

Tagungsbericht 12/1987

Mathematische Modelle in der Biologie

15.3. bis 21.3.1987

The mathematical research Institute Oberwolfach has early recognized that the few mathematicians interested in Mathematical Biology around 1970 would stimulate a wide-spread interest in this field, and it has supported and enhanced their efforts by inviting to conferences in 1975, 1978, 1981, 1984, organized by the late Helmut Werner (Münster/Bonn), K.P.Hadeler (Tübingen), Willi Jäger (Heidelberg). In contrast to the situation in Physics there is no clear distinction between Theoretical Biology, Mathematical Biology and Biomathematics. Very often a scientist covers the whole field from formulating a model in close contact with experimentalists to the mathematical investigation of this model and possibly to generalizations which are of mathematical interest in themselves. The Oberwolfach conferences have contributed in shaping a community of scientists who work on mathematical problems related to Biology. This community is not organized but fluctuating, and it is closely connected by personal contacts and joint research activities. The present conference, due to a long list of proposals, a generous director, and unexpectedly many affirmative answers, started with about 40 proposed contributions. Such number hardly agrees with the concept of Oberwolfach to organize small groups for cooperative research. The organizers decided to have some lectures in the mornings and special sessions of a rather informal character in the afternoons and sometimes evenings. This schedule has produced a rather liberal and informal atmosphere and a very active participation.

Various fields have been covered, contributions on population dynamics were most numerous. There is generally a strong interest in populations structured by age, level of infection, size or other characters. Ecology is a field of active research, in particular persistence of species is a biologically relevant concept for the many situations where global stability does not hold. Epidemiology has been and will be a field of importance, even if the results will not answer the urgent demands of the public.

Aggregation, chemotaxis, pattern formation are fields in which hard experimental data are available; the same is true for various problems in physiology, in particular neurobiology, cardiology, and muscular contraction.

Sometimes it is necessary to return to basic ideas and to discuss whether diffusion, growth, attraction, biomass ect. are valid concepts and which phenomena are described by such notions. One has to recall that, in contrast again to Physics, in Mathematical Biology most quantities are phenomenological.

The participants came from various countries, the atmosphere was relaxed, some joint work was continued or got started. The invariably good care of Mr. Fürstendorf and his staff is gratefully acknowledged.

Vortragsauszüge

Tom Aldenberg

Liebig's Law and Ecosystem Model Response.

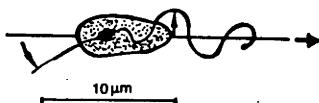
Liebig's Law of the Minimum (1855) states that the nutrient present in a minimum amount relative to the needs of a plant will limit the yield (crop). In the framework of ecosystem models, a generalization of the limiting factor concept can be obtained by calculating standing stock sensitivity coefficients with respect to nutrient input concentrations (or input light intensity) through Tomovic sensitivity analysis. In a one-species-two-nutrients algal culture, Liebig's Law results from a bifurcation of the steady state solutions for each nutrient depleted. Variable quota (nutrient biomass ratio) models can be analyzed similarly.

In trophic situations (e.g. water quality models) nutrient and light sensitivity can be monitored in their transfer from the primary to the secondary trophic level. The sensitivity approach seems also applicable to assessing the so-called indirect effects in ecotoxicology.

Wolfgang Alt

Searching Behavior of Male Ectocarpus Gametes.

After release from gametangia, female gametes of the brown algae species *Ectocarpus siliculosus*, settle on surfaces (of rocks) and produce



the sexual pheromone ectocarpene. The male gametes first swim in 3-D water, then upon hitting a 2-D surface perform more or less curved paths, whereby the pheromone (a) decreases the tendency to leave the surface, (b) increases the mean turning rate b_0 and (c) induces sharp turns in paths pointing down the gradient. The stochastic process for the

$$\text{angle } d\Phi_t = B_t dt$$

$$\text{and the turningrate } dB_t = \lambda(b_0 - B_t) + \sqrt{\beta} dw_t$$

is compared with experimental data (movies produced by Annette Geller) by estimating b_0 and plotting the variance of

$$\Phi_\tau = \frac{\beta}{\lambda^2} \left(\tau - \frac{1}{\lambda} [1 - e^{-\lambda\tau}] \right).$$

With the aid of simulations this model is compared to another one, in which B_t represents the alternating strokes of the front flagellum (see picture).

The *spiral search strategy* (within a range $\leq 400\mu\text{m}$ distance from the female) provides an intense area covering exploration, although the macroscopic motility is reduced. However, due to the chemotactic response, the mean searching time becomes finite - according to an explicit formula based on a *diffusion approximation*

$$\partial_r u = \frac{1}{r} \partial_r \{r(\mu \partial_r u - \chi u)\}.$$

The further strategy of male gametes to leave a surface at low pheromone concentration in order to randomly search for other surfaces even increases the mating probability, if a sparse random distribution of female gametes on different surfaces (rocks in the sea) is assumed.

Bernd Aulbach

The Past in Short Hypercycles.

