied to 1) structure models of metapopulations; 2) structure models of communities consisting from n populations; 3) structure models of populations with complicated life cycles; 4) gap-modelling of forest communities; 5) succession forest models; 6) ergodic theorems for structural models.

"Ergodic hypothesis in biology" asserts that the climax state of the succession system of plant biocenoses possesses the following property: The area under i-th biocenose must be proportional to a "proper time" of its development. This hypothesis is a particular case of ergodic theorems that are proved for general structural models of communities.

Markus Kirkilionis

Numerical continuation of equilibria of physiologically structured populations

Numerical methods for the continuation and bifurcation analysis of invariant sets had a major impact for the understanding of finite dimensional dynamical systems given by maps and ODE's. Such systems are widely used in population dynamics to describe the interaction of species. However, it became clear that quite often a population's dynamics can only be understood if individual differences are taken into account, a good example is cannibalism. In this case the species' behaviour could never be described under the assumption that all individuals are equal. Also, models of physiologically structured populations (or short PSPM's) can be used to derive mechanistically from a micro-level (here the individual level) models on a macro-level (here the population-level), which might then be describable by a finite dimensional system like an ODE. To understand the additional properties arising from a population consisting of individuals, numerical tools for bifurcation analysis are under development. They are hopefully giving the same kind of insights as they did in the finite-dimensional case.

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PSPM's can be given in different forms, birth of individuals in the individual state space Ω (a space containing all possible individual's state positions as given by length, size, energy content etc.) can be continuously distributed over (subsets of) Ω or concentrated only at finitely many points, births can be continuous in time or being events etc. We have chosen a deterministic setting with just one possible state-at-birth and continuous reproduction, formulated as coupled integral equations. The coupling is given by so-called environmental interaction variables I, and the model becomes nonlinear only by dependence of ingredients on I. This has the advantage that every population can be modelled first independently by a linear submodel, and only in a second step nonlinear feedback is taken into account. This formulation has also advantages for the implementation of the numerical algorithms.

In this talk we addressed specifically the problem of numerical continuation of equilibria. To do so, we need to construct a finite-dimensional approximation of a map $G : X \times \Lambda \to X$, where the infinite-dimensional space X contains the possible population states and Λ is a finite-dimensional parameter space. Given G and a fixed $\alpha \in \Lambda$, an equilibrium can be calculated by solving the equation $G(x, \alpha) = 0$, $x \in X$. We gave a recipe how to obtain a finite-dimensional approximation G^* of G in the case $\dim(\Lambda) = 1$. Essentially the idea was to follow individual characteristics in Ω and to stop computing the characteristics after finite time. The usual continuation algorithms can be used with G^* to compute the dependence of equilibria on a single parameter. After a formal linearisation of G and the derivation of a characteristic equation $F : X \times \mathbf{C} \times \Lambda$, now with $dim(\Lambda) = 2$ and $\mathbf{C}$ being the complex numbers, we are able to calculate stability boundaries of equilibria in two parameter space, again with a similar finite-dimensional approximation F^* of F. In this case we use the combined system $G^*(x, \alpha) = 0$ and $F^*(x, i\omega, \alpha) = 0$ which implicitly define the stability boundary.

René Lefever

Modelling of vegetation patterns by non-local Verhulst-Fisher equations

A non-local Verhulst-Fisher model is presented which describes the dynamic vast classes of terrestrial plant communities growing in arid semi-arid regions throughout the world. On the basis of this model, we show that the vegetation stripes ("tiger bush") formed by these communities result from an interplay between short range cooperative interactions controlling plant reproduction and long range self-inhibitory interactions originating from plant competition for environmental resources. Isotropic as well as anisotropic environmental conditions are discussed. We find that vegetation stripes tend to orientate themselves in the direction parallel or perpendicular with respect to the direction of anisotropy depending on whether this anisotropy influences the interactions favouring or inhibiting plant reproduction; furthermore, we show that ground curvature is not a necessary condition for the appearance of arcuate vegetation patterns. In agreement with *in situ* observations, we find that the width of the vegetated bands increases when environmental conditions get more arid and that patterns formed of stripes orientated parallel to the direction of a slope are static, while patterns which are perpendicular to this direction exhibit an upslope motion. Moving front *interfacial instabilities* are predicted.

Jürgen Lenz

Transmission of tensional patterns across cell boundaries

Moving cells exert tension on their immediate surroundings. Tension is generated within the filamentous actin cytoskeleton and transmitted across the cell membrane via certain membrane proteins which are bound to the cytoskeleton and to the extracellular matrix at the same time.

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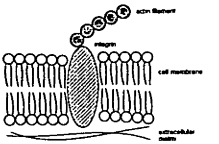
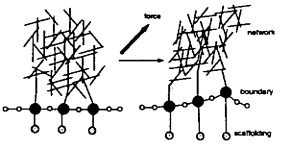


There is a strong interaction between the kind of transmission or percolation of tensional patterns across the membrane and the microarchitecture of their molecular assemblies performing the transmission.

This interaction was investigated using a many particle model based on a microscopic Brownian dynamics approach. Simulations were presented which show the deformation and tension distribution of a preformed filamentous network attached to a scaffolding structure via a boundary layer after exertion of an external force pattern.



Lines of high tension appear within the network which "map" the exposed force pattern to a tension distribution within the scaffolding structure.

These results indicate how tensional patterns can be transmitted across the cell boundary and how the internal tension state of the cytoskeleton may represent the action of an underlying force pattern. This points to the possibility of interpreting the transmission and storage of tension as a kind of information processing.

Moreover, this model emphasizes the worth of structural approaches in simulating events of assembly with large structure-function relationships within the cytoplasm which, as a whole, is highly structured.

