MATHEMATISCHES FORSCHUNGSINSTITUT OBERWOLFACH

T a g u n g s b e r i c h t 51/1993

Mathematische Modelle in der Biologie

21.11. – 27.11.1993

This meeting on Mathematical Biology (now an established field on an international scale) has brought together a reasonably small group of scientists from many countries whose domains of research cover a large portion of the field. Quite a number of young scientists have presented their results.

The meeting has been organized by P. Maini (Oxford), L. Segel (Rehovot), K.P. Hadeler (Tübingen). Major topics were morphogenesis and immunology, along with neurobiology, population dynamics, epidemiology and other fields.
From the mathematical point of view various areas have been covered, in particular ordinary and partial differential equations and stochastic processes. It could be observed that some problems of Mathematical Biology use most recent and advanced tools and results from rather distant mathematical fields, e.g. the effective investigation of certain pattern formation systems uses results on curvature flows from differential geometry.

We shall not review the contributions in detail but rather refer to the abstracts. We just list some of the topics covered: Pattern formation, aggregation, motion of cells and microorganisms, chemotaxis, foraging and search strategies, growth of tissues, skin morphogenesis and wound healing, cell biology, immunology, surface receptors and binding, structured population models, with applications to epidemiology, optimal vaccination strategies, sexually transmitted and parasitoid diseases, neural networks and discrete dynamical systems, population genetics, evolution and toxonomy.

The facilities of the Institute have been great as ever and the assistance of the staff has made this conference not only scientifically effective but also a pleasant event.

Vortragsauszüge

Wolfgang Alt:

Stochastic modeling of search behavior and homing strategies

General aspects of search behavior are envisaged: locomotion itself, capability of orientation and possible storage of information about "goals" of search. The importance of stochasticity in these processes is briefly discussed. In particular, experimental findings and theoretical concepts on the homing search of desert isopods (Hemilepistus reaumuri) are presented. Using the general framework of stochastic differential equations for the angular turning rate of a migrating individual, search paths with characteristic loops and meanders can be modelled and simulated. Search success is quantified by measuring the degree of path overlap and by computing an index of area search intensity. Quantities are plotted versus path length, both for observed isopod data and for typical simulated search paths. Certain elements of a systematic search are described and explained by a hypothesis about temporal locomotion control, based on the isopods' ability for path integration and directional compensation. Finally, possible effects of orientational cues are mentioned.

Viggo Andreasen:

Genotype proportions in hybrid zones

A hybrid zone between two populations that differ at one locus is studied for a diploid organism. The heterozygote fitness is reduced by $(\beta + \delta)$ (β is the birth rate deviation and δ is the death rate deviation). The population extends along a one dimensional continuous habitat and migration occurs by simple diffusion of individuals. A simple continuous time model without age-structure models the demographic process for each genotype and the system is transformed into three new variables, the total population size N, the gene frequency p and the deviation from Hardy-Weinberg proportions F. The gene frequency in the steady state cline always follows closely a hyperbolic tangens. Analysis of the asymptotic behavior of the cline far from the hybrid zone suggests a qualitative prediction of the shape of N, p, and F over the zone. For slow selection the shape is determined by a central steepness of $\sqrt{(\beta + \delta)/4\sigma}$ as observed by Bazykin in 1969, where σ is the diffusion coefficient. For strong selection the cline is less steep than the Bazykin cline and the form is dominated by the migration process. The steepness at the center of the cline is close to $\sqrt{b/4\sigma}$ where b is the birth rate of homozygotes.