The so-called short hypercycles

$$\dot{x}_i = x_i(x_{i-1} - \sum_{j=1}^n x_j x_{j-1}), \quad i = 1, \dots, n, \quad (x_0 = x_n), \quad n = 2, 3, 4$$

are known to have simple dynamics as far as future time is concerned. In fact, any trajectory in the interior of the state simplex S converges to the unique interior equilibrium as $t \rightarrow \infty$. In this talk the past behavior is examined which turns out to be less simple. As $t \rightarrow -\infty$ there are two types of asymptotic behavior: either (I) a trajectory converges to an equilibrium on the boundary of S or (II) it oscillates aperiodically approaching the closed polytope which is formed by the nonstationary edges of S . The case $n = 2$ has only type (I) trajectories whereas all trajectories in case $n = 3$ are of type (II). In case $n = 4$ both types of solutions exist.

Erich Bohl

SV-40-Replication.

The mechanism of SV-40-replication consists of three main steps. A model was presented incorporating these steps one after another to illustrate their influence on the system.

Stavros Busenberg

An Age-Structured Epidemic Model.

An epidemic model is analyzed with fertility, mortality and transmission rates dependent on the age of the affected population. Endemic threshold criteria are

derived and the stability of steady state solutions is analyzed for certain forms of the force of horizontal infection. The relation between age-structured epidemic models of this type and catalytic curve models of epidemics is derived. The possibility of identifying vertically transmitted diseases from the catalytic curve is demonstrated.

Pierluigi Colli

Mathematical Modelling of heterogeneous Muscle Fibre.

One considers a mathematical model of a contracting muscle fibre, which is assumed to be non-homogeneous in order to account for the differences between the tension-length relationship determined in short segments of the fibre and the one observed in the whole muscle fibre. The model gives a system of nonlinear and nonlocal hyperbolic equations; the existence and the uniqueness of the solution are proven.

Piero Colli-Franzone

A Mathematical Model of Cardiac Sources and Propagation Wavefronts Spreading in Myocardial Excitable Tissue.

We introduce a mathematical model describing the potential distribution elicited by the electrical activity of the heart in the depolarization phase of the ventricular tissue. By means of singular perturbation techniques we derive jump relationships of the potential through the excitation wavefront and various equations concerning the dependence of the propagation wavefront velocity on the electric properties of the medium. Numerical simulation in 2-dimensional medium are presented.

James D. Cushing

Asymptotic Dynamics of Some Discrete Models for Structured Population Growth.

The existence and stability of equilibria are discussed for general nonlinear, discrete matrix models for populations structured into an arbitrary number of categories. The model allows transitions between any two categories (not necessarily in a progressive manner). Nonlinear Leslie and Usher models are included as special cases. An observation of Leslie is proved concerning the existence and stability of a persistent solution ("stable age distribution") for a certain type of nonlinearity.

Odo Diekmann

Bistability in a Prey-Predator- Patch Model.

The interaction between, for instance, rose plants, spider mites and predatory mites is characterized by the fact that local mite colonies go extinct while on a larger spatial scale the system persists. One can model such a situation by viewing

the population as an ensemble of local colonies (which are characterized by the number of spider mites and predatory mites) and, in addition, free patches (plants), searching spider mites and searching predatory mites (the so-called air plancton). Thus we obtain a rather complicated structured population model, with colonies as "individuals". By a time scale argument, which amounts to the assumption that local colonies have a negligible lifetime, one can reduce the model to a system of three ordinary differential equations which inherits some of the characteristics of the structured model. The o.d.e. system has bistable behaviour suggesting that biological control can only be successful if predatory mites are introduced in large quantities.

The lecture is a progress report on joint work with Hans Metz and Mous Sabelis (from the University of Leiden), which is far from finished. One of the aims is to bridge the gap between relatively simple qualitative o.d.e. models and very complex quantitative simulation models in the hope that a whole continuum of models gives, when taken together, more insight than each of them separately.

Klaus Dietz

Dynamics of Sexually Transmitted Diseases.

The classical models for sexually transmitted infections assume homogeneous mixing either between all males and females or between certain subgroups with heterogeneous contact rates. This implies that everybody is all the time at risk of acquiring an infection. These models ignore the fact that the formation of a pair of two susceptibles renders them in a sense temporarily immune to infection as long as the partners do not separate and have no contacts with other partners. The present model, whose stability conditions are investigated jointly with K.P. Hadeler, takes into account the phenomenon of pair formation by introducing explicitly a pairing rate and a separation rate. The infection transmission dynamics depends on the contact rate within a pair and the duration of an infection. One can specify explicitly a lower bound for the number of life time partners for the persistence of the infection. This bound decreases considerably as the average duration of a partnership increases.

Herbert I. Freedman

Models Incorporating Prey Behaviour as Modified by a Parasite leading to Predator Survival.

The prey population in a predator-prey model is divided into susceptibles and infectives with respect to a parasite. The predator functional responses of the infectives are altered leading to criteria for survival of the predators. Criteria are also obtained for there to exist a globally asymptotically stable equilibrium.

Jean-Pierre Gabriel

Hemodialysis and Urea Kinetics.

