MATHEMATISCHES FORSCHUNGSINSTITUT OBERWOLFACH

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Mathematische Biologie

24.10. – 30.10.1999

Organizers: O. Diekmann (Utrecht University) and K.P. Hadeler (University of Tübingen).
This meeting on Mathematical Biology brought together distinguished researchers, who represented a wide area of recent research. In 35 talks particular emphasis was given to the following fields:

- Models for immunology, diseases, parasites and viruses (N. Bellomo, L. Esteva, M. Mackey, J. Müller A. Pugliese, D. Rand)
- Stochastic and deterministic models for spatial spread, internal dynamics and pattern formation (W. Alt, V. Capasso, A. Deutsch, D. Grünbaum, S. Gueron, M. Gyllenberg, T. Hillen, M. Kirkilionis, M. Lewis, K. Painter, B. Schönfisch, A. Stevens)
- Models for evolution, mutation and selection (E. Baake, R. Bürger, U. Dieckmann, W. Gabriel, P. Hammerstein, N. Heino, V. Hutson, H. Metz, M. Möhle)
- Theoretical ecology (C. Cosner, A. Hastings, H. Heesterbeek, J. Hofbauer, F. Kelpin, J. Saldana).
- In addition there was a contribution on psychophysics by U. an der Heiden and a lecture on a generalized law-of-mass-action by R. Schimming. M. Baake participated in discussions along the whole meeting.

In the sequel you will find detailed abstracts of the talks.
The relevant levels of scaling in biological systems and the transition from individual behavior to macroscopic models turned out to be a major question in most of the talks.

The organizers were quite sensitive to the atmosphere of the meeting and initiated four round table discussions corresponding to the four main topics of this conference.

- Balance laws when individuals are characterised by both a physiological state and position in space (Chair: Daniel Grünbaum)
- Ecology (Chair: Alan Hastings)
- Cells, molecules and genes (Chair: David Rand)
- Population genetics (Chair: Ellen Baake)

These discussions were of great success. Interpretations of different results were discussed, important open problems have been stated and future research directions were streamlined. We are sure that all participants agree to thank the organizers for this good initiative and we hope that this motivates other meetings and conferences to include round table discussions in small groups as well.

February 2000, Fleur Kelpin and Thomas Hillen.

Abstracts of talks

Dynamics of Dense Swarms and Cell Aggregates

W. Alt

Skeins (1-dimensional "queues") of travelling birds typically show oscillating swarm extension and, often, "compression" waves that start at the leading bird and travel backwards.

These dynamic phenomena can be fairly reproduced by a discrete stochastic ordinary differential equation system modelling the force balance between the individual tendency to attain a preferred speed and mutual interaction forces as an attraction/repulsion potential and an entrainment of speeds among nearest neighbours.

Defining a discrete "volume density" as the ratio between body size δ and distance of neighbours, one easily derives continuum mass and force balance equations in the hydrodynamic limit $\delta \to 0$. Indeed, one obtains the 'classical' compressible Navier-Stokes equation with a density dependent stress function $f(u)$ and viscosity coefficient $\mu(u)$. The natural boundary condition at the moving boundary (along characteristics of the hyperbolic equation) arises as a singularly perturbed no-stress condition, namely an inhomogeneous Neumann condition $f(u) + \mu(u)\partial_x v = 0$ for the parabolic equation for the velocity v.

Discretisation and numerical solutions of this PDE-problem (eventually after introduction of stochastic perturbation) show similar effects of oscillations and damped transition waves as the original stochastic discrete ODE-model.

Advantages of both treatments, PDE and ODE, are mentioned including nonlinear eigenvalue computations and correlation analyses. Generalisations include models for cell aggregates (with application in tumour growth or wound healing), where cell width $B_i(t)$ can grow with time, or split with eventual cell division - both depending on local density.

Distance Measures and Substitution Processes in Molecular Phylogeny

E. Baake

Molecular phylogeny, the art of reconstructing the history of a sample of sequences from the leaves of a tree, relies on the concept of additive metric trees. If a tree-additive distance measure is available between leaves, the tree topology and the branch lengths may be reconstructed. One very general distance concept is the so-called "paralinear distance" as defined as a function of the pairwise joint probabilities of the letters at the leaves, is tree-additive if the underlying substitution process is a Markov process on a tree, where the transition matrices may vary from edge to edge. We consider two questions:

1. How are the branch lengths corresponding to the paralinear distance related to the substitution process?

2. Can information about the substitution process itself (as opposed to just the tree geometry) be inferred from pairwise joint distributions of letters at the leaves?

Answers:

1. The paralinear branch length may be understood as the sum of the relative probability fluxes, integrated over the edge, and averaged over the forward and reversed directions, where the averaging reflects our ignorance of the position of the rod.

2. Markov transition matrices for the edges may not be singly inferred, but return-trip matrices (forward and back again across an edge or path) may be inferred up to conjugacy in case of internal edges.

Tumor Immune System Interactions

N. Bellomo

The development of mathematical models towards an immuno-mathematical theory is a promising, however difficult field of applied mathematics. Although the activity in the field of theoretical immunology is still at the stage of pioneer work, it is worth to be searched, considering the great impact it can have in improving quality of life.

The development of tumor growth models is of interest for the simulation and optimization of tumor treatment plans. From a mathematical point of view it is interesting in the context of the development of structures and pattern formation. Biologically it can lead to a deeper insight into tumor immune system interactions. The final aim of research activity in the field is: **the development of an immuno-mathematical theory able to describe, by means of evolution equations, the interactions and competitions between tumors and the immune system**.