Nicola Bellomo:

Kinetic models in biology and immunology

The physical system to model consists in tumor cells which grow in vivo and interact with the host and the immune system. The immune system has the potential capability of producing some significant anti-tumor reactions. It recognizes

tumor-associated membrane antigenes or mutuated peptides presented by the histocompatibility complex. The ensuing reaction can affect tumor growth, both by impairing or enhancing it. In natural conditions, however, the progressive tumor growth suppresses the immune reaction, induces host cachexia, and eventually results in host death.
The research line developed in collaboration with the Center of Immunogenetics of the National Research Council Italy, Torino University, attempts to develop a mathematical model, based on the methods of non equilibrium statistical mechanics, suitable to predict the tumor evolution starting from interactions, at a cellular level, of tumor cells and host system cells.
The final objective is to obtain a prediction of the evolution of the tumor focusing the activities of the immune system towards the inhibition of certain tumors.
The model consists in a set of integrodifferential equations which are studied at a qualitative and quantitative level having in mind the objective stated in the preceding item.

Vincenzo Capasso:

Modelling HIV transmission via shared drug equipment in groups of injecting drug users

Notification data in Italy show that about 70% of reported cases of AIDS are related to drug addiction. Kaplan in 1989 has proposed a mathematical model of transmission of HIV via shared drug injection equipment in "shooting galleries". Actually in Italy injection equipment is not difficult to acquire, so that interaction among drug users occurs more likely because of sharing the equipment in a friendship group of drug users.
By importing some of the basic ideas of Kaplan's model we propose here a modification which takes into account grouping of drug users as the main mechanism of transmission. A mathematical model based on a system of ODE's is thus proposed in which the force of infection is obtained via a stochastic model of friendship grouping and sharing of infecting equipment. The qualitative analysis is carried out showing the role of R_0, the reproduction ratio, as a threshold parameter for a globally asymptotically stable nontrivial endemic state.
Extensions to structured populations are also pursued together with computer simulations of the solutions. A sensitivity analysis of the parameters has also been shown.

Carlos Castillo-Chavez:

Demographic pair formation models for heterogeneously mixing populations

We consider a heterosexually mixing population where $m = [m_1, \ldots, m_n]^t$ and $f = [t_1, \ldots, t_n]^t$ denote the single male and female populations, respectively. Let Q_{ij} denote the number of pairs with type i-male and type j female; M_m and M_f

the per capita removal rates for male and females resp.; Λ_i^m and Λ_i^f the recruitment rates – assumed constant – of single male and females for type i, resp; $C_i(m,f)$ and $B_i(m,f)$ the per capita pair formation rates of type i singles, male and female resp.; $p_{ij}(m,f)[q_{ij}(m,f)]$ the probability that an i-male pairs with a j-female [i-male with a j-male] given that he [she] pairs with somebody. The dynamics can then be described (τ_{ij} denotes the pair dissolution rate) by the following ODE system:

$$\begin{aligned}
\frac{dm_i}{dt} &= \Lambda_i^m - (M_m + C - i(m,f))m_i + \sum_j (M_f + T_{ij})Q_{ij}, \\
\frac{df_i}{dt} &= \Lambda_i^f - (M_f + B_i(m,f))f_i + \sum_j (M_m + T_{ji})Q_{ji}, \\
\frac{d}{dt}Q_{ij} &= C_i(m,f)m_i p_{ij}(m,f) - (M_m + M_f + T_{ij})Q_{ij}, \\
& \qquad i = 1,\ldots,n; \qquad j = 1,\ldots,n \qquad (*) \\
\text{where} \quad & \sum_i^n C_i(m,f)m_i = \sum_i B_i(m,f)f_i, \\
& \sum_j p_{ij}(m,f) = \sum_j q_{ij}(m,f) = 1, \\
& m_i C_i(m,f) P_{ij}^{(m,f)} = f_j B_j(m,f) q_{ji}(m,f).
\end{aligned}$$

We further assume that

$$\begin{aligned}
&\frac{\partial}{\partial m_i}(m_i C_i(m,f)) \geq 0\,, \qquad \frac{\partial}{\partial f_i}(f_i B_i(m,t)) \geq 0, \quad i = 1,\ldots,n \\
&\frac{\partial}{\partial m_j} C_i(m,f) \leq 0\,, \qquad \frac{\partial C_i(m,f)}{\partial f_j} \leq 0\,, \\
&\frac{\partial}{\partial m_j} B_i(m,f) \geq 0\,, \qquad \frac{\partial}{\partial f_j} B_i(m,f) \leq 0\,, \quad j = 1,\ldots,n
\end{aligned}$$