The importance of mathematical modeling in dialysis arose recently as a consequence of the achievement of individualized treatment therapies. Two distinct models are basically used, namely the urea kinetic model and the direct dialysis quantification, for the estimation of the urea distribution volume and the urea generation rate. Unfortunately they lead to different results for the same patient. It seems that the underlying hypotheses of the models are poorly described in the literature. The aim of the talk is an attempt to fill this gap and to show that the observed discrepancy is not surprising at all.

Annette Grabosch

A Cell-Cycle Model Based on Unequal Division.

Of concern is a mathematical model proposed by Kimmel et al. which describes the cell cycle of eukaryotic cells, which are characterized by their RNA content. The model is based on three assumptions: (i) in mitosis a cell divides into two daughter cells of possibly different sizes, (ii) the RNA content at the beginning of the cell cycle determines the RNA content at the end of the cycle (i.e. at division), (iii) the RNA content at the beginning of the cell cycle determines the duration of the cycle. These assumptions lead to an integral equation which describes the cells dividing at time t which have an actual RNA-content x

$$(*) \quad m(t, x) = \int_0^{\infty} k(x, y) m(t - q(x, y), y) dy, \quad t \geq 0, \quad m(t, x) = g(t, x), \quad t < 0.$$

For all $g \in L'([-r, 0] \times [0, \infty)) =: E$ there exists a unique solution of (*) which moreover can be described by a one-parameter semigroup of positive linear operators on E . Results from positive operator and spectral theory are used to show that $m(t, x) \sim e^{\lambda_0 t} h(x)$ for large t . This restates essentially the result of Arino and Kimmel (1987) by using more recent functional analytic methods. Moreover, using strong positive properties (such as irreducibility) one can show that $\text{supp } h$ is bounded from below away from 0 and from above.

Michael R. Guevara

Spatiotemporal Patterns of Block in Cardiac Tissue.

Block of propagation of the cardiac impulse is the underlying cause of many cardiac arrhythmias. A model of a one-dimensional cable of cardiac Purkinje fibre is investigated numerically. The proximal end of the cable is stimulated with a periodic train of current pulses. At sufficiently low rates of stimulation, for every stimulus pulse, there is a wave of excitation that propagates through the cable to its distal end. At high rates of stimulation not every wave traverses the cable -

some impulses are blocked in the interior of the cable. Many different patterns of block resembling clinically observed rhythms (such as Wenckebach and Mobitz I periodicity) are seen. These are described as a function of one parameter: the rate of stimulation. Clinical examples are presented in which it is shown that the dynamics can be reduced to that of a one-dimensional difference equation.

Mats Gyllenberg

Age-Size Structure in Populations with Quiescence.

In many populations not all individuals are actively growing, but some are in a quiescent state. Under certain circumstances a normally growing individual can become quiescent and later it may return to the normal state again. Often an individual can undergo several transitions back and forth from one state to the other.

A mathematical model (a system of PDE's) for the continuous age-size distribution of a population with both normal and quiescent individuals is given. The theory of positive operator semigroups is used to show that under general assumptions about individual behaviour the age-size distribution converges to a stable distribution. Some of the features of the model are illustrated by a simple example.

The presentation is based on joint work with Glenn Webb.

K.P. Hadeler

Models for Infectious Diseases and Parasitic Infections.

Three approaches towards models for infectious diseases and parasitic infections are presented. In a first model (R. Waldstätter, K.P. Hadeler, G. Greiner) the population is subdivided into a class of noninfected and a class of infected, which is structured according to the level of infection $x \in \mathbb{R}_+$. The model is formulated as a diffusion problem on $\{P\} \cup \mathbb{R}_+$ where P is a point. In other words, the state of the population is a measure with a density on \mathbb{R}_+ and a point mass at zero. In view of a Lotka birth law the problem is not formally self-adjoint. Mathematically the problem is treated, after a Liouville transformation, as a self-adjoint problem with non-self-adjoint, relatively bounded perturbation. In a second approach (M. Kretzschmar, K.P. Hadeler, K. Dietz) a host population is classified according to discrete parasite numbers, i.e. is described by a linear multitype birth and death process with killing (of the host). The related characteristic differential equations show a remarkable similarity to Lotka-Volterra systems and the equations of evolutionary game dynamics (vector Riccati equations). For the third class of models (sexually transmitted diseases) see the lecture of K.Dietz.

Henk Heijmans

On the Simplification of Structured Population Models.

When developing structured population models, one usually makes all kinds of simplifying assumptions on the level of the individual. This is unavoidable if one is to end up with a problem which is amenable to mathematical analysis. The best known type of approximation is by time-scale arguments. In this lecture a different type of simplification is considered, one which could be called: "From state jumps to reduced growth".

In the linear case, one can give a mathematical justification of such a simplification by the Trotter-Kato theorem for C_0 -semigroups. If the equations are nonlinear, then things become more difficult, but there is good hope that the results extend to the nonlinear case.

Josef Hofbauer

Saturated Equilibria and Applications to Boundedness, Persistence, and Stability of Lotka-Volterra Equations.