Philip Maini

Propagating patterns in morphogenesis and wound healing

Propagating patterns arise in developmental biology and in wound healing. In both cases cells respond to external cues and also influence the cues, resulting in "dynamic reciprocity". One example from morphogenesis concerns the development of multicellularity in the slime mold *Dictyostelium discoideum* (Dd). Following starvation, periodic waves of the chemical cAMP initiate the aggregation of Dd amoebae via a cell streaming mechanism. A model coupling cell chemotaxis and cAMP reaction-diffusion is derived and it is shown that aggregation can occur as the consequence of the growth of a small amplitude pattern in cell density forced by the large amplitude cAMP waves.

In wound healing, the alignment of the extracellular matrix (ECM) on which cells move plays a key role in the quality of healed tissue. A model involving fluxed induced alignment is developed and analysed, and experimentally testable predictions are made on how alignment can be influenced by manipulating key parameters.

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Hans Metz

Towards a Bifurcation Theory of ESS's?

Evolutionarily Stable Strategies, are strategies such that if the whole population plays them no alternative strategy can invade the population. The calculation of such strategies provides us with predictors for the possible long term outcomes of the evolutionary process.

To get more specific we need the concept of fitness. Initially a mutant is present in such small numbers that its environment is essentially set by the resident population. Therefore the dynamics of the population descending from it is essentially linear. The dominant Lyapunov exponent of this linear dynamics we shall call $sX(Y)$, where the Y refers to the trait value characterising the mutant's strategy as opposed to the resident strategy X. X and Y are assumed to take values in some nice subset of R^n. Y can(not) invade X when $sX(Y) > 0$ (< 0).

By necessity $sX(X) = 0$. We assume that X persists. So the population dynamics has to proceed to an attractor with the X population neither growing nor declining in the long run. In other words the X-population has exponential growth rate zero, and so have all mutants indistinguishable from it. I shall assume for simplicity that the population dynamical attractor is unique. An ESS is such a value X^* of X that $sX^*(Y) < 0$ for all YX^*. Often it is difficult to calculate s itself, whereas it is still possible to find some nice expression in X and Y that is monotonically related to s in Y for each value of X. Or else some expression which is sign equivalent to s. In those cases we can first maximise s for Y and then set Y equal to X to obtain X^*. For one dimensional trait spaces one can deduce both the position of the ESS's and the evolutionary convergence to them by plotting the sign pattern of s in the (x,y)-plane. I shall refer to this plot as the Pair-wise Invasion Plot. Mutants for which s is positive can invade. They can take over only when $sy(x) < 0$. s changes sign on the diagonal and possibly on some other curves. Where these curves cross the diagonal we have (local) Evolutionarily Singular points. These points correspond to either fitness maxima or fitness minima in the y-direction.

It is possible by subsequent mutant substitutions to converge to or diverge from a singular point, be it a fitness minimum or a maximum. This can be read of from the PIP. If convergence is to a fitness maximum the population stays there. These are the good evolutionary attractors. These attractors are a subset of the ESS's only. If it converges to a fitness minimum the population will start to become dimorphic.

The dimorphic region of the (x_1,x_2)-plane is characterised by the fact that x_1 and x_2 can invade into each other. Dimorphic populations can be analysed in the same manner as monomorphic ones. We ask which mutants can invade and possibly take over. For simplicity we shall from now on consider the case of small mutational steps. This allows us to draw evolutionary isoclines in the subset of (x_1,x_2)-plane corresponding to dimorphisms.

It is possible to write down a full classification of the singular points in terms of the second partial derivatives of s in the x and y directions. Intriguingly these quantities also determine the evolutionary progression in the dimorphic region near to the diagonal. This is due to the fact that a dimorphic population with two equal resident types provides the same environment for an invading mutant as the corresponding monomorphic resident population.

A next step is to classify the possible bifurcation patterns of such singular points when a model parameter is changed. This effort is hampered by the fact that at the crucial point $x_1 = x_2 = x^*$ the function $sx_1x_2(y)$ only allows directional derivatives in the (x_1,x_2)-plane, and not a full derivative. But other regularities can be exploited. On the boundary of the polymorphism set in the (x_1,x_2)-plane one of the two types goes extinct while the other type remains. So basically the invasion problem close to such a boundary resembles the invasion problem in the corresponding monomorphic population. This allows us i.a. to tell where the isoclines cross the the boundaries. The lack of differentiability combined with these constraints

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leads to a collection of bifurcation patterns which differ in many ways from those commonly observed for differential or difference equations.

The classification of the common bifurcation patterns is based on geometric considerations only. Finding good algebraic characterisations is very much an open problem.

Masayasu Mimura

A phenomenological model of bacterial colonies

It is known that one bacterial species, *B. subtilis* exhibits diverse growth patterns depending on the environmental conditions; the concentrations of nutrient and agar. If the environment is quite poor (hard agar with poor nutrient) there appear very complex patterns with branched structures. It resembles DLA clusters. On the other hand, if the environment is rich, it shows a disk like patterns which propagate outward with constant velocity.

In order to theoretically understand such diversity and complexity of patterns, we propose a space time continuous model for the bacterial cells and the nutrients. The essential ansatz in modelling is that bacterial cells consist of two types: one is active cells and the other inactive cells. It is numerically demonstrated that our model generates very satisfactory patterns which are in quite good agreement with experiments. By this result it could be confirmed that such diverse patterns are generated by the same underlying principles.