If $\sigma_{ij} = \sigma\ \forall i,j$ then the following results where established:

R1 If $(*)$ has only one equilibrium then it is a global attractor and

$$\begin{aligned}
\lim_{t\to\infty} \frac{Q_{ij}(t)}{\sum_j Q_{ij}(t)} &= p_{ij}(m^*, f^*) \\
\lim_{t\to\infty} \frac{Q_{ij}(t)}{\sum_i Q_{ji}(t)} &= q_{ji}(m^*, f^*)
\end{aligned}$$

R2 If

$$C_i(m,f) = \frac{\alpha_i \sum_k \beta_k f_k}{\sum \alpha_k m_k + \sum \beta_k f_k}\,, \quad B_i(m,f) = \frac{\beta_i \sum \alpha_k m_k}{\sum \alpha_k m_k + \sum \beta_k f_k}$$

or

$$B_i(m, f) = \beta_i ,$$
$$C_i(m, f) = \alpha_i .$$

α_i and β_i are constants, then $(*)$ has a unique positive equilibrium which is globally asymptotically stable.

Joint work with Wenzhang Huang (Cornell University), Jia Li (Univ. of Alabama, Huntsville).

J. Demongeot:

Dependence of the asymptotic behavior of neural networks on:

a) the mode of updating the state of the neurons taking into account the state of their neighbours

b) the boundary conditions

A real neural network, partially or fully connected, presents different possible characteristics for its asymptotic behavior. The richness of this behavior (in terms of number or complexity of attractors (resp. confiners) in case of a deterministic (resp. stochastic) transition rule) is directly related to global properties of the network like:

- memory capacity
- speed of convergence
- entrainability,...

The complexity of the asymptotic behavior is highly depending on structural properties of the network such as:

- connectivity
- mode of updating the neurons (sequentially, block- sequentially or massively parallelly)
- boundary conditions (active or silent behavior on the frontiers of the network)
- form of the input signal (more or less correelated, second order stationary or not,...)
- degree of additional noise,...

We will focus on the dependence on the mode of updating and on the boundary condidtions and we will give examples of applicating these theoretical results.

Odo Diekmann:

Reflections on structured population models

It is argued that a convenient (both from a biological and from a mathematical point of view) formulation of structured population models is given by the system

of integral equations

$$B(t) - B(s) = \int_{-\infty}^{t} (K_E(t,\tau) - K_E(s,\tau))B(d\tau)$$
$$E(t) = \int_{-\infty}^{t} Q_E(t,\tau)B(d\tau)$$

where E is the environmental state and B the cumulative number of birth (as a measure on the space of individual birth states) and where K_E describes cumulative offspring production in the time interval specified by the arguments and Q_E the contribution to the environmental state. Two concrete examples were intended to be presented (but shortage of time reduced this to one). The talk is based on joint work with Mats Gyllenberg, Hans Metz and Horst Thieme.

Stephen Dunbar:

Models of saltatory search in optimal foraging

Many searching animals move in a jerky, or "saltatory" fashion: they move forward, pause briefly, and move forward again. Modelling this foraging movement views scanning-search and body-forward-movement as interdependent time-distance functions to allow not only for the possibility of oscillations implied by saltatory search, but other movement patterns as well, including cruise search. The modelling elements are:

1. Movement reduces the acuity of prey detection so animals must stop or slow down to detect prey successfully.
2. Animals must stop or slow down to minimize the cost of moving.

These assumptions are combined in an energy functional. Some simplifying assumptions make analysis possible. The existence of an oscillation solution imposes some necessary conditions on the convexity of the acuity and cost of movement functions. The Euler-Lagrange equations create a piece-wise linear system which can have a periodic or oscillating solution. The necessary conditions for a periodic solution imply parameter inequalities which can be experimentally tested.