We call an equilibrium \bar{x} of an ecological differential equation $\dot{x}_i = x_i f_i(x_1, \dots, x_n)$ saturated if missing species cannot invade the system at \bar{x} : if $\bar{x}_i = 0$ then $f_i(\bar{x}) \leq 0$. Two main results: 1) Interior solutions $x(t) > 0$ converge to an equilibrium $\bar{x} \Leftrightarrow \bar{x}$ is saturated. 2) Index Theorem: The sum of the indices of all saturated equilibria is +1. In particular, every ecological system has at least one saturated equilibrium. There are obvious applications to *persistent* systems: As they cannot have saturated equilibria on $\text{bd}\mathbb{R}_+^n$ they must have an interior fixed point. Based on a characterization of Lotka-Volterra equations $\dot{x}_i = x_i(r_i - (Ax)_i)$ with bounded orbits in terms of "B-matrices" ($\forall x \geq 0, x \neq 0 : \exists i : x_i > 0, (Ax)_i > 0$) we derive criteria for the existence, uniqueness of saturated equilibria, their local and global stability in terms of algebraic properties of the interaction matrix.

James P. Keener

Wave Propagation in Parallel Nerve Fibres and its Implication to Fibrillation Onset.

We discuss the effects of anisotropy, excitability and refractoriness in models of action potential propagation in myocardium. We show the significant difference between discrete models and continuous models with respect to propagation failure. We use this difference to suggest a possible mechanism to explain one dimensional propagation in two dimensional anisotropic media and to suggest how this mechanism may also lead to permanently rotating waves of propagation in the myocardium. The theory is quantitative and predicts a window of vulnerability to premature stimuli. It remains to check this analytically determined window of vulnerability against experimental observations on fibrillation onset.

A. Lasota

Statistical Stability, Periodicity and Chaos in Population Dynamics.

The dynamics of a discrete dynamical system may be described from the statistical point of view by the sequence of iterates of a positive operator P (The Frobenius-Perron operator P). A convenient way to study such iterates is to use the lower bound function theorem. Roughly this theorem says that if the iterates $P^n f$ are bounded from below ($P^n f \geq h + \epsilon_n$) then they must converge to a unique stationary density ($P^n f \rightarrow f_*$, $Pf_* = f_*$). The lower bound function theorem was first proved for positive, norm-preserving operators (Lasota-Yorke) and recently extended to positive operators which may not preserve the norm (Rudnicki). Thus the theorem may be applied to systems in which the population either grows or becomes extinct. Particularly interesting applications in biology are related to the problem of modeling cell cycle dynamics (Lasota-Mackey, Tyson).

Douglas A. Lauffenburger

A Dynamic Model for Cell Adhesion.

The adhesion of cells to surfaces is a key event in many physiological and pathological processes such as the immune response and the metastatic spread of cancer. This adhesion is typically mediated by the binding of cell membrane receptors to complementary ligand molecules and the adhesive surface. In order to understand this phenomenon quantitatively, we present and analyze a dynamical mathematical model for receptor-mediated cell adhesion to a ligand-coated surface in a fluid shear flow. The model is comprised of a pair of nonlinear ordinary differential equations which can be analyzed in the phase plane.

Markus Löffler

Modeling Hemopoietic Stem Cell Regulation.

Red and white blood cells and blood platelets have a common ancestor stem cell. Although the cell kinetic parameters of the blood forming proliferation and maturation scheme are fairly well known it is still unclear how the regenerative activity of the stem cells may be controlled. A simple two compartment model (stem cells, differentiated cells) based on ordinary non-linear differential equations will be presented which enables a classification of the basic control hypotheses. Two stem cell properties are considered to be controlled independently: the proliferative activity and the growth fraction. Examining the parameter space of the coupling coefficients reveals conditions for stability and bifurcation. The analysis gives suggestion for a reasonable choice of values. Some unsatisfactory features of previously published models will become apparent. In addition numerical results of a more complex model describing the interaction of granulo- and erythropoiesis on the stem cells will be presented.

Michael Mackey

The Dynamics of Platelet Production.

In certain clinical situations, the number of circulating platelets in the blood stream display oscillatory dynamics which may either be periodic or aperiodic. A physiologically realistic model of platelet production yields a first order delay-differential equation for the number of circulating platelets (P). The equation is nonlinear and contains two significant time delays, one of which is state dependent as it depends on the value of P in a monotone increasing fashion.

Analysis plus numerical simulations suggest that increasing the random destruction of circulating platelets leads to a succession of bifurcations of platelet dynamics, finally culminating in aperiodic variations in P . These results are in correspondence with the clinically observed phenomena.

(Frank van den Bosch and) Hans Metz

Applying the Diekmann-Thieme Model for the Spatial Spread of Epidemics and Populations.

The Diekmann-Thieme model is a spatial extension of the Kermack- McKendrick functional differential equation model for the development of an epidemic. For this model Diekmann and Thieme independently proved the existence of an asymptotic speed of radial expansion. To apply the Diekmann-Thieme model in practice one has to devise well fitting submodels with few parameters for the integral kernel, and corresponding parameter estimation procedures. The talk describes the results of a cooperative project to this end by Frank von der Bosch, Jan Zadoks from the Agricultural University in Wageningen and myself. The agreement between the observed and predicted rate of focus expansion turned out to be surprisingly good. Further topics addressed were approximation formulas for calculating the speed, the connection with Fisher's equation, the extension to the spread of general structured populations and to non-rotationally symmetric space kernels (a necessary extension if one wishes to study large scale spread of plant epidemics). The (conjectured) results were applied to the spread of musk rat, collared dove and rabies.