Johannes Müller

Scaling methods and approximative equations for homogeneous reaction diffusion systems and applications to epidemics

We consider a reaction–diffusion equation which is homogeneous of degree one. This homogeneity is a symmetry. The dynamics is factorised into trivial evolution due to symmetry and nontrivial behavior. This is done by a projection into an appropriate hyper manifold. The remaining evolution equations are rather complex. We examine the bifurcation behavior of a stationary point of the projected system. Therefore techniques for dimension reduction similar to the Ginzburg–Landau approximation (GL) are used. Since we are not in the classical GL situation, the remaining approximative equations have a quadratic nonlinearity and the amplitude does not scale with ϵ but with ϵ^2. Moreover, the symmetry enforces that not only one but two equation are necessarily to describe the behavior of the system. This result is used to analyze an epidemic model.

Jürgen Nauroschat and Uwe an der Heiden

Transmembrane signaling via stimulatory G-Proteins

Guanine-nucleotide regulatory proteins ("G-proteins") are universal elements of the transmembrane signaling system, modulating and conducting external messages on their way from membrane receptors to effector units which control signal-specific intracellular processes. The effector most frequently involved is the enzyme adenylate cyclase, releasing the "second" messenger cAMP to the cytoplasmic domain.

We present a mathematical model of the receptor/stimulatory G- protein/ adenylate-cyclase network. The model is based on the biomolecular mechanisms underlying the activation and inactivation procedures of the pathway. In particular, a recently discovered negative feedback loop is taken into account by which activation of the G-protein favours receptor kinases to

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phosphorylate the agonist-occupied receptor, thus inducing inhibition of receptor/G-protein coupling. Another feature of the model is the inclusion of the so called receptor-sequestration which enables dephosphorylation of receptors in vesicles rich in phosphatase.

The model is expressed in terms of rate equations for a total of eleven biochemical species. By evaluation of quasi-steady-state conditions and conservation laws finally a system comprising four nonlinear differential equations is obtained. The remaining "essential" dependent variables represent the free and the agonist-bound receptors, the G-protein activity, and the output cAMP. The ordinary differential system is non-autonomous because of the external influence of the agonist signal.

The system is analyzed with respect to different stimulus-configurations. There is a bounded domain with the shape of a prism containing all biologically relevant trajectories, no matter which stimulus-configuration is applied. Of course, the prism contains the steady-states occuring under stationary input conditions. These steady-states can be shown to exist uniquely, to be locally asymptotically stable, and to depend monotonously on the input strength. This dependence is nonlinear, exhibiting saturation effects. The mathematical analysis is continued with respect to time-varying inputs and responses. The response to the onset of stimulation of a system adapted to the resting state is immediate for the two receptor states, but delayed for active G-protein and cAMP.

Numerically we illustrate several properties of the model, such as hypersensitivity and desensitization/resensitization-behavior, which are important characteristics of biological information processing.

Hans Othmer

Adaptive models for movement: from microscopic rules to macroscopic equations

The ability to detect external signals and respond to them by altering behaviours is characteristic of biological systems ranging from the cellular to the organismic level. Motile individuals must be able to detect food sources, the presence of prey, noxious substances, etc., and respond by altering their pattern of movement or other behaviour. Since most biological systems maintain a barrier between inside and outside, they must also have mechanisms for transducing external signals into internal signals. Many sensory systems are also able to adapt to constant stimuli, by which we mean that these systems are in effect "derivative sensors": a step change in external signal produces a transient rather than a permanent response.

The signal detection/transduction response systems for several cell types are now understood at the molecular level. These include the cellular slime mold *Dictyostelium discoideum* and the bacterium *E. coli*. In the first part of this lecture we discuss a new model for signal transduction in *E. coli*. We show that the model responds to both step changes in the attractant level and to slow exponential ramps in time, the two most commonly used experimental protocols. With additional assumptions about how the chemotactic proteins interact with the flegellar motor, we can also reproduce the observed bias in the swimming behaviour.

In the second part of the lecture we introduce a mathematical framework for incorporating the internal dynamics into the partial differential-integral equation that describes the evolution in space and time of the density of non-interacting individuals in a population. With begin with a so called velocity jump process and reduce it top a hyperbolic system in one space dimension. We prove that in certain cases steady state aggregation, i.e. a non-constant spatial distribution of the density, is impossible unless the sensory system adapts as described earlier.

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Andrea Pugliese

Evolution of virulence: interaction of population and evolutionary dynamics

In order to explain the evolution of virulence in microparasites, it is generally accepted that a trade-off exists between the transmission coefficient (β) and the disease-related mortality (ν).

If one assumes that the evolutionary time scale is slower than the time scale of epidemiological interactions, the ESS is obtained at the virulence level that maximizes $R_0 = \frac{\beta}{\mu+\nu}$, where μ is the mortality rate.

Assuming on the other hand that evolution of parasites occurs at the same time scale as hosts' demography (as it appears from several studies in viral evolution), the natural variable is the distribution of the various viral types. I use the variable x to describe "virulence", assume that every infected host is infected with a single type of parasites (this implies that type substitution within a host occurs on a faster scale) and that mutations occur isotropically in x. Approximating this last process with a diffusion operator, one obtains the system:

$$\begin{aligned} \frac{dS}{dt} &= b(S+I) - \mu S - S\int \beta(y)i(y,t)\,dy \\ \frac{\partial i(x,t)}{\partial t} &= \gamma\frac{\partial^2 i}{\partial x^2} + S\beta(x)i(x,t) - (\mu+\nu(x))i(x,t) \end{aligned}$$

that has to be complemented by boundary conditions.

When the parasite-induced deaths are large enough to regulate the population, there exists a unique positive equilibrium. The value of S at equilibrium increases with γ. If one assumes density-dependence in b, the result is the same, and the condition becomes a usual threshold condition.

In order to better understand the system, I used an approximated system of ODE, whose variables are S, I, m (the mean virulence) and V (its variance). If $\beta''(x) \leq 0 \leq \nu''(x)$ (an assumption usually made in the β-ν trade-off), this system admits a unique positive equilibrium that is locally asymptotically stable. The approach to the equilibrium may be oscillatory, in particular m may undergo large fluctuations. The mean virulence at equilibrium is always higher than the level that maximizes R_0; the interaction of time-scales thus changes not only the approach to equilibrium, but also the evolutionary equilibrium itself.