The evolution of the tumor-immune system interactions can be described by the following main features:

- Loss of differentiation and replication of tumor cells;
- Activation and defense, or inhibition and cooperation of the immune system;
- Interaction and competition between tumor and immune cells;
- Cytokine signal emission and reception regulating cell activities;
- Condensation of tumor cells, macroscopic diffusion, and angiogenesis.

This characterization suggests to identify three **natural scales** also connected to different stages of the disease: the actions on the **cellular scale** are triggered by signals stemming from a **sub-cellular level** and have an impact on a **macroscopic scale**, i.e. on the organism, if tumor cells condense and when tumors grow and spread.

In the following we will describe these three levels more in detail.

The sub-cellular scale

The evolution of a cell, as described by Forni et alii [1], and others, is regulated by the genes contained in its nucleus. Receptors on the cell surface can receive signals which are then transmitted to the cell's nucleus, where the fore-mentioned genes can be activated or suppressed. The capability of receiving particular signals can modify the usual behavior of a cell. In extreme situations, particular signals can induce a cell to reproduce itself in the form of identical descendants, that is the so-called clonal expansion, or to die and disappear apparently without trace, that is the so-called apoptosis or programmed death. Clonal expansion activates a competition between tumor cells and cells of the immune system. If the immune system is active and able to recognize the tumor cells, then it may hopefully be able to develop a destruction mechanism. Otherwise, tumor growth may develop progressively. The activation and disactivation of immune cells, too, can be regulated by cytokine signals.

The cellular scale

The fact that the evolution of tumors and their competition with the immune system has to be modelled on a cellular level is well recognized in the literature, as documented in the paper by Tomlison and Boomer [2]. In this work simple models are proposed to simulate the effects of the failure of programmed cell death and of the loss of cell differentiation. These two events are recognized to cause the proliferation of tumor cells. If and when a tumor cell is recognized by immune cells, a competition starts, as documented in [3], which may end up either with the destruction of tumor cells or with the inhibition and depression of the immune system. Cellular interactions are regulated by signals emitted and received by cells through complex image recognition processes. Therefore, the connection to the

fore-mentioned sub-cellular scale is evident: interactions apparently developed at the cellular level, are ruled by interactions which are developed at a lower scale [5]. On the other hand, the development of tumor cells, if not suppressed by the immune system, tends towards condensation into a solid form so that macroscopic features become important.

The macroscopic scale

After a suitable maturation time tumor cells start to condense and aggregate into a quasi-spherical nucleus and interact with the outer ambient, say environment cells and immune system. These interactions usually occur on the surface and within a layer where angiogenesis phenomena take place. Here, one has the overlap of cellular phenomena with typical macroscopic behaviors such as diffusion phenomena or, more in general, phenomena that can be related to the conservation or evolution of macroscopic variables such as tumor size.

The first step is the identification of the typical features of tumor growth following the early stage of free cells. A very schematic description is the following: Tumor cells start to condense into molecular clusters and finally into a quasi-spherical solid state, which may be constituted by several multicellular aggregates. Then, a quasi spherical tumor grows and interacts with the outer ambient. A description of this stage requires the identification of two zones divided by two mobile frontiers: The inner zone of the necrotic cells which die due to the absence of nutrients, and the outer zone of active tumor cells growing due to the support of environmental cells penetrating into the tumor zone by capillary sprouts (angiogenesis).

Several interesting contributions, which develop continuum models where the relevant phenomena are described by simple diffusion equations, are available in the literature. The relevant literature is cited in the review paper [5].

The analysis of mathematical problems generated by the application of models generates several sophisticated mathematical problems. The following ones are indicated among several ones.

i) Models of cellular theory are stated by nonlinear integro differential equations similar to those of nonlinear kinetic theory (the Boltzmann equation). The mathematical analysis should develop a qualitative theory with special attention to bifurcation phenomena. In particular, the bifurcation separates the evolution where the immune system is able to control the neoplastic growth, from those where the immune system is inhibited by tumor cells.

ii) The analysis of macroscopic models refers to moving boundary problems for systems of nonlinear partial differential equations.

References

[1]Forni G., Foa R., Santoni A., and Frati eds., **Cytokine Induced Tumor Immunogeneticity**, (Academic Press, New York, 1994).

[2]Tomlison I., and Boomer W., Failure of programmed cell death and differentiation as causes of tumors: some simple mathematical models, *Proc. Natl. Acad. Sci. USA*, 92, 11130–11134, (1995).

[3]Bellomo N., Preziosi L., and Forni G., On a kinetic (cellular) theory of the competition between tumors and the immune host system, *J. Biolog. Systems*, 4, 479–502, (1996).

[4]Bélair J., Glass L., an der Heiden U., and Milton J. eds., **Dynamical disease - Mathematical Analysis of Human Illness**, (American Institute of Physics Press, Williston, 1995).

[5]Bellomo N. and De Angelis E., Strategies of applied mathematics towards an immuno-mathematical theory of tumors and immune system interactions, *Math. Models Meth. Appl. Sci.*, 8, (1998).

Evolution of Genetic Variability and the Advantage of Sex and Recombination in Changing Environments

R. Bürger

The role of recombination and sexual reproduction in enhancing adaptation and population persistence in temporally varying environments is investigated on the basis of a quantitative-genetic multilocus model. Populations are subject to density-dependent regulation with a finite growth rate, diploid, and either asexual, or randomly mating and sexual with or without recombination. A quantitative trait is determined by a finite number of loci at which mutation generates genetic variability. The trait is under stabilizing selection with a optimum that either changes at a constant rate in one direction, or exhibits periodic cycling, or fluctuates randomly. It is shown by Monte-Carlo simulations that if the directional-selection component prevails, then freely recombining populations gain a substantial evolutionary advantage over nonrecombining and asexual populations that goes far beyond that recognized in previous studies. The reason is that in such populations, the genetic variance can increase substantially and thus enhance the rate of adaptation. In nonrecombining and asexual populations, no or much less increase of variance occurs. It is explored by simulation and mathematical analysis when, why, and by how much genetic variance increases in response to environmental change. In particular, it is elucidated how this change in genetic variance depends on the reproductive system, the population size and the selective regime, and what the consequences for population persistence are.