Jaroslav Milota

Stability in Population Models with Infinite Delay.

Several biological models lead to partial differential equations of the type

$$\dot{u}(t) = d\Delta u(t) + f(u(t), u_t).$$

The theory for linearized equations is developed. This yields sufficient conditions for asymptotic stability of equilibria and also bifurcation results. As an example, the Volterra equation

$$\dot{u}(t) = d\Delta u(t) + au(t)[1 - bu(t) - e \int_{-\infty}^0 k(s)u(t+s)ds]$$

is treated.

Piero de Mottoni

A hyperbolic System of Conservation Laws of Degenerate Type Arising in a Pursuit-Escape Model.

The object of the present report (based on a joint work with Hsiao Ling, Peking) is the system of conservation laws

$$\begin{aligned}
 &u_t + (u(1-v))_x = 0 \\
 (*) \quad &v_t + (v(1+u))_x = 0 \quad x \in \mathbb{R}, \quad t > 0
 \end{aligned}$$

This is motivated by a model, originally proposed by Murray and Cohen, describing nonlinear advection phenomena for two populations, the "pursuers" and the "fugitives". According to this interpretation u, v , are the space gradients of population densities $U(x, t), V(x, t) \geq 0$ where U denotes the fugitives and V the pursuers. Since U, V obey the system (where only the total mass $\int_{\mathbb{R}} (U+V) dx$ is conserved)

$$\begin{aligned}
 U_t + (U(1-V_x))_x &= -UV_{xx} \\
 V_t + (V(1+U_x))_x &= +VU_{xx}
 \end{aligned}$$

in which $1 - V_x, 1 + U_x$ represent the advection velocities of the U 's, respectively of the V 's, this means that the U 's provoke the V 's into the pursuing action by moving away, while the V 's cause the U 's to flee by running after them. Moreover, the terms on the right-hand side say that the fugitives, when built up into a peak, are "stronger" than the pursuers, for they cause the pursuers to be eaten if they overtake a peak of fugitives; instead, the rearguard of the fugitives is eaten by the pursuers. In turn, the pursuers' forerunners eat the fugitives, but being grouped into a peak is disadvantageous for the pursuers, because the fugitives will feed on any peak of pursuers which happens to overtake them.

After studying rarefaction waves, shock waves and contact discontinuities for (*), the existence and uniqueness of the solution of the Riemann problem is proved. Then the possible wave interactions are studied in order to apply Glimm's method (in a somewhat modified form) and hence to establish the existence of a solution of the initial-value problem for (*). The qualitative properties of the solutions are studied in case of specific initial data.

Hans G. Othmer

Oscillations, Relay and Signaling in Dictyostelium discoideum.

The cellular slime mold *Dictyostelium discoideum* exhibits several of the morphogenetic processes, including cell-cell communication, cell movement and chemotaxis, and pattern formation and regulation. For this reason it serves as a model system from which insight into the control of these processes can be obtained. In this lecture we report on joint work with Peter Monk and Gary DeYoung on a mathematical model that reproduces the experimental observations on relay and

adaptation. Numerical computations show that this model predicts propagating waves of the correct amplitude, speed and wave form in an aggregation field. The computations also show that when an aggregation field is stimulated periodically at a sufficiently high frequency there is "conduction block" or "gating" of the waves, as is observed experimentally. We also address the question as to whether a single cell can serve as a pacemaker in an aggregation field and show that it can for parameter values suitable to cells of that age.

Günter Palm

Stability and Threshold Control in Neural Networks.

Investigations on associative memory and observations in real neural networks suggest that it should be possible to stabilize the total activity at relatively sparse activity patterns, i. e. patterns in which only a low percentage of neurons is active. Moreover, it should be possible to regulate this overall level of activity by some global parameter (here the threshold).

By means of a simple analysis of randomly connected neural networks one can show that this is indeed possible with plausible amounts of excitation and inhibition.

Manfred Peschel (coauthors W. Mende and F. Breitenecker)

Models of Biodynamical Systems with the Lotka-Volterra Approach.

Direct Iteration as a simulation concept

$$x_i' = x_i \prod_{G_{ij} > 0} (1 + DG_{ij}x_j) / \prod_{G_{ij} < 0} (1 - DG_{ij}x_j)$$

for Lotka-Volterra systems

$$\dot{x}_i = x_i \sum G_{ij}x_j, \quad i = 0, 1, \dots, n-1, \quad D \text{ step - width.}$$

Special cases are Hypercycle

$$x_i' = x_i (R_i F_i x_i^{k_i} (1 + Dx_{i+1}) / (1 + D\phi)), \quad \phi = \sum x_i x_{i+1}, \quad i \bmod n$$

and chaotic Lotka-Volterra networks of the form

$$x_i' = R_i F_i x_i^{k_i} (1 - x_i^{v_i})^{l_i} \prod_{G_{ij} > 0} (1 + DG_{ij}x_j) / \prod_{G_{ij} < 0} (1 - DG_{ij}x_j)$$

$0 < R_i \leq 1$, and normalization factors F_i , as alternative proposals for neural networks. Control-factors of the forms

$$U = (1 + KRg(xs)) / (1 + KRg(x)) \text{ resp. } U = (1 + KRg(xs)/g(x)) / (1 + KR)$$

with $g(x)$ monotonous functions are discussed. Bifurcations and chaos in $x' = xU$ may arise.