David Rand

Fluctuations and correlations on evolutionary dynamics

Most models for ecological, evolutionary, epidemiological and immunological dynamics are mean field models or PDE's. On the other hand the biological systems themselves, as well as being spatial, are also stochastic and have populations made up of individuals. What is the relevance of this for biological phenomena and how can we model such systems in a way that is mathematically controllable?

In the first part of the talk I considered some examples where simulations suggest new explanations of biological phenomena. Firstly I explained self-evolved criticality in host-pathogen systems. In these systems there is a critical transmissibility for the parasite and the system evolves so as to set the transmissibility to this value. Also, evolution in this system is 2-3 orders of magnitude slower than that in mean-field models.

The second example concerned a new explanation for the evolution and maintenance of sexual reproduction. This has long been an outstanding problem of evolutionary theory because the costs of sex are very high while the conjectured advantages are very weak. Our explanation

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involves the fact that parasites maintain high genetic diversity of the hosts which is distributed in space. Thus parasites attacking the sexual hosts have no evolutionary target. On the other hand, those attacking asexual hosts have a target and can therefore evolve to efficiently attack/exploit them.

The final example concerned the evolution of altruism. This was a problem for evolution recognised by Darwin who suggested a resolution in terms of group selection. Such explanations are now discredited and instead there are three new explanations: i) selection in trait groups, ii) kin selection and iii) reciprocal altruism. I presented a new explanation in which one considers the spatial structure of an invading population of altruists. By clumping they benefit each other and can get sufficient advantage in order to be able to invade.

The second part of the talk was concerned with the description of a correlation equation formalism for modelling such problems. One considers the underlying biological process and derives equations for low-order correlations and corrections. One tries to determine which correlations it is necessary to include in order for the correction terms to be a small scale stochastic variable that can be replaced by an approximate noise term. I then discussed how this formalism performs in terms of the above biological problems.

André de Roos

The spatial scale of interaction between predators and their prey

The main topic in this presentation is the influence of the spatial scale of interaction between predators and their prey on the ultimate dynamics of the system.

As one example, I will discuss the dynamics of a predator-prey interaction in which the predator individuals forage on a broad spatial scale while the prey individuals exhibit only restricted use of space. Predators are characterized by a non-linear functional response which depends on the local prey density. Prey are assumed to occupy patches, forming a metapopulation with low migration among patches. The predator population is assumed to exert a globally uniform predation pressure on the prey subpopulations. The non-linearity in the functional response to local prey density results in the occurrence of multiple equilibria, which differ in the fraction of prey patches that are (nearly) empty. Equilibria with a larger fraction of empty prey patches are more stable. The system tends to approach equilibria with a sufficiently high number of empty prey patches, so that global population dynamics are stable. If unstable dynamics are observed, the fluctuations in local prey density exhibit predictable characteristics. Hence, a non-linear response of the predator to local prey density can induce pattern formation in prey density and global stabilization. These results carry over to situations in which prey migration between patches does occur or the spatial domain occupied by the prey population is continuous instead of subdivided into patches.

Joan Saldaña

Evolutionarily stable growth rates in continuously size-structured populations

The *general life history problem* can be formulated as the following question: "How should an organism optimally allocate its resources to growth, survival and reproduction?" Here, by means of maximising the intrinsic growth rate λ of the population of consumers, we find the evolutionarily stable allocation of the energy uptake between growth and reproduction in the following size-structured population model (endowed with a positive initial condition (u_0, v_0, r_0)):

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$$
\begin{cases}
u_t + [V(x,r)\,u]_x = -m(r)\,u, \quad x \in [0,l),\ l \le \infty, \quad t > 0, \\
V(0,r)\,u(0,t) = \displaystyle\int_0^l \beta(x,r)\,u(x,t)\,dx + \beta(l,r)\,v(r), \quad t > 0, \\
v' = -m(r)v + \lim_{x \to l}(V(x,r)\,u), \quad t > 0, \\
r' = g(r)r - f(r)\,L(u,v), \quad t > 0,
\end{cases}
$$

where $u(x,r)$ denotes the density of the *growing individuals* with size x at time t, $v(t)$ denotes the *non-growing individuals* at time t and $r(t)$ denotes the *resource level* at time t. Further, we assume that $V(x,r) = f(r)\,k(x)$ with $f(0) = 0$, $f(r) > 0$ for all $r > 0$ and $f'(x) > 0$; $\beta(x,r) = f(r)[1 - k(x)]\,b(x)$ with $0 < k(x) \le 1$ and $b(x) \ge 0$ for all $x \in [0,l)$; $m(r) > 0$ with $m'(r) < 0$; $g'(r) < 0$ with $g(r_c) = 0$ for some $r_c > 0$; and $L(u,v)$ is a positive continuous linear functional.

In the model, the energy uptake is channeled between growth -in a proportion k- and reproduction -in a proportion $(1-k)$- in such a way that this partition in growing individuals depends on their size. The aim of the present study, that has been carried out in collaboration with Àngel Calsina, is to find an allocation function $k(x)$ that maximises λ.

Nick Savill and Paulien Hogeweg

(Some) evolutionary consequences of self-structured spatial patterns

We are interested in how self-structured spatial patterns can influence the ecological and evolutionary dynamics of populations and the feedback of the evolutionary changes on the spatial patterns.