References: Genetics 153: 1055-1069 (1999).

From the Individual Behavior Subject to Stochastic Fluctuations to the PIDE Describing the Global Behavior of Aggregating Populations

V. Capasso

Starting from field experiments, we consider animal grouping due to the interplay of interaction between individuals which tend to the formation of spatially concentrated patterns and dispersion caused by repulsion to avoid overcrowding. As a specific example the social behaviour of a slave-maker species of ants (Polyergus Rufesceus) is taken.

As detected in field experiments carried out by the authors, during their raids, Amarous tend to aggregate in a transversally organized army, still avoiding overcrowding. We interpret this phenomenon as a combination of aggregative and repulsive social forces acting on each individual. A relevant phenomenon is the spatial dependence of the social parameters on different environmental conditions that may impose restrictions on the sensory range of individuals. We describe the individual dynamic, in a group of N by means of N stochastic differential equations (SDE's) where the drift depends upon the social "forces" and random dispersal is modelled by independent Brownian motion. We assume for the aggregation "force" a long range dependence upon the (empirical) distribution of particles, and the repulsion "force" a mesoscale range dependence. Simulations show a good agreement with data. For N tending to infinity the multiple scale approach for aggregation and repulsion kernels lets us make use of the "moderate" limit theory of large numbers as developed by K. Oelschläger. A rigorous derivation shows that the limiting distribution of particles admits a density satisfying a deterministic advection-diffusion integro-differential equation, which corresponds to models present in literature (see e.g. Minura et al.).

Modeling the Effects of Aggregation in Population Dynamics

C. Cosner

The dynamics of populations can be strongly influenced by the way that the populations are distributed in space. This can be seen in simple mean-field models and also in spatially explicit models incorporating dispersal and population dynamics. A factor that can influence population dynamics is the degree

to which populations tend to aggregate. In the case of simple predator- prey models, the standard assumption is that populations are well mixed, this leads to a mass action law for the encounter rate of predators and prey. Typically a mass action law then leads to a functional response depending only on prey density. Assuming that predators are localized in some way, eg. by aggregation, leads to functional responses which depend on both prey and predator densities. That in turn can alter predictions about the persistence (coexistence) of competing predators. In a spatially explicit model with logistic growth but nonlinear diffusion, the assumption that the diffusion rate decreases as population density increases can lead to the conclusion that the population experiences an Allee effect (i.e. decline at low densities but growth at high densities), even if the population dynamical terms (per se) are purely logistic!

Migration Automata: a Model Concept for Simulation and Analysis of Cell-based Pattern Formation

A. Deutsch

Migration automata offer a modelling perspective to typical examples of cellular pattern formation based on direct *cell-cell interactions*, e.g. street formation of Myxobacteria or sorting out of cells during gastrulation. Migration automata can be alternatively viewed as stochastic cellular automata or extensions of lattice-gas automata.

We have characterized basic, in particular density and orientation dependent interactions. Density-dependent interaction provides a model of differential adhesion while orientation-dependent interaction yields a model of collective motion or swarming. Coupling of various "interaction modules" leads to models of more complex pattern formation. For example, differential adhesion together with orientation-dependence may explain pigment pattern formation of salamander larvae.

Migration automata can be used as simulation tool of spatio-temporal pattern formation but also allow for straightforward analysis. In particular, Fourier analysis permits to deduce important orientational and spatial aspects of simulation outcomes and to view the onset of swarming and aggregation as phase transitions.

Evolutionary Branching in Sexual Populations: A New Model for Sympatric Speciation

U. Dieckmann, M. Doebeli

Understanding speciation is a fundamental problem in evolutionary biology. While it is generally accepted that many species have originated through allopatric divergence in geographically isolated populations of the same ancestral species, the possibility of sympatric speciation has often been dismissed. Recent results in the theory of adaptive dynamics, however, suggest that once density and frequency dependence, naturally arising from the ecological feedback between a population and its environment, are properly incorporated into models of evolutionary change, convergence to disruptive selection becomes a common and robust phenomenon. The resulting process of evolutionary branching, where a population with a unimodal distribution for a metric character undergoes directional selection to a state at which selection turns disruptive, has been suggested as a paradigm for sympatric speciation in clonal species. Here we extend the results of clonal adaptive dynamics to sexual populations. We use explicit multilocus genetics to describe sexual reproduction in an individual-based model, and we consider the evolution of assortative mating, depending either on the character under disruptive selection or on a selectively neutral marker trait. In both cases we show that, for generic models of resource competition, evolution of assortative mating often leads to reproductive isolation between ecologically diverging subpopulations.

Fixation of Clonal Lineages under Muller's Ratchet

W. Gabriel, R. Bürger

For clonal lineages that differ in their deleterious mutational effects s the probability of fixation is investigated by mathematical theory and Monte-Carlo simulations. If s in one or both lineages is sufficiently small, the lineage with the smaller s will become fixed with high probability. If, however, the deleterious effects are larger than roughly 0.1 in both lineages, the probability of fixation is independent of s and depends only on the initial frequencies of the lineages. Then the competition is not driven by the ratio of mean fitnesses of the lineages but by the relative sizes of the zero-mutation classes, which are independent of s. After the loss of the zero-mutation class of a lineage the other lineage will spread to fixation with high probability and within a short time span. The independence of the fixation probability on s in a single population leads to dramatic effects in metapopulations: lineages with larger s have a much higher fixation probability. The range of advantageous values s is expanded to even lower values if the migration rate between the subpopulations becomes small. As soon as a lineage with a higher s is established, it can spread because it is protected from invasion of lineages with lower s.