Edith Geigant:

A differential-integral equation with application to anisotropic distributions of F-actin

The cytoskeleton of a cell contains many actin proteins which form orthogonal meshworks or parallel bundles under the influence of actin-binding proteins. To explain these structures we present a model consisting of a nonlinear ordinary differential-integral equation for the anisotropic directional distribution of actin filaments.
In the mathematical part of the talk we derive

1) properties of the discretization for 2 directions of the differential-integral-equation, e.g. bifurcation of stationary solutions from constant solutions, and
2) the behaviour of solutions with small/big masses, the stability of constant solutions and the long-time behaviour of solutions.

Then we are interested in stationary solutions and symmetries. The mathematical analysis as well as the numerical simulations show, that the model is well apt to explain the formation of orthogonal and parallel structures.

Byron Goldstein:

The kinetics of ligand binding and dissociation with cell surface receptors

In biological systems chemical reactions often occur between reactants that are not well mixed. In many cases one of the reactants is confined to a surface while the other is distributed over a volume. Here we consider a simple example, the reversible binding of ligands in solution to receptors on cell surfaces. For a ligand to bind it must diffuse to the vicinity of the cell surface and then react with a receptor. To predict the binding kinetics requires solving a diffusion-reaction problem. Surprisingly, this is rarely done when ligand-cell surface receptor kinetic binding studies are analyzed. Rather a chemical rate equation (an ODE) is solved that has the same form as for a well mixed system except that the fundamental rate constants k_q and k_r which are functions of the free receptor concentrations, i.e.

$$\dot{B} = k_f(R)LR - k_r(R)B, \qquad (1)$$

where B is the bound ligand concentration, L the bulk ligand concentration and $R = R_T - B$ the free receptor concentration. We show how, starting from the diffusion equation and appropriate boundary conditions, using the Method of Weighted Residuals, one can obtain Eq. (1) with the usual forms for k_f and k_r, i.e.

$$k_f = k_{on}/(1 + Rk_{on}/k_+) \quad \text{and} \quad k_r = k_{off}/(1 + Rk_{on}/k_+) \qquad (2)$$

where k_+ is the diffusion limited forward rate constant, i.e. for a ligand with diffusion coefficient D diffusing to a sphere of radius a, $k_+ = 4\pi Da$. We also show how Eq. (1) can be generalized to the case when there is more than one receptor population on the cell surface that binds the ligand or (2) when the cell releases a ligand that it can also bind. Finally, we look at binding studies that test Eq. (1).

K.P. Hadeler:

Reaction telegraph equations

In the classical models for particles that move and multiply (KPP, Fisher's equation) Brownian motion is replaced by a correlated random walk. Then one arrives (in one space dimension) at hyperbolic systems. For these scaling properties,

stationary solutions on bounded intervals, the spectrum of generators, and, in particular, the problem of travelling fronts has been investigated.

Hans Heesterbeek:

Threshold quantities for helminth infections

For parasitic worms we give threshold quantities for invasion into virgin populations in autonomous and periodic environments for models that are described in terms of mean parasite burdens. The theory for the periodic case holds, with suitable reinterpretations of ingredient, also for invasion by micro-organisms. The mathematical view point leads naturally to a dominant Floquet multiplyer as candidate for the threshold quantity in the periodic case. A more "biological" approach leads to two additional quantities Q_0 and P, and one can show that all three have the same threshold behaviour. Q_0 has the interpretation: expected number of adult worms produced per adult worm is the absence of density dependent constraints. P has the interpretation: expected number years of adult life produced per year of adult life. Only when the environment is constant do P and Q_0 coincide and are the equal to what one would call R_0 for macro-parasites. In general all are different but P lends itself best to the development of approximation formulae.