An example model system is described that demonstrates these ideas: namely the evolution of parasitoid aggregation in a spatially extended host-parasitoid model. In the model it turns out that the direction and strength of the selection pressure on the parasitoids is determined by the spatial pattern the parasitoids find themselves in (spirals and turbulence in this case). Moreover, there is competition on the level of the patterns which determines the evolutionary outcome of the aggregation strength. It is then useful to think of the spiral waves as entities in their own right. This leads to questions like "Is there selection on the level of spirals?", etc.

This behaviour comes about because of the interaction of processes across spatial and temporal scales.

Birgitt Schönfisch

Dimer automata

We define a class of discrete dynamical systems which we call dimer automata. In dimer automata the new states of *two* neighbouring cells are functions of the states of those two cells, whereas in cellular automata the new state of *one* cell is a function of the states in the neighbourhood. Synchronous dynamics gives rise to conflicts but with asynchronous dynamics such systems are very natural. Dimer automata are very simple, they have some advantages in modelling spatial spread. We present a definition, a classification, a first approach to determine approximate asymptotic densities and examples how to determine the long term dynamical behaviour. Finally we give an example applying the dimer concept to an alignment model.

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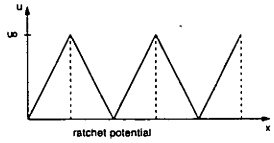
Frank Schweitzer

Generation of directed motion by means of active Brownian particles

The transition of Brownian (disoriented) motion into a directional (ordered) motion can be considered as a virtual pattern formation. We introduce a model based on active Brownian particles, which i) are able to store energy in an internal energy depot, which can be converted into kinetic energy, and ii) are able to change their environment by modifying a local potential, which in turn influences the further motion.

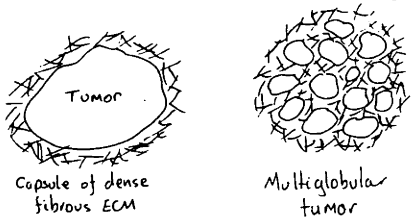
Different examples to generate directed motion are discussed: i) the quasi-periodic motion of pumped Brownian particles between a localised energy source and a potential minimum, ii) the origination of directed motion in a ratchet potential (periodic, asymmetric potential), iii) the generation of directed motion based on chemotactic response of the particles.



Jonathan Sherratt

Mathematical modelling of tumor invasion

Correlations of cell phenotype driving invasion is a key cause for understanding tumor dynamics and for efficient implementation of anti-invasive therapies. We have modelled this using a system of partial differential equations governing benign and invasive cells, extracellular motion, degradative enzyme concentration and degradation products. Simplified submodels show the importance of haptotaxis and proteolysis actin together driving invasion, and also different benign tumor morphologies, in particular capsule formation and multi-lobularity. The full model framework enables these various components to be studied together, for example showing the way in which protease production can lead to the dissolution of a tumor capsule.



Angela Stevens

Pattern formation of interacting particles, induced by diffusing and non-diffusing media

In this talk the connection between localisation results for a single particle doing a reinforced random walk in one dimension, aggregation results for many interacting particles, doing the same and continuous chemotaxis equations were presented. This was done to understand the aggregation of myxobacteria which tend to glide on so called slime trails. The question is whether slime trail following accounts for the final aggregation. Davis (1990) showed that only

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a superlinear reinforcement of an attractive information accounts for localisation of a particle undergoing a reinforced random walk in one dimension. The diffusion approximation of this random walk leads to:

$$\begin{aligned} \partial_t p &= D\partial_x \left(\partial_x p - \left(\frac{p}{v} \partial_x v \right) \right) \\ \partial_t v &= \lambda p \text{ or } \lambda v p \end{aligned}$$

where p denotes the probability density and v the density of the reinforcement information conditions on the path. For Neumann boundary conditions, an initial peak for p and $\partial_t v = \lambda v p$, p blows up in finite time, $\partial_t v = \lambda p$ the initial peak of p breaks down. So this result agrees nicely with Davis' (1990) result. The same can be done in two dimensions with similar findings. Simulations of the reinforced random walk for many particles show that not only the reinforcement has to be strong to account for aggregation but also the positive reaction towards the existing trails has to be stronger. This gives rise t the question: When does the chemotaxis describe the gliding of interacting populations of bacteria?

If one sets up stochastic equations for each particle in an N particle system, equivalent to the above mentioned Focker-Plank equation, and adds rules for the interaction of the particles - it should be moderate interaction - the chemotaxis system can be derived rigorously.

Sabine Stöcker

Models for fish schools

Schooling behavior is a challenging topic in the context of animal aggregation. It is also of economic importance for the estimation of stock sizes. An individual based movement model will be developed, taking into account energetic advantages of schooling. This model is a cellular automaton with a hexagonal grid. The latter considers the geometry of a school, where fish swim in a diamond-shape configuration in order to make use of the velocity, induced by the tail strokes of preceding fish. Furthermore, knowing the induced velocity field allows to consider the energetic needs of fish swimming in that school and to describe the break up of schools due to oxygen depletion. This allows to estimate maximum school sizes.

Catelijne van Oss, Andreas Deutsch and Wolfgang Alt

A spatial model of dynamic instability in microtubules

Microtubules are long, thin polymers that constitute an important part of the cytoskeleton of living cells. One of their functions is to separate the duplicated chromosomes during cell division. Both *in vivo* as *in vitro* it is observed that microtubules can show a unique dynamic behaviour called "dynamic instability", in which phases of slow polymer growth alternate with rapid shrinkage [7]. Apparently, the transitions between these phases occur at random. In a microtubule solution, the states (growing or shrinking) of the microtubules can be either uncorrelated or nearly synchronous. Even traveling waves of microtubule assembly/disassembly are observed. The phenomenon of dynamic instability is associated with a change in the energy state of the monomer following polymerisation, which makes the polymer less stable. This results in polymer shrinkage if the rate of energy change exceeds the polymerisation rate, and polymer growth in the reverse case [5,9]