Helmut Schwegler

Stefan problems in Modeling of Self-Maintaining Systems.

Recently "protocell models" have been discussed as examples of self-maintaining and proliferating systems being governed by simple physical mechanisms of diffusion, reaction and solidification. Mathematically these mechanisms condense into a free boundary problem. For the aim of understanding better the mathematical questions here a 1-dimensional version model of such models is investigated. It consists of a diffusion equation for a building material with a production term which is constant over the whole length of the 1-dimensional object (size dependent nutrition). This building material can condense at the ends (pointlike surface) of the object giving rise to growth or shrinkage according to the excess of material transported to the ends by diffusion beyond a constant loss. This balance gives the so-called Stefan equation for the change of size. It depends on the one hand on the gradient of the concentration of the building material and determines on the other hand the boundary for the diffusion of the material. It can be shown that under sufficiently high nutrition there exist stationary solutions for the size of the object and the concentration profile, i. e. the object is self-maintaining. The stability of one branch of stationary solutions can be shown by explicitly solving the equations in the neighbourhood of the stationary solutions.

Karl Sigmund

A Maximum Principle for Frequency Dependent Selection.

It is well known that the classical selection equation of Fisher, Haldane and Wright is a gradient (with the average fitness as potential) if the state space, i.e. the probability simplex, is provided with a certain Riemannian metric first introduced by Shahshahani. If the fitness parameters are frequency dependent, this is no longer valid in general. However, if the fitness is given by a game whose dynamics is a Shahshahani gradient, then the corresponding frequency dependent selection equation is also such a gradient. This is the case in particular if the genotypes correspond to convex combinations of the alternatives.

Brian D. Sleeman

Complex Behaviour of Biological Models and Hamiltonian Dynamics.

Discrete time models from population genetics, ecology, physiology may often be formulated as

$$u_{n+1} = Q[u_n] \quad (1).$$

where, for example, $u_n(x)$ represents the gene fraction or population density at time "n" at the point x of the habitat and Q is an operator on a certain set of functions on the habitat. The habitat may be one, two or three dimensional. It may be discrete in which case x ranges over a discrete set of niches. Under certain monotonicity conditions on Q it is known that (1) supports "discrete" travelling fronts. If this condition is relaxed then (1) may exhibit quite complex characteristics. For a class of biological models based on Fisher's equation we attempt to distinguish between complex behaviour appearing at each generation and that due to diffusion throughout the habitat. Typically if (1) is continuous in space and has period-2 solutions in time then the spatial behaviour may be described in terms of Hamiltonian dynamics leading to non-integrable systems (implying stochasticity) to which KAM theory may be applied as well as the ideas of Melnikov.

Hal Smith

Oscillations and Multiple Steady States in a Cyclic Feedback System with Repression.

The classical Goodwin equations modeling the control of protein synthesis in the cell and variants which include multigene expression in a single feedback loop are studied. In the case that an even number of genes are involved in the loop, it is shown that convergence to steady state is the rule. In this case there can be multiple stable steady states if the nonlinearities are sufficiently strong. If an odd number of genes are involved in the loop, a general result is stated which implies that periodic solutions occur when the steady state is unstable (strong nonlinearities).

Betty Tang

Competition in the Gradostat.

The chemostat is a well-studied model ecosystem in which all components, in particular the nutrients, are assumed to be homogeneously distributed. The gradostat, which essentially is a concatenation of chemostats, was devised to study growth along a nutrient gradient. When only one species grows in the gradostat, there is an interesting spatial distribution of the population. When there are two competing species, so far we have been able to obtain conditions for coexistence as well as globally asymptotically stable steady state in a 2-vessel gradostat. In the general n-vessel gradostat, coexistence as a steady state can be shown to be possible. This is different from the chemostat where competitive exclusion holds.

Petre Tautu

Qualitative Aspects of Tumor Growth.

A stochastic spatial model for tumor growth is introduced in the framework of the theory of interacting biological cell systems. Essential biological characteristics of normal and neoplastic growth are discussed leading to the construction of a general growth model on an infinite d -dimensional ($d \geq 1$) lattice. Three classes of growth models are mentioned: (i) Eden models, (ii) Williams-Bjerknes models, and (iii) a multivariate Markov configuration model. These belong to the family of "voter" models having the advantage of existence of dual processes. Among many qualitative aspects of tumor growth, the (weighted) occupation time will be analyzed in this talk; a parallelism with a class of measure-valued processes will be particularly mentioned.