Uwe an der Heiden:

Higher order delay-differential equations and hormonal control

We study feedback systems of the form of the differential-difference equation

$$\sum_{i=0}^{n} a_i \frac{d^i x}{dx^i}(t) = f(x(t-\tau)) \qquad (1)$$

with constants $a_i \in \mathbb{R}, \tau > 0$, and a nonlinear function $f : \mathbb{R} \to \mathbb{R}$. Applications arise in hormonal systems, population dynamics, neurophysiology, servodevices, and economics.
For $n = 0$ Eq. (1) corresponds to a difference equation with continuous time:

$$x(t+1) = f(x(t)).$$

Note that e.g. for $f(\xi) = 4\xi(1-\xi)$ this equation has a chotic attractor of Hausdorff dimension ∞. $n = 1$ gives the Mackey-Glass equation

$$dx(t)/dt + ax(t) = f(x(t-\tau))$$

which, as we conjecture, has a chotic attracors of arbitrary finite dimension depending on the form of f. Existence of chaos (with dimension between 1 and 2) has been proved earlier (an der Heiden & Walther: J.Diff. Eqs. 47, 273-295(1983),

an der Heiden & Mackey: J. Math. Biol. 16, 75-101(1982)). Recently for the case $n = 2$ Wolfdietrich Bayer and I could prove the existence of chaos in the equation

$$d^2x(t)/dt^2 + x(t) = f(x(t-r))$$

when f is piecewise constant ($f(\xi) = 1/2$ if $0 \leq 1/2$, $f(\xi) = -1/2$ otherwise).

Mike Hendy:

Which method should I use to build an evolutionary tree from my sequence data? (joint work with M.A.Charleston)

Biologists have more than 100 different methods available to reconstruct evolutionary trees from genetic sequence data. Advice on their relative performance is not generally available and can be limited to superficial evidence. In our simulation study we tested the performance of a number of methods:

CO (Compatibility analysis), CT (closest tree), Li (Li's method), NJ (neighbour joining), MP (maximum parsimony), ST (neighbourliness), and UPMGA, together with some variations.

Given (T, P), where T is a phylogenetic tree for n sequences and P is a set of probabilities describing the evolution of (2 or 4-state) character sequences on T, we can use Hadamard conjugation to calculate the expected frequency of each possible site pattern among the sequences. For each n, $4 \leq n \leq 10$, and for each tree "shape", we generated sample sequences (randomly selected using the expected frequencies) for many variations of P. We tested the accuracy of each of the tree building methods on each sample sequence.

The results presented are from more than 1200 combinations of the initial parameters, each trial being the average performance on 1000 sample sequences, the same set for each method. With one exception (UPGMA) the accuracy of methods were not greatly dissimilar. Sequence length and the lengths of short internal edges appear to be the most critical parameters affecting accuracy.

Pauline Hogeweg:

Pattern formation and multilevel evolution

We investigate pattern formation as a side effect of evolutionary dynamics. This pattern formation influences the evolutionary fate of the entities profoundly. For example there will be positive selection for early death if spiral wave patterns are formed. We investigate the attractors found dependent on the occurence of pattern formation or its absence. We conclude that evolution "lives" by side effects.

Frank Hoppensteadt:

VCON Networks

Oscillatory neural network models can process information in stable ways similar to some physiological networks. This is illustrated by various VCON networks which have the form

$$\frac{dx_j}{dt} = w_j + \alpha_j \cos x_j + S\{\sum_{i=1}^{N} c_{ij}(t)V(x_i)\} \quad \text{for} \quad j = 1, \ldots, N$$

where V is a voltage wave form (e.g. $V(x) = \cos_+^4 x$), S is a sigmoidal function (e.g. $S(u) = \tan ha$), C is a matrix of connection strengths (e.g. $C_{ij}(t) = c_0 + \frac{A}{t}\int_0^t V(x_i)V(x_i)$) and α_j and w_j are characteristic parameters. [see FCH, An Introduction to the Mathematics of Neurons, Camb.U.Press, 1986]. Six networks are presented that describe recent work: The attention model [FCH, SIAM Review 34 (1992) 426-444]; The pencil column model [FCH and R.Borisyuk, in progress]; The thin pencil model; Periodic Array of pencils; The atoll oscillator; and a storage network. Analysis of these networks in noisy environments [FCH, H.Salehi; A.Skorokhod, Randomly perturbed integral equations and some of their applications] and computer simulations of them are presented.