Until now, models of dynamic instability in microtubules have merely focused on temporal behaviour (see for instance [1,2,4,6]). The first spatial model was made by [8] to describe the

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spatial organization of microtubules growing from a central nucleation center (the centrosome). Our aim is to study microtubule oscillations and spatial pattern formation without the presence of an organising centre. For this, we set up an individual-oriented model, in which the individuals are the monomers (similar individual-orientated models have proven to be successful in other systems that display spatial structures, see for instance [3]). The monomers are characterized by their (x, y) position and a state variable. The state can be either of the following: free monomer, monomer situated at the tip of a polymer, monomer situated inside a polymer. In addition, a monomer in each of these three states can be either energy-rich or energy-poor, which results in a total of six possible states. Dependent on their own state and that of their neighbours, monomers can diffuse, change their energy state, assemble into polymers and disassemble. With this model at hand, we are able to assay the influence of local monomer concentrations on the behaviour of individual polymers. Also, the model allows investigation of spatial patterns resulting from "communication" between neighbouring polymers mediated by the local monomer concentration.

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Nick Savill and Maarten Boerlijst.

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Tagungsteilnehmer

Prof.Dr. Fred Adler
Dept. of Mathematics and Biology
University of Utah

Salt Lake City , UT 84112
USA

Dr. Maarten C. Boerlijst
Department of Zoology
University of Oxford
South Parks Road

GB-Oxford OX1 3PS

Prof.Dr. Wolfgang Alt
Abteilung Theoretische Biologie
Botanisches Institut
Universität Bonn
Kirschallee 1

53115 Bonn

Prof.Dr. Jim M. Cushing
Dept. of Mathematics
University of Arizona

Tucson , AZ 85721
USA

Prof.Dr. Ovide Arino
Departement de Mathematiques
Universite de Pau, Appl. URA 1204
B.P. 290
Avenue de l`Universite

F-64000 Pau

Dr. Andreas Deutsch
Abteilung Theoretische Biologie
Universität Bonn
Kirschallee 1

53115 Bonn

Dr. Ellen Baake
MPI für Entwicklungsbiologie
Spemannstr. 35/IV

72076 Tübingen

Dr. Ulf Dieckmann
Wissenschaftskolleg zu Berlin
Wallotstr. 19

14193 Berlin

Prof.Dr. Nicola Bellomo
Dipartimento di Matematica
Politecnico di Torino
Corso Duca degli Abruzzi, 24

I-10129 Torino

Prof.Dr. Odo Diekmann
Vakgroep Wiskunde
Universiteit Utrecht
Postbus 80.100

NL-3508 TA Utrecht

Gefördert durch
DFG Deutsche Forschungsgemeinschaft

Prof.Dr. Regis H. Ferriere
Institute d'Ecologie
Univ. Paris 6
7 quai Saint-Bernard

F-75252 Paris Cedex 05

Prof.Dr. Mats Gyllenberg
Institute of Mathematical Sciences
University of Turku

SF-20014 Turku

Eckhard Finke
Institut für Ökologie
Universität Jena
Neugasse 23

07743 Jena

Prof.Dr. Karl Peter Hadeler
Lehrstuhl für Biomathematik
Universität Tübingen
Auf der Morgenstelle 10

72076 Tübingen

Prof.Dr. Marino Gatto
Dipartimento di Elettronica e
Informazione
Politecnico di Milano
Piazza Leonardo Da Vinci 32

I-20133 Milano

Prof.Dr. Andreas V.M. Herz
Institut für Biologie
Humboldt-Universität
Invalidenstr. 42

10115 Berlin

Prof.Dr. Daniel Grünbaum
Dept. of Mathematics
University of Utah

Salt Lake City , UT 84112
USA

Thomas Hillen
Lehrstuhl für Biomathematik
Universität Tübingen
Auf der Morgenstelle 10

72076 Tübingen

Prof.Dr. Shay Gueron
Department of Mathematics
Technion
Israel Institute of Technology

Haifa 32000
ISRAEL

Prof.Dr. Georgi P. Karev
Center of Ecology and Production of
Russian Academy of Sciences
69 Novocheremushkinskaja

117418 Moscow
RUSSIA

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Markus Kirkilonis
CWI
Dynamical Systems Lab.
Kruislaan 413

NL-1098 SJ Amsterdam

Prof.Dr. Masayasu Mimura
Dept. of Mathematics
Hiroshima University

Hiroshima 730
JAPAN

Prof.Dr. Rene Lefever
Chim. Physique II
Universite Libre
Campus Plaine U.L.B.
Code Postal n. 231

B-1050 Bruxelles

Johannes Müller
Lehrstuhl für Biomathematik
Universität Tübingen
Auf der Morgenstelle 10

72076 Tübingen

Prof.Dr. Jürgen Lenz
Abteilung Theoretische Biologie
Botanisches Institut
Universität Bonn
Kirschallee 1

53115 Bonn

Jürgen Nauroschat
Fakultät für Naturwissenschaften
Universität Witten/Herdecke
Stockumer Str. 10

58453 Witten

Prof.Dr. Philip K. Maini
Centre for Mathematical Biology
Oxford University
24 - 29, St. Giles

GB-Oxford OX1 3LB

Prof.Dr. Hans G. Othmer
Dept. of Mathematics
University of Utah

Salt Lake City , UT 84112
USA

Prof.Dr. Hans A.J. Metz
Inst. of Evolutionary and
Ecological Sciences
Rijksuniversiteit Leiden
Kaiserstraet 63

NL-2311 GP Leiden

Prof.Dr. Andrea Pugliese
Dipartimento di Matematica
Universita di Trento
Via Sommarive 14

I-38050 Povo (Trento)