Internal State-mesiated Biological Random Walks With and Without Spatial Memory

D. Grünbaum

In this talk I gave several examples of biological systems in which organisms or cells within organisms perform biased random walks to climb environmental gradients, and in which the random walk behavior is mediated by internal state variables. Examples included bacteria with surface receptors, zooplankton with phenotypically plastic morphologies, and seabirds with cognitive assessments of their surroundings. Populations of individuals that use these behaviors can be described exactly using a linear Boltzmann equation, in which a vector of internal state variables are accounted for together with the more usual position and velocity variables. In the model I presented, the internal states can undergo continuous change in response to the environmental variable (e.g. increasing hunger level with increasing time since feeding), and can also undergo finite "jumps"(e.g. a large decrease in hunger when a large food item is encountered). When spatial gradients in the population and the environmental variable are sufficiently small, the Boltzmann equation can be scaled with a small parameter reflecting the difference between relatively short spatial scales of movement between turns and relatively long spatial scales of environmental variation. In that case, a perturbation expansion leads at first order to a solution for the local equilibrium state-velocity distribution. I showed that at second order the particular solution (that leads to population flux) can be expressed in terms of the solutions to two reduced partial differential equations. The integrals of these solutions over velocity and state are the diffusion and chemotaxis coefficients in the parabolic approximation to the original hyperbolic system. I showed a comparison between an individual-based simulation and the approximating PDE that shows an excellent agreement in the predicted state-space distribution. In the final part of the talk, I showed another type of random walk, in which a male moth attempts to climb a pheromone trail to locate a female under turbulent atmospheric conditions. I presented a preliminary analysis of moth trajectories in a wind tunnel that are suggestive of a spatial memory. I then showed a simulation model of a moth behavior that uses a simple spatial memory to climb gradients much more effectively than comparable behaviors without spatial memory. I argued finally that since many organisms can be shown to use biased random walks and also to have a spatial memory, incorporating spatial memory into biological models will be a challenging and useful research direction.

Birth and Death Processes, and Mass Action Laws in Biology and Chemistry: an Interacting Particle System Approach

S. Gueron

Birth-death processes describe the stochastic evolution in time of a random variable whose value increases or decreases by one in a single event. Many models, for example in chemistry and in population biology, can be viewed as (coupled) birth-death processes, although this interpretation is not often made explicitly.

A typical approach for modeling a stochastic process is implemented by writing down deterministic differential equations for its time evolution. Such deterministic models hope to approximate the expectation of the stochastic process when the state space is sufficiently large. However, some examples like the group size distributions of coagulation-fragmentation processes show that this is not always the case.

In this address, we compare use the dynamics of stochastic and deterministic models using ergodic birth-death processes on a finite state space with N states. We focus on asymptotically linear and mass action type birth-death processes, that have applications to population biology and chemistry. Asymptotic expansions of the equilibrium expectations of these processes are derived and compared with their deterministic counterparts. We show that as $N \to \infty$, both asymptotic expansions agree up to the first or second leading orders.

Lack of Uniqueness in Structured Population Models

M. Gyllenberg

I give examples, where the initial value problem

$$\begin{aligned} \frac{\partial}{\partial t} n(t,x) + \nabla \cdot g(I(t),x) n(t,x) &= 0, \quad t > 0,\ x \in \mathbf{R}^n \\ I(t) &= \int_{\mathbf{R}^n} \gamma(x) n(t,x) dx, \quad t > 0 \\ n(0,x) &= n_0(x),\ x \in \mathbf{R}^n \end{aligned}$$

has infinitely many solutions. I emphasize the main features leading to nonuniqueness and draw conclusions concerning modelling principles for structured populations.

Conflict and Cooperation Within the Organism

P. Hammerstein

In the early days of theoretical biology, Ronald Fisher identified the selective forces that operate in sex ratio evolution. His explanation of why the sexes are produced in roughly equal numbers had major impact on both theoretical and empirical research in biology. Quite unexpectedly, sex ratio theory helped to understand intraorganismic conflicts in animals and plants. One example is the worker-queen conflict concerning proportions of male and female reproductive forms in superorganisms of social hymenoptera. Another example is the sex ratio conflict between cytoplasmic and nuclear DNA. Bacteria of the genus Wolbachia illustrate this conflict impressively. They induce sex change, parthenogenesis, and cytoplasmic incompatibility in their hosts. The invasion dynamics of Wolbachia in host populations has been modelled and is roughly understood. In contrast, the evolutionary dynamics has received little attention and needs to be explored more extensively. This could shed some light on endosymbiont evolution and on the "parliament of genes" problem. As far as conflict within the nuclear genome is concerned, sex ratio theory has led to the empirical discovery of the B-chromosome PSR, a prime example of ultraselfish DNA. PSR disrupts transmission of the entire genome of males in a parasitic wasp, thereby inducing sex change in a female's offspring. This resembles some of Wolbachia's manipulations.

Complex Dynamics in Ecology

A. Hastings

The long standing paradigm has been to match persistent ecological systems with asymptotic behavior of simple differential equation models. Yet because of the short time scales of ecological systems, this may be inappropriate. Simple systems consisting of 2 linked populations in discrete time show long transients for those parameter values for which basins of attraction are also complex. More complex behavior emerges with more patches. A study of a system of 2 linked predator-prey equations shows that complex dynamics may lead to transients which occur for parameter values far from those leading to stable aymptotic behavior. Thus transients can change the view of what allows ecological communities to persist.