Putting these networks together gives a circuit analogous to the brain circuit.

$$\text{Stimulus} \rightarrow \text{Thalamus} \rightleftharpoons \begin{matrix}\textit{Reticular}\\ \textit{Complex}\end{matrix} \rightarrow \text{Neocortex} \rightarrow \text{Memory} \rightarrow \text{Response}$$

Volker Lendowski:

A deterministic model for the motion of *Listeria*

Listeria monocytogenes is a bacterium living inside human host cells. It uses the host cell actin to form a long "tail" that seems to push the bacterium forward. We applied a deterministic actin phase/solution phase flow model by Dembo, Harlow, Alt to calculate concentration and velocity of actin as a function of space and time. Three different approaches for a pushing force that determines the speed of the bacterium have been considered:

(i) polymerization in a neighbourhood of listeria and pushing by the total amount of stress leads to small effects because of a low concentration of actin at the surface.

(ii) Polymerization at the surface as a source term improves the results.

(iii) Polymerization at the surface as the source of the pushing force (an idea of G.Oster et al.) also seems to give reasonable results.

To each of these approaches numerical calculations in one space dimension have been presented.

Markus Löffler:

Stochastic branching processes in the intestinal epithelium

We provide arguments that the intestinal crypt epithelium is organized in the following way

(1) stochastic cellular branching process of stem cells with state dependent transition probabilities
(2) threshold dependent fission process of crypts if the number of stem cells exceeds a critical value
(3) pedigree concept of cellular development of transient proliferating cells
(4) cell displacement organized by local cell-cell-interactions acting on pedigree properties.

This concept is supported by simulation studies using stochastic cellular automata and iterative renormalisation procedures on the branching processes.

Dimitri O.Logofet:

When growing flowers is a matter of mathematics

In a variety of possible answers to the question there is a particular one that treats the "flower" as a visible form for a diagram of logical relations among various notions of matrix stability which occur in application areas like e.g. multi- species community dynamics. Under a few simple and natural conventions it turns out to be possible to construct a "flower" of relations, with the "petals" corresponding to particular subsets of real stable matrices $n \times n$ (community matrices). Mutual allocation of petals has required a certain number of statements concerning matrices to be either found in the literature or proved anew, especially those with the new class of "quasi-recessive" matrices. Each of the petals has its own meaning in terms of stability behavior in the corresponding class of dynamic models, yet the hierarchy is valuable in itself as a convenient framework to study new classes of matrices or/and to search for their characterizations in terms of matrix entries.

Michael C. Mackey:

Multistability in a population of replicating and maturing cells

If a population of cells has maturation $x \in [0,1]$ with maturation velocity $V(x)$ and is simultaneously proliferating with cell cycle time $\tau > 0$, then the evolution equation for the number $u(t,x)$ of cells at time t and maturation level x is given by a nonlinear transport equation with both temporal and maturation nonlocality:

$$\frac{\partial u(t,x)}{\partial t} + \frac{\partial (V(x)u(t,x))}{\partial x} = \mathrm{L}(u(t,-\tau, e^{-g(V(x))\tau}x))$$

with initial function $f(t',x)$, $(t',x) \in [0,\tau] \times [0,1]$.
Depending on f, the solution u may display a variety of limiting ($t >> 0$) spatio-temporal (ST) patterns ranging from ST constant solutions through ones in which

the ST pattern is highly irregular. A correspondence is drawn between the variety of these patterns and certain idiopathic hematological diseases as well as patient response following whole body irradiations and subsequent bone marrow transplant.

Philip K. Maini:

Sequential pattern formation in a model for skin morphogenesis

During morphogenesis regular patterns often develop behind a frontier of pattern formation which propagates across the domain. Here we consider the propagating patterns exhibited in two dimensions by a tissue-tissue interaction mechanochemical model for skin pattern formation. We show that the model can exhibit travelling waves of complex spatial pattern formation. We present two alternative mechanisms that can produce such sequential patterning. In particular, we show that the specification of a simple quasi-one-dimensional pattern is all that is required to determine a complex two-dimensional pattern. We relate our model solutions to pattern propagation during chick feather primordia morphogenesis.