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Prof.Dr. David Rand
Mathematics Institute
University of Warwick
Gibbert Hill Road

GB-Coventry , CV4 7AL

Dr. Frank Schweitzer
Institut für Physik
Humboldt Universität Berlin
Unter den Linden 6

10099 Berlin

Prof.Dr. Andre M. de Roos
Dept. of Pure and Appl. Ecology
University of Amsterdam
Kruislaan 320

NL-1098 SM Amsterdam

Prof.Dr. Jonathan A. Sherratt
Mathematics Institute
University of Warwick
Gibbert Hill Road

GB-Coventry , CV4 7AL

Prof.Dr. Joan Saldana
Dep. de Matematiques i Informatica
Estudis universitaris de Vic
c/Miramarges 4

E-08500 Vic, Catalonia

Dr. Angela Stevens
Institut für Angewandte Mathematik
Universität Heidelberg
Im Neuenheimer Feld 294

69120 Heidelberg

Nicholas Savill
VAKGROEP Theoretical Biology and
Bioinformatics
Padualaan 8

NL-3584 CH Utrecht

Sabine Stöcker
Pelagic Fisheries Research Program
University of Hawai, Jimar
1000 Pope Road

Honolulu , HI 96822
HAWAI

Birgitt Schönfisch
Lehrstuhl für Biomathematik
Universität Tübingen
Auf der Morgenstelle 10

72076 Tübingen

Catelijne Van Oss
Abteilung Theoretische Biologie
Botanisches Institut
Universität Bonn
Kirschallee 1

53115 Bonn

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Fred Adler
Department of Mathematics and Biology
University of Utah
Salt Lake City, UT 84112
USA
tel: +(1)801-581-6848
fax: +(1)801-581-4148
email: adler@math.utah.edu

Wolfgang Alt
Theoretische Biologie
Universitaet Bonn
Kirschallee 1-3
D-53115 Bonn
GERMANY
tel: +(49)228-73-5577
fax: +(49)228-73-5513
email: wolf.alt@uni-bonn.de

Ovide Arino
Departement de Mathematiques
Universite de Pau, Avenue de l'Universite
64000 PAU
FRANCE

Ellen Baake
Zoologisches Institut
Luisenstr. 14
D-80333 Munchen
GERMANY
tel: +(49)7071-601-402
fax: +(49)7071-601-448
email: ellen@mpib-tuebingen.mpg.de

Nicola Bellomo
Department of Mathematics
Corso Duca degli Abruzzi 24
10129 Torino
ITALY
tel: +(39)11-5647514
fax: +(39)11-5647599
email: Bellomo@Polito.it

Maarten Boerlijst
Department of Zoology
South Parks Road
Oxford, OX1 3PS
UK
tel: +(44)1865-271279
fax: +(44)1865-310447
email: mcb@einstein.zoo.ox.ac.uk

James Cushing
Department of Mathematics, BLDG 89
University of Arizona
Tucson, AZ 85721
USA
tel: +(1)520-621-6863
fax: +(1)520-621-8233
email: cushing@math.arizona.edu

Andreas Deutsch
Theoretische Biologie
Universitaet Bonn
Kirschallee 1-3
D-53115 Bonn
GERMANY
tel: +(49)228-73-2081
fax: +(49)228-73-5513
email:deutsch@sn-bota-1.bota.uni-bonn.de

Ulf Dieckmann
International Institute for
Applied Systems Analysis
Adaptive Dynamics Network
2361 Laxenburg
AUSTRIA
tel: +(43)2236-807-386
fax: +(43)2236-71313
email: dieckman@iiasa.ac.at

Odo Diekmann
Vakgroep Wiskunde
Universiteit Utrecht, Postbus 80.010
3584 CD Utrecht
THE NETHERLANDS
tel: +(31)30-2531487
fax: +(31)30-2518394
email: o.diekmann@math.ruu.nl

Regis Ferriere
Lab. d'Ecologie
Ecole Normale Suprieure
tel: +(33)1-4329 ext 3778
fax: +(33)1-8172
email: ferriere@wotan.ens.fr

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46, rue d'Ulm
75230 Paris Cedex 05
FRANCE

Eckhard Finke
Institut fur Okologie
FG Theoretische Okologie u.
Systemanalyse, Neugasse 23
D-07743 Jena
GERMANY
tel: +(49)3641-630354
fax: +(49)3641-630425
email: Eckhard.Finke@rz.uni-jena.de

Marino Gatto
Dipartimento di Elettronica
Politecnico di Milano
Piazza Leonardo Da Vinci 32
20133 Milano
ITALY
tel: +(39)2-23993536
fax: +(39)2-23993412
email: gatto@elet.polimi.it

Danny Grunbaum
Department of Mathematics
University of Utah
Salt Lake City, UT 84112
USA
tel: +(1)801-585-7663
fax: +(1)801-581-4148
email: grunbaum@math.utah.edu

Shay Gueron
Department of Mathematics
Technion I.I.T.
Haifa 32000
ISRAEL
tel: +(972)4-8294092
fax: +(972)4-8324654
email: shay@math.technion.ac.il

Mats Gyllenberg
Department of Mathematics
University of Turku
20014 Turku
FINLAND
tel: 358-2-3336567
fax: 358-2-3336595
email: matsgyl@utu.fi

Karl-Peter Hadeler
Lehrstuhl fur Biomathematik
Universitaet Tubingen
Auf der Morgenstelle 10
D-72076 Tubingen
GERMANY
tel: +(49)7071-2976898
fax: +(49)7071-294-322
email: k.p.hadeler@uni-tuebingen.de

Andreas Herz
Department of Theoretical Physics
University of Bremen
D-28359 Bremen
GERMANY
tel: +(49)421-2182856
fax: +(49)421-2184869
email: herz@physik.uni-bremen.de