Models involving continuous and discrete time: a challenge in agriculture

J. A. P. Heesterbeek

We consider hybrid models for the following situation: continuous periods of interaction between two species are separated by discontinuous changes in the abundance of one of the two at regular intervals. One can think for example of an agricultural crop and interaction with a plant pathogen or weed, or of a herd of farm animals and interaction with a parasite. At regular intervals the crop or animals are harvested and replanted/restocked with a new cohort. The pathogen, weed or parasite has to employ free-living stages (spores, larvae, cysts, seeds) or attack some alternative host in order to bridge the gap between two consecutive growing seasons. During the growing season the environmental reservoir of the pathogen, weed, or parasite increases in size due to interaction with the host. Usually, there is an added complication of density dependence in the survival, reproduction or development of the pathogen, weed, or parasite (collectively: the pest species). The typical applied question is: if one would have a control measure aimed at the pest species and if one would observe a decrease in the reservoir at the start of a number of consecutive years, can one conclude that control is successful?

We studied this question with a minimal model that includes the three basic ingredients: continuous/discrete time, environmental reservoir, and density dependence. The model consists of differential equations for the interaction within the season and has resetting of the host population at all integer time points. We study the one-dimensional map that describes dynamics of the environmental reservoir at the start of the season. The map is unimodal. One can show that periods of all orders exist and calculate the regions in which they are stable. It turns out that control can actually make matters worse, by bringing the system into a region of chaotic behaviour and possibly long cycles. A series of years with decreasing reservoir is therefore no clue as to the success of the control measure. The analysis shows the importance of incorporating the three ingredients into models, and highlights an area of great potential use in agriculture which does not receive the attention that is due from mathematicians.

On the Biochemical Basis of Psychophysical Laws - A Mathematical Bridge

U. an der Heiden

Psychophysics investigates the relationship between physical stimuli and human or animal sensation and perception. Best known is the Weber-Fechner-law on the logarithmic dependence of visual sensation on the intensity of light. We try to explain such and other phenomena on the basis of mathematical models (in the form of systems of nonlinear ordinary differential equations) for biochemical processes taking place in sensory cells, and interestingly, with more or less strong variations, in essentially all cells of organisms when the cells underly certain stimuli in their environment (light photons, heat, hormone molecules, antigenic agents etc.). The equations incorporate in particular several (two or more) feedback loops within the biomolecular pathways in the transmembrane signalling system of the cells involving

various proteins like e.g. receptors, guanine nucleotide regulating proteins ("G-proteins"), adenylate cyclase, and "second messengers" like cAMP. It can be shown by evaluating the mathematical model with realistic parameter values that in the rod photoreceptors two of the biochemical feedback loops are able to broaden the reliable range for light discrimination with a factor of about 1000. The models explain also a variety of adaptation and sensitisation phenomena observed by psychophysics. Remark: This is joint work with Juergen Nauroschat

The Adaptive Dynamics of Functional Traits

M. Heino, U. Dieckmann

We have extended the framework of adaptive dynamics to infinite-dimensional traits. Such adaptive traits naturally arise in many areas of evolutionary ecology. We denote the function-valued trait as $s(a)$, where a is determinant value. The equation describing the expected dynamics of $s(a)$ in clonally reproducing populations under mutation-limited evolution is given as

$$\dot{s}(a) = \frac{1}{2}\mu_s \bar{n}_s \int \sigma_s^2(a', a) D_s \bar{f}(a') da' \tag{1}$$

where μ_s is mutation rate, $\bar{n}_s$ average population size on the resident attractor, $\sigma_s^2(a', a)$ is the variance-covariance function of the mutation distribution, and $D_s \bar{f}(a')$ is the selection gradient, or functional derivative of the fitness function $\bar{f}$ at s. The integral in (1) can be positive or negative and determines the direction that evolution can take. Equilibria of (1) can be of various types. (i) *Selection-induced equilibria*, where the selection gradient vanishes ($D_s \bar{f}(a) = 0 \; \forall a$). (ii) *Covariance-induced equilibria*, where the variance-covariance function is singular, such that $\int \sigma_s^2(a', a) D_s \bar{f}(a') da'$ vanishes despite $D_s \bar{f}(a) \neq 0$. (iii) *Constraint-induced equilibria*, where the evolutionary dynamic reaches boundaries of feasible trait space.

Parabolic Limit of Transport Equations and Chemotaxis

T. Hillen

(Joint work with H.G. Othmer)
In this talk we discuss the diffusion approximation to velocity jump processes. We show that under an appropriate scaling of space and time, the asymptotic behavior of solutions of the resulting transport equation can be approximated by the solution of a diffusion equation obtained via a regular perturbation expansion. In general the resulting diffusion tensor is anisotropic, and we give necessary and sufficient conditions under which it is isotropic. The method presented here simplifies previous derivations and we give a minimal set of necessary assumptions which lead to a parabolic limit.

We use this approach to derive the limiting equation under a variety of external biases imposed on the motion (chemotaxis). Depending on the strength of the bias, it may lead to an anisotropic diffusion equation, to a drift term in the flux, or to both. Some examples lead to the classical Patlak-Keller-Segel model.

[1] Hillen, T. and Othmer, H.G. Chemotaxis equations from the parabolic limit of velocity jump processes. submitted to *SIAM J. Appl. Math.*

Intermingled Basins for Two Species Systems

F. Hofbauer, J. Hofbauer, P. Raith, T. Steinberger

We present discrete time two-species competition systems

$$x_i' = x_i f_i(x_1, x_2), \qquad \frac{\partial f_i}{\partial x_j} < 0 \quad \forall i, j = 1, 2$$

which have the following property: *From almost all initial conditions one of the two species dies out. But the survivor is unpredictable.* More precisely: The state space $\mathbb{R}^2_+$ splits into three pairwise disjoint sets $\mathbb{R}^2_+ = B_1 \cup B_2 \cup D$, such that (1) Every orbit starting in B_i converges to the x_i-axis. (2) For every open set $U \subset \mathbb{R}^2_+$, both sets $B_1 \cap U$ and $B_2 \cap U$ have positive Lebesgue measure. (3) The set D has zero Lebesgue measure.