Stephen Merrill:

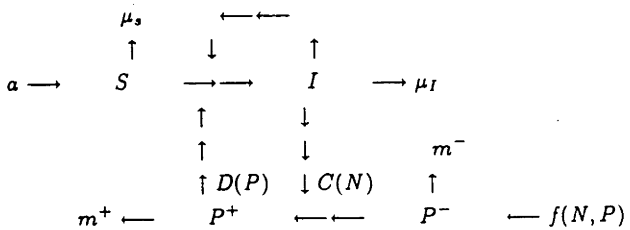
Modeling the early stages of HIV infection

The biology of the stages of HIV infection prior to "full blown AIDS" is described. Features of mathematical descriptions are argued to need a description of $CD4'$ T cell and macrophage infection, a description of the development of new strains and the decline of the immune response, and stochastic methods.
A branching process with immigration is suggested.

Jaroslav Milota:

Sexually transmitted disease with a high risk group

A model which could partly describe the transmission of sexually transmitted diseases by uncontrolled prostitution near the Czech-German border is presented. This is expressed by a system of four ODEs for susceptible and infective customers and for positive and negative prostitutes according to the following diagram:



where $N = I + S$, $P = P^+ + P^-$, the functions C, D, E are increasing, and $f(\cdot, P)$ is increasing, $f(N, \cdot)$ is decreasing.

It is shown that the model is epidemiologically well-posed and there is a threshold number R(# of new cases/infective) with the properties:

$R < 1$ $\Rightarrow \exists!$ (disease free) equilibrium which is locally asymptotically stable

$R > 1$ $\Rightarrow$ (i) disease free equilibrium is unstable

(ii) $\exists!$ endemic equilibrium, which is globally asymptotically stable provided

$m_- = m_+, \mu_- = \mu_+$

(iii) disease is uniformely persistent, i.e. $\exists \varepsilon > 0$.
such that $\underline{\lim} I(t) \geq \varepsilon, \underline{\lim} p^+(t) \geq \varepsilon$ (if $I(0), p^+(0), > 0$).

Masayasu Mimura:

Aggregating pattern formations in a chemotaxis model

A population model with diffusion, chemotaxis and growth is considered from the aggregating pattern formation view point. Assuming that the diffusion and chemotaxis rates of individuals are very small compared with the diffusion rate of the chemotactic substance, we discuss the pattern dynamics of localized solutions which biologically indicates the aggregation of individuals. For the study of such pattern formation, we derive a new equation which describes the boundary of aggregating region and study theoretically and complementarily numerically the dynamics of the aggregating patterns.

Johannes Müller:

Optimal vaccination strategies in age-structured populations

Within the framework of homogeneous age structured demographic models an optimization problem for vaccination strategies is considered.
In the model every person has a vaccination certificate: In this certificate the birthdate, the number of vaccinations applied to the person and the date of the last vaccination are written. Thus the population is structured by age, number of vaccinations and time since the last vaccination.
The reproduction number and the costs are introduced for a fixed vaccination strategy. Two problems, to get at given costs a strategy with minimal reproduction number or to get at given reproduction number a strategy with minimal costs, are defined. An existence theorem is proved. In special cases the form of optimal strategies is determined.

Hans G. Othmer:

Aggregation, blowup and collapse: The ABC's of taxis in reinforced random walks

Biological and probabilistic motivation is given to formulate the following question: Is aggregation in a population of motile individuals possible in the absence of longrange signaling? Beginning with a master equation for a random walk, we derive a number of taxis equations that differ in how the local environment is sensed. Computational results show that aggregation, blowup and collapse, are all possible, depending on the initial data, the chemotactic sensitivity function, and the local dynamics for the production of a non-diffusible substance that confronts transition rates.