Horst R. Thieme

How to Estimate the Efficacy of Control Measures in Epidemic Plant Diseases.

In their paper "A model for spread of plant disease with periodic removal" (J. Math. Biology 21 (1984), 149-158) S. Fishman and R. Marcus present a model for the spread of the Citrus Tristeza virus in a citrus orchard. The trees are planted in rows and are periodically inspected. Detected infected trees are removed. Unfortunately it is unknown how large the percentage of detected trees (among the infected trees) actually is and whether the control efforts are sufficient to keep the disease down. We show how the success of the control measures can be judged by appropriately combining the data from all rows collected at single inspections and comparing the combinations from subsequent inspections.

Robert T. Tranquillo

Stochastic Model of Leukocyte Chemosensory Movement.

We propose a unifying hypothesis to explain the component of directional randomness observed in tracks of leukocytes in both random motility and chemotaxis. It is based on a description of the leukocyte as an integrated system sensing and responding to a "noisy" receptor signal: noise inherent in receptor-sensing of chemoattractants underlies the directional randomness. The unbiased random walk characteristic of random motility arises from perceived fluctuating gradients without a mean reference direction and the biased random walk in chemotaxis arises due to the occurrence of perceived concentration fluctuations around the mean gradient.

Analysis of the stochastic model yields an objective index of directional randomness in random motility, the "directional persistence time", in terms of model parameters associated with receptor binding, receptor signal transduction, and a cell turning response. Simulation of the model equations yields cell tracks from

which the orientation behavior in a chemoattractant gradient can be characterized in terms of the same model parameters. This work elucidates the relationship between persistence and orientation in terms of the sensing, transduction, and response mechanisms.

John J. Tyson

**A Stochastic Model of Cell Division
(with application to fission yeast).**

Cellular, genetic and molecular studies suggest that cell division in lower eukaryotes is controlled by the interaction of an activator and an inhibitor of mitosis. From experimental evidence we construct a stochastic model of cell division and derive therefrom the characteristic statistical properties of cell cultures in balanced exponential growth. Comparing the implications of the model with experimental observations, we predict the mitotic activator to be an unstable protein present in approximately 200 copies per cell at division.

Gail Wolkowicz

A Predator-Prey Model Involving Group Defence.

A class of ODE's of generalized Gause type, modelling predator-prey interaction involving group defence by the prey is considered. By group defence we mean the phenomenon whereby the prey are better able to defend or disguise themselves when their numbers are large.

Using the carrying capacity of the environment as the bifurcation parameter, it is shown that the model exhibits rich dynamics: As well, the results give strong support for Rosenzweig's paradox of enrichment since the model predicts that sufficient enrichment leads to extinction of the predator for almost all initial conditions.

The model will then be used to motivate how the connection matrix could be used in the analysis of biological models.

Berichterstatterin: M. Kretschmar

Tagungsteilnehmer

Dr. T. Aldenberg
R. I. V. M.
Postbus 1

NL-3720 BA Bilthoven

Prof. Dr. P. Colli
Dipartimento di Matematica
Universita di Pavia
Strada Nuova, 65

I-27100 Pavia

Prof. Dr. W. Alt
Abteilung Theoretische Biologie
Universität Bonn
Kirschallee 1

5300 Bonn 1

Prof. Dr. P. Colli-Franzone
Dipartimento di Matematica
Corso C. Alberto, 5

I-27100 Pavia

Dr. B. Aulbach
Mathematisches Institut
der Universität Augsburg
Memminger Str. 6

8900 Augsburg

Prof. Dr. J. Cushing
Dept. of Mathematics
Building 89
University of Arizona

Tucson , AZ 85721
USA

Prof. Dr. E. Bohl
Fakultät für Mathematik
der Universität Konstanz
Postfach 5560

7750 Konstanz

Prof. Dr. O. Diekmann
Stichting Mathematisch Centrum
Centrum voor Wiskunde en
Informatica
Kruislaan 413

NL-1098 SJ Amsterdam

Prof. Dr. S. Busenberg
Dept. of Mathematics
The Claremont Colleges
Harvey Mudd College

Claremont , CA 91711
USA

Prof. Dr. K. Dietz
Institut für Medizinische Biometrie
Universität Tübingen
Westbahnhofstraße 55

7400 Tübingen

Prof. Dr. H. I. Freedman
Dept. of Mathematics
University of Alberta
632 Central Academic Building

Edmonton, Alberta T6G 2G1
CANADA

Prof. Dr. J. P. Gabriel
Departement de Mathematiques
Universite de Fribourg

CH-1700 Fribourg-Perolles

U. Gaedke
Limnologisches Institut
Universität Konstanz
Mainaustraße 212

7750 Konstanz

Dr. A. Grabosch
Department of Mathematics
Georgetown University

Washington, D. C. 20057
USA

Prof. Dr. M. R. Guevara
Dept. of Physiology
McGill University
3655 Drummond Street

Montreal, Quebec H3G 1Y6
CANADA

Prof. Dr. M. Gyllenberg
Institute of Mathematics
Helsinki University of Technology
Otakaari 1