These examples are constructed as suitable perturbation from degenerate competition systems $x_i' = x_i f(x_1 + x_2)$, where the one-dimensional map $x \mapsto xf(x)$ has a chaotic attractor (more precisely it should be unimodal with negative Schwarzian derivative and satisfy the Collet-Eckmann condition). The logistic map $x \mapsto Rx(1-x)$ and the Ricker–Moran map $x \mapsto Rxe^{-ax}$ satisfy these assumptions for parameters R from a set of positive measure.

The Evolution of Dispersal

V. Hutson

A model is considered where there is no direct selection and in the simplest case two phenotypes with diffusion rates $\mu_1 < \mu_2$:

$$\frac{\partial u_i}{\partial t} = \mu_i \Delta u_i + u_i[a(x,t) - u_1 - u_2] \quad (i = 1, 2),$$

on Ω, a finite domain with zero Neumann conditions. It is assumed that there are semitrivial equilibria $(\tilde{u}_1, 0)$, $(0, \tilde{u}_2)$. One can show that in the autonomous case the lower diffusion rate is always preferred. The key is that $(\tilde{u}_1, 0)$ is asymptotically stable, which follows from the variational formula. An interesting extension of the model is to include time periodicity. It is natural to study the stability of $(\tilde{u}_1, 0)$, $(0, \tilde{u}_2)$, which are of course periodic orbits, by using the idea of a periodic-parabolic eigenvalue. However, the operator is not now self-adjoint, and the problem is much harder. On the other hand, it leads to many mathematically interesting questions. Most significantly, one can show that under certain circumstance there is selection for higher diffusion, and there may even be coexistence. This is in direct contrast with the autonomous case.

Collaborators: J. Dockery, K. Mischaikow, M. Pernarowski, P. Poláčik, W. Shen, G. Vickers

A Structured Population Model With Discrete Reproduction

F. Kelpin

Individuals do not usually produce a constant stream of offspring. Instead, they often reproduce at discrete moments in time. We study a rotifer species using the dynamic energy budget (DEB) theory developed by Kooijman. In our structured population model, the rotifer 18 constantly allocates energy to reproduction, but only lays an egg when enough energy has been allocated to reproduction. We show the results of parameter estimations for chemostat transients for a food chain of nutrients, algae and rotifers after a pulsed addition of algae or nutrient.

Modelling the Development of Hydra
M. Kirkilionis

The talk was concerned with recent modeling approaches to understand the development and regeneration properties of different Hydra species. Hydra is a freshwater polyp that has a number of fascinating properties. First there are the early cutting experiments that show that every Hydra can regenerate missing parts of its body. Then there are tissue replantation experiments which show that Hydra tissue has a so-called 'positional value', an notion introduced by Prof. Wolpert (London). Such a positional value is needed to ensure that cells 'know' whether they are positioned near the food or head of the body. A traditional explanation is that positional value is determined by the concentration of an 'activator' which is a morphogen that changes the internal state of cells. To derive gradients of activator concentrations, one must also introduce an inhibitor. Via the classical Turing-instablity analysis one can then derive conditions when such a system allows for pattern formation, given the diffusion rates of activator and inhibitor are very different (Applications to Hydra by Gierer & Meinhard). Another problem is that this analysis is usually done for fixed bounded domains, whereas during development and regeneration the tissue is growing. Activator-inhibitor systems with growing domains usually show varying patterns in time, but changing patterns would contradict experimental evidence. This is still an unsolved problem. Prof. Mueller (Heidelberg) has recently proposed that positional value is determined by the numbers of receptors for a morphogen on the cell surface. Based on this proposal different models have been formulated, working with the numbers of free and bounded (bounded with the morphogen) receptors and a morphogen as state variables. This leads in general to coupled systems of reaction-diffusion and purely reactive systems. There is still some more analysis needed to show which patterns such systems can produce. But again the issue of growing tissue has to be considered, also for receptor-based equations. One new type of model has been presented that takes into account division rates of cells, together with some specific characteristics of the Hydra tissue. In Hydra, new cells are usually only formed at the gastric region. The cells are still not differentiated, but attain their positional value and function while wandering around as single cells in the space between endo- and epidermis.

Spread Rate for a Nonlinear Stochastic Invasion
M. Lewis

It has been long conjectured that intrinsic factors association with interacting individuals can slow the spread of a population or disease, even in a uniform environment. In this talk I analyse the effect of such factors when individuals interact locally over small neighborhoods, formulating a set of equations describing the dynamics of spatial moments of the population. Although the full equations cannot be expressed in closed form, a mixture of moment closure and comparison methods can be used to derived upper and lower bounds for the expected density of individuals. Analysis of the upper solution gives a bound on the spread rate of the stochastic invasion process which lies strictly below the spread rate for the deterministic model. Finally, I propose a heuristic formula for estimating the true rate of spread for the full nonlinear stochastic process based on a scaling arguments for moments. This gives speeds that are close to those calculated numerically by Monte Carlo simulations.