Thomas Hillen
Lehrstuhl fur Biomathematik
Universitaet Tubingen
Auf der Morgenstelle 10
D-72076 Tubingen
GERMANY
tel: +(49)7071-29-78827
fax: +(49)7071-294-322
email: thomas.hillen@uni-tuebingen.de

Georgy Karev
Centre of Ecology and Production of
Russian Academy of Sciences
69 Novocheremushkinskaja
117418 Moscow
RUSSIA
tel: 095-332-6990
fax: 095-332-2917
email: karev@spepl.msk.su

Markus Kirkilonis
CWI
Kruislaan 413
tel: +(31)20-592-4221
email: markus@cwi.nl

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1098 SJ Amsterdam
THE NETHERLANDS

Reni Lefever
Faculte des Sciences
Universite Libre de Bruxelles
Campus Plaine C.P. 231
1050 Brussels
BELGIUM
tel: +(32)2-650-5791
fax: +(32)2-650-5767
email: rlefever@ulb.ac.be

Jurgen Lenz
Theoretische Biologie
Universitaet Bonn
Kirschallee 1-3
D-53115 Bonn
GERMANY
tel: +(49)228-73-7467
fax: +(49)228-73-5513
email: lenz@sn-bota-1.bota.uni-bonn.de

Philip Maini
Centre for Mathematical Biology
Mathematical Institute
24-29 St. Giles
OXFORD, OX1 3LB
UK
tel: +(44)1865-273553
fax: +(44)1865-273583
email: maini@maths.ox.ac.uk

Hans Metz
EEW - Section Theoretical Biology
University of Leiden, PO Box 9516
2300 RA Leiden
THE NETHERLANDS
tel: +(31)10-4953070 (home)
tel: +(31)71-5274937 (work)
fax: +(31)71-5274900
email: metz@RULSFB.LeidenUniv.nl
Metz@iiasa.ac.at

Masayasu Mimura
Grad. School of Mathematical Sciences
University of Tokyo
3-8-1 Komaba, Meguro-ku
Tokyo 153
JAPAN
tel: +(81)3-5465-7025
fax: +(81)3-5465-7025
email: mimura@ms.u-tokyo.ac.jp

Johannes Muller
Lehrstuhl fur Biomathematik
Universitaet Tubingen
Auf der Morgenstelle 10
D-72076 Tubingen
GERMANY
tel: +(49)7071-2976843
fax: +(49)7071-294322
email: johannes.mueller@uni-tuebingen.de

Jurgen Nauroschat
Department of Mathematics
University of Witten/Herdecke
Stockumer Str. 10
D-58453 Witten
GERMANY
tel: +(49)2302-669-214
fax: +(49)2302-669-220
email: nauro@natwi.natwi.uni-wh.de

Hans Othmer
Department of Mathematics
University of Utah
102 Widstoe Building
Salt Lake City, UT 84112
USA
tel: +(1)801-581-3901
fax: +(1)801-581-4148
email: othmer@math.utah.edu

Andrea Pugliese
Dipartimento di Matematica
Universita'di Trento
38050 Povo
ITALY
tel: +(39)461-881686
fax: +(39)461-881624
email: pugliese@science.unitn.it

David Rand
Nonlinear Systems Lab.
tel: +(44)1203-523599
fax: +(44)1203-524182

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Mathematics Institute
University of Warwick
Coventry, CV4 7AL
UK
email: dar@maths.warwick.ac.uk

Andre de Roos
Department of Pure and Applied Ecology
University of Amsterdam
Kruislaan 320
1098 SM Amsterdam
THE NETHERLANDS
tel: +(31)20-5257-747
fax: +(31)20-5257-754
email: aroos@bio.uva.nl

Joan Saldana
Departament de Matematiques i
Informatica
Estudis Universitaris de Vic
08500 Vic, Catalonia
SPAIN
tel: 34-3-8861222
email: saldana@gregal.euv.upc.es

Nick Savill
Theoretical Biology and Bioinformatics
Utrecht University
Padualaan 8
3584 CH Utrecht
THE NETHERLANDS
tel: +(31)30-2533695
fax: +(31)30-2513655
email: njs@behold.biol.ruu.nl

Birgitt Schonfisch
Lehrstuhl fur Biomathematik
Universitaet Tubingen
Auf der Morgenstelle 10
D-72076 Tubingen
GERMANY
tel: +(49)7071-2976843
fax: +(49)7071-294-322
email: birgitt.schoenfisch@uni-tuebingen.de

Frank Schweitzer
Institute of Physics
Humboldt University
Unter den Linden 6
D-10099 Berlin
GERMANY
tel: +(30)2093-7636
fax: +(30)2033-7638
email: frank@summa.physik.hu-berlin.de

Jonathan Sherratt
Mathematics Institute
University of Warwick
Coventry, CV4 7AL
UK
tel: +(44)1203-523870
fax: +(44)1203-524182
email: jas@maths.warwick.ac.uk

Angela Stevens
Institut fur Angewandte Mathematik
Universitaet Heidelberg
Im Neuenheimer Feld 294
D-69120 Heidelberg
GERMANY
tel: +(49)6221-54-8980
fax: +(49)6221-54-5331
email: stevens@iwr.uni-heidelberg.de

Sabine Stocker
JIMAR
University of Hawaii
1000 Pope Road
Honolulu, HI 96822
USA
tel: +(1)808-956-5909
fax: +(1)808-956-4104
email: stoecker@soest.hawaii.edu

Catelijne van Oss
Theoretical Biology and Bioinformatics
Utrecht University
Padualaan 8
3584 CH Utrecht
THE NETHERLANDS
tel: +(31)30-2533688
fax: +(31)30-2513655
email: cvo@binf.biol.ruu.nl

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