SF-02150 Espoo

Prof. Dr. K.P. Hadeler
Institut für Biologie II
Universität Tübingen
Auf der Morgenstelle 28

7400 Tübingen

Prof. Dr. U. an der Heiden
Fakultät für Naturwissenschaften
Universität Witten/Herdecke
Stockumer Str. 10

5810 Witten -Annen

Prof. Dr. H.J.A. Heijmans
Mathematisch Centrum
Centrum voor Wiskunde en
Informatica
Postbus 4079

NL-1009 AB Amsterdam

Dr. J. Hofbauer
Institut für Mathematik
Universität Wien
Strudlhofgasse 4

A-1090 Wien

Prof. Dr. W. Jäger
Institut für Angewandte Mathematik
der Universität Heidelberg
Im Neuenheimer Feld 294

6900 Heidelberg

Prof. Dr. D. Lauffenburger
Department of Chemical Engineering
University of Pennsylvania
311 Towne Bldg.
220 S. 33rd Street

Philadelphia, PA 19104 USA

Prof. Dr. P. Jagers
Dept. of Mathematics
Chalmers University of Technology
and University of Göteborg
Sven Hultins gata 6

S-412 96 Göteborg

Dr. M. Löffler
Abteilung LFI/EDV
Universitätsklinik 1
Joseph Stelmannstr. 9

5000 Köln 41

Prof. Dr. J. P. Keener
Dept. of Mathematics
University of Utah

Salt Lake City, UT 84112
USA

Prof. Dr. M. C. Mackey
Department of Physiology
McGill University
3655, Drummond Street

Montreal P. Q. H3G 1Y6
CANADA

M. Kretzschmar
Lehrstuhl für Biomathematik
Universität Tübingen
Auf der Morgenstelle 10

7400 Tübingen

Prof. Dr. J. A. J. Metz
Institut voor Theoretische Biologie
Rijksuniversiteit Leiden
Groenhovenstraat 5

NL-3211 BT Leiden

Prof. Dr. A. Lasota
Institute of Mathematics
UMCS
pl. Marii Curie-Skłodowskiej 1

20-031 Lublin
POLAND

Prof. Dr. J. Milota
Dept. of Mathematics
University Karlov
MFF UK
Sokolovska 83

186 00 Praha 8 CSSR

Prof. Dr. P. de Mottoni
Dipartimento di Matematica
Universita di Roma II
Via Orazio Raimondo

I-00173 Roma

Prof. Dr. J. Rinzal
National Institute of Health
Building 31, Room 48-53

Bethesda, MD 20205
USA

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

Salt Lake City, UT 84112
USA

Dr. W. Rittgen
Institut für Dokumentation,
Information und Statistik
Deutsches Krebsforschungszentrum
Postfach 10 19 49

6900 Heidelberg 1

Dr. G. Palm
Max-Planck-Institut für
Biologische Kybernetik
Spemannstraße 38

7400 Tübingen

Prof. Dr. F. Rothe
Fachbereich Informatik
Hochschule der Bundeswehr
Werner-Heisenberg-Weg 39

8014 Neuburg

Prof. Dr. M. Peschel
Forschungsbereich Mathematische
Kybernetik, Akademie der
Wissenschaften der DDR
Rudower Chaussee 6

DDR-1199 Berlin

Dr. R. Schaaf
Institut für Angewandte Mathematik
der Universität Heidelberg
Im Neuenheimer Feld 294

6900 Heidelberg

L. Pilz
Institut für Epidemiologie und
Biometrie
Deutsches Krebsforschungszentrum
Postfach 10 19 49

6900 Heidelberg 1

Prof. Dr. H. Schwegler
Fachbereich Physik
Universität Bremen
Universitätsallee

2800 Bremen

Prof. Dr. K. Sigmund
Institut für Mathematik
Universität Wien
Strudlhofgasse 4

A-1090 Wien

Dr. H. R. Thieme
Sonderforschungsbereich 123 "Stoch.
mathem. Modelle i.d. Naturwiss."
der Universität Heidelberg
Im Neuenheimer Feld 294

6900 Heidelberg

Prof. Dr. B. D. Sleeman
Dept. of Mathematical Sciences
University of Dundee

GB- Dundee , DD1 4HN

Prof. Dr. R. Tranquillo
Centre for Mathematical Biology
University of Oxford
24 - 29, St. Giles'

GB- Oxford OX1 3LB

Prof. Dr. H. L. Smith
Department of Mathematics
Arizona State University

Tempe ,AZ 85287
USA

Prof. Dr. J. J. Tyson
Dept. of Biology
Virginia Polytechnic Institute

Blacksburg , VA 24061
USA

Prof. Dr. B. Tang
Dept. of Mathematics
University of Southern California
University Park

Los Angeles , CA 90089-1113
USA

Prof. Dr. G.S.K. Wolkowicz
Department of Mathematics
Mc Master University

Hamilton, Ontario L8S 4K1
CANADA

Dr. P. Tautu
Institut für Epidemiologie und
Biometrie
Deutsches Krebsforschungszentrum
Postfach 10 19 49

6900 Heidelberg 1

11