Effects of Competing Virus Strains in Vector-transmitted Diseases
E. Lourdes

(Joint work with K.P. Hadeler)
Many parasites use variability to circumvent the defense strategies of the immune systems. There are cases of high variability within one host as the HIV infection or Hepatitis C infection, and others in which one finds several distinct types of parasites which coexist in the host population but each host

typically carries only one type. As an example we have different strains (distinguished by serotype) of virus in dengue fever. Each serotype causes immunity against it, but not against other serotypes. For dengue fever there have been extensive public health studies (Gubler (1986), Hulstead (1992), WHO (1986)), and the spread of the disease has been studied in terms of epidemiological models. In this work we formulate a deterministic model for the spread of a vector transmitted disease taking into account the different serotypes (or types) of the same virus. It is shown that such a system which includes virus diversity together with transmission by vectors, leads to hysteresis phenomena when the vector is subject to control measures.

Understanding Neutrophil Dynamics in the Grey Collie

M. Mackey

Cyclical neutropenia (CN) is a disease (affecting both humans and grey collies) in which circulating levels of white blood cells, red blood cells, and platelets oscillate in a regular fashion. The period in humans ranges from 15 to 44 days and from 9 to 14 days in the grey collie. In the grey collie, high amplitude oscillations are associated with second and higher order harmonics (relative to the fundamental) in the power spectrum of circulating cell numbers. Previous work has shown that a destabilization of the peripheral regulation of white blood cell numbers (mediated by colony stimulating factor–CSF) is not the origin of the disease. Rather, the disorder must originate in the hematopoietic stem cell compartment leading to an oscillatory cellular influx into all cell lines.

A mathematical model for this peripheral feedback control of white blood cell numbers has been formulated, including: 1) The negative feedback regulation of apoptosis due to colony stimulating factor; and 2) The distribution of (maturation) time delays. Under the assumption that this control system is receiving an oscillatory stem cell input, we have been able to precisely reproduce the temporal patterns of neutrophil numbers and the Fourier spectral properties for nine grey collies. The modeling and parameter determination further predicts that the apoptotic rate of white blood cell precursors in the bone marrow of the grey collie is elevated relative to normal collies. This has been confirmed by further laboratory studies.

Limit Relations Between Metapopulation Models

H. Metz

I considered heuristically the relations between various metapopulation models. The starting model consists of infinitely many equal finite patches of size omega coupled by migration through a common disperser pool. The local populations follow independent birth and death processes. Random catastrophes set the local populations independently back to zero. Two tunable parameters alpha and gamma measure overall migration speed and catastrophe rate. Then I let omega go to infinity and alpha or gamma to zero, in various concerted manners, while rescaling the local population sizes and time, to see what limits result. The usual Levins limit (blinking patches, without further structure) is recovered by setting gamma zero and then letting omega go to infinity and alpha to zero in a concerted manner. The unfortunate outcome is that the interesting dynamics takes place on a biologically unrealistically long time scale. A less expected limit results if one sets omega equal to infinity and then lets both alpha and gamma go to zero in a concerted manner. In this limit the patches follow independent semi-Markov chains with states close-to-zero and close-to-carrying-capacity. The switching rates between the semi-states are independent of the size of the migration stream as long as it is nonzero.

Ancestral Coalescent Structures in Haploid and Diploid Population Models
(tutorial lecture)
M. Moehle

A class of population models with non-overlapping generations and fixed population size N is considered. It is assumed that the family sizes within a generation are exchangeable random variables. A weak convergence criterion is established for a properly scaled ancestral process as N tends to infinity. It results in a full classification of the coalescent generators in the case of exchangeable reproduction. In general the coalescent process allows for simultaneous multiple mergers of ancestral lines. The standard (Kingman) coalescent appears if and only if triple mergers are asymptotically negligible in comparison to binary mergers.

Contact Tracing in Stochastic and Deterministic Epidemic Models
J. Müller, M. Kretzschmar, K. Dietz

We consider a simple unstructured individual based stochastic epidemic model with contact tracing. Even in the onset of the epidemic, contact tracing implies that infected individuals do not act independently of each other. Nevertheless, it is possible to analyze the embedded non-stationary Galton-Watson process. Based upon this analysis, threshold theorems and also the probability for major outbreaks can be derived. Furthermore, it is possible to obtain a deterministic model that approximates the stochastic process, and in this way, to determine the prevalence of disease in the quasi-stationary state and to investigate the dynamics of the epidemic.

How Well Do PDE Models Capture Chemotactic Motion? Comparisons Between Numerical Simulations of a PDE and Particle Model
K. Painter

Chemotaxis can be described as the movement of organisms induced by response to an environmental signal. Mathematically, this can be thought of as the movement along concentration gradients of a chemical cue. Mathematical models of chemotaxis have been proposed to describe a range of biological phenomena, from fields as diverse as ecology, immunology to developmental biology. The most widely studied models of chemotaxis are the PDE models originally proposed by Keller and Segel (1970) to describe pattern formation in bacterial populations. The PDE models offer a number of advantages, including straightforward numerical simulation and relatively easy mathematical analysis. However, a number of assumptions are made to derive the PDE system, including the assumption of a continuous density distribution and scalings of time and length scales such that a diffusion model can be derived. It is therefore questioned how well PDE models capture biological chemotaxis.

To explore this question, we compare simulations of the PDE model with Monte Carlo simulations for a population of individual particles jumping on a lattice. We show that in the majority of situations, PDE models accurately capture the behaviour of the individual model. However, a number of simulations demonstrate significant differences in the result. It is therefore important to consider the two approaches when attempting to model chemotaxis.

Different Approximations in Models for Macroparasites

A. Pugliese

In the talk I presented some qualitative and quantitative comparison between an infinite system of differential equations [3] for the interaction of macro-parasites with their hosts, and some low-dimensional approximations, in which the parasite distribution is assumed to be negative binomial [1]. The most surprising result is that the approximation where aggregation is variable, and promoted by multiple infections [5] yields results identical to the infinite system. Qualitatively, the effect of parameters on the existence of an endemic equilibrium and its stability are similar in all models, except that in [1] the parameter region where the equilibrium is stable is much larger.

Considering two species of macroparasites on one host, I studied the invasibility conditions in the infinite system; I found [4] that, if there is a trade-off between virulence and transmissibility, coexistence of two species is possible, but only when the parameters fall in a very narrow region. If, on the other hand, one species is more virulent and less transmissable, it will be competitively excluded. I also showed that the width of the coexistence region is insensitive to the aggregation of parasite distributions. These results are rather different from what found [2] in an approximate model; in this context, therefore, the approximation is not appropriate, especially because of the introduction of parasite aggregation and correlations as parameters, instead of byproducts of interactions.

[1] Anderson, R. and May, R. (1978). J. Anim. Ecol. 47:219–247.
[2] Dobson, A. (1985). Parasitology 91:317–347.
[3] Kostizin, V.A. (1934). Symbiose, parasitisme et évolution (étude mathémati- que). Hermann, Paris.
[4] Pugliese, A. (1999). Theor. Pop. Biol. , in press
[5] Pugliese, A., Rosà, R., and Damaggio, M. L. (1998). J. Math. Biol. 36:419–447.

Explaining the T-Cell Repertoire

D. Rand

A major problem in immunology is to explain how T-cells are able to mount an effective response while distinguishing antigen from foreign pathogens from antigen derived from self proteins. This problem has been made harder by recent experimental findings which show that contrary to previous assumptions the affinity of the binding between T cell receptor and MHC:peptide complexes is low and the overall signalling process is highly dynamic. I presented a mathematical model whose analysis provides a possible resolution to this paradox. The model integrates (i) stochastic analysis of the molecular processes involved in antigen presentation with (ii) the behavior of the T cells at a population level to determine overall probabilities that a foreign invader will be recognised and that self will be tolerated. The most important of the mathematical tools used in the analysis is a study in terms of large deviations of the fluctuations in signalling due to the choice of T cell clonotype and the antigen presentation profile.

A Height-structured Forest Model With Spatial Competition in the Recruitment

J. Saldaña, M. Kirkilionis

By means of bookkeeping arguments, a spatially averaged n-species height-structured forest model is derived assuming four main hypotheses. First, the shape of the trees of all species are tubular-like and the light energy uptake of a tree depends on the available light that this tree is able to absorb along its canopy. Second, the availability of light at a given height level h, $L(t, h)$, depends on the total shading produced by those trees that are above this level. This quantity will define the first *interaction variable* of the model.

Third, it is assumed that trees are distributed uniformly in the area occupied by the forest, i.e., no spatial correlations are present. Fourth, there exists a spatial competition of germinating seeds for filling

the *free* sites with new trees. Therefore, the recruitment of a species s is the product of how many seeds are produced by this species, $p_s(t)$, times the probability that a seed of this species occupy a free site, $p_s(t)/\sum_s p_s(t)$, times the probability that this seed is at a free site where it can successfully germinate, which it is assumed to be $L(t,0)/L_\infty$, with L_∞ the maximal (averaged) light energy per unit area. The total seed production, $\sum_s p_s(t)$, will define the second interaction variable of the model. Finally, a result on the existence and uniqueness of a local solution of the model equations is presented.

Generalizations of Mass Action Kinetics

R. Schimming

There are three typical steps in the modelling of kinetics: (i) A network structure, where the vertices are compartments or reservoirs for some substance and the edges are channels through which the substance can flow. (ii) Balance equations for the amounts of substance in the compartments. (iii) Dynamical laws; some systematics of these is proposed in the lecture. In particular, generalized additive mass action kinetics is discussed.

Cellular Automata with Activation and Inhibition

B. Schönfisch

Our models were inspired by ideas from Reaction-Diffusion systems, namely that there is a short range activation and a long range inhibition. The aim was to see what effects emerge from very simple systems. Therefore the particles do not move and there is only one species or substance. Formally we consider cellular automata on a finite grid $G \subset \mathbf{Z}^2$, with the set of elementary states $\{0,1\}$ where 0 is regarded as resting and 1 as active. The traditional Moore neighborhood is divided in activating and inhibiting. A cell becomes active if at least s_e neighbors in the activation neighborhood and at most s_i neighbors in the inhibition neighborhood are active, otherwise it becomes resting. The dynamics is asynchronous. Depending on the activation and inhibition threshold different patterns evolve. For $s_i = 4$ we get a well known class of monotone and totalistic automata. They always end in a stationary state which here can be characterised exactly. Also for $s_e > 3$ and $s_e = 2, s_i = 0, 1$ the dynamics can be identified. The most interesting patterns evolve with $s_e = 0, 1$. For $s_e = 0$ or 1 and $s_i = 0$ we found a function V which we call a discrete lyapunov function mapping states of the grid onto real numbers. V has a lower bound, only a finite number of possible values and is decreasing if a cell changes state. It follows that in these cases the automaton reaches a stationary state. With simulation results and rules derived from the local function we characterised the patterns obtained with $s_e = 0, 1, 2$. Future work is to imbed this model in a general framework and compare it to real biological systems.

Wave Propagation in Inhomogeneous Media

A. Stevens

(joint work with: Steffen Heinze and George Papanicolaou)

We consider a scalar reaction-diffusion equation with bistable nonlinearity in a medium with spatially varying diffusion and drift coefficients. A major problem in reactive flows is the derivation of upper and lower bounds for the effective speed of propagation. Using a min/max characterization of the traveling wave velocity we provide such estimates for shear flows, equations near the homogenization limit and a spatially discretized problem which models the propagation of calcium waves in cardiac tissue. The method presented can be applied to any other problem possessing a maximum principle.

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