Birgitt Schönfisch:

Differential equations and cellular automata as models for epidemics

On the one side we consider the Kermack-McKendrick model of differential equations. On the other side we define a cellular automaton $(G \subset \mathbb{Z}^2, U, E, f_0)$ where U is the Moore neighborhood, E is a set of elementary states $E = \{0, \ldots, e\}$ with a infectious and g recovered states and 0 as the susceptible state. Two local functions are investigated "a susceptible cell is infected with $p(s) = p^* s$ neighbors are infectious" (where s is the number of infectious neighbors) and "a susceptible cell is infected if at least $\bar{s}$ neighbors are infectious". A quasi-stationary distribution $(\hat{S}, \hat{I}, \hat{R})$ is defined and it is shown that $\frac{1}{a}\hat{I} = \frac{1}{g}\hat{R}$ (as required from the DGL model) is satisfied. Computer simulations imply that the same automata, with high migration introduced, correspond to the Kermack-McKendrick model with an infection term βSI for the stochastic rule and a term including the binomial distribution in the deterministic case. At most parameter sets the trajectories, the equilibrium and even the stability are apparently similar.

Lee Segel:

Honorable discharge of segnalling molecules from vesicles to granules

Here "honorable discharge" means discharge of (i) neurotransmitter from vesicles, and (ii) of histamine of most cell granules, that is in accord with key experimental observations. These observations include the facts that (i) is fast (almost complete discharge occurs in 0.1 msec), and that in (i) and (ii) the resides (granules) contain negative fixed changes to which positive transmitter and cations can bind. It is shown that diffusion cannot be responsible for (i), mainly because A is too slow. Futhermore it is demonstrated (via space-averaged Nernst-Planck + binding ODE's) that cation exchange can set up elective fields to provide honorable dischange of signalling molecules, both in cases (i) and (ii).

Hiromi Seno:

On dynamics of group formation and the community structure

The group size is determined, following some rules related to the fitness of the members within groups and the newcomers. Without any conflict, the group size continues to grow. However, once the gap between the benefits of group member and another (immigrant, subordinate member, member of other group) appears, the conflict in terms of the benefits validated by the fitness occurs. In this case, the cost for the conflict taken into account, the compromised resolution of the conflict can be formulated, which gives the rule to determine the final group size. The group size cannot grow beyond the final size. Since the final size is identified distinctly for each of inter-group processes: immigration; ostracism; fusion; decomposition, the ultimately approached size is determined depending on which inter-group process is relevant compared to the others. Indeed, with a simple numerical calculation, oscillation of the group size can occur for a set of parameters.

As for the structure of the community constructed by a number of groups, a mathematical modelling approach with a type of von Foerster equation is possible. For the stationary distribution of group size, assumed that the logistically growing groups make the community and reproduce the new group with the fixed minimal size N_0, it is shown that the rank-size relation for the community could appear as Zipf-Pareto law for sufficiently small size, that is, for sufficiently high rank.

The full scope for these topics is to give some mathematical modelling, with biologically significant sense, for the inter-group dynamics within the community. The next stage will be to consider the inter-group reaction dynamics which affect the structure of the community.

Jonathan A.Sherratt:

Spatiotemporal oscillations and chaos behind invading predators

Spatially homogeneous populations of predators and prey can coexist either at constant population densities or at densities that vary periodically in time. A much wider range of behaviours occurs in the spatially inhomogeneous case, including the invasion of a prey population by predators, leaving behind stable coexisting population densities. I use a reaction-diffusion model to consider the problem of invasion by predators when this coexisting steady state is unstable, so that homogeneous oscillations would evolve into periodically oscillating population densities. Intuitively, one might expect that the invading predators would simply leave behind homogeneous oscillations, but I show that the model I use predicts that this does not occur, and that rather the invading predators leave behind spatiotemporal oscillations. These oscillations can be regular or chaotic, depending on the parameter values. I will show that the regular oscillation are periodic plane waves, and that irregular oscillations arise when these solutions are unstable. Biologically, these results suggests a novel way in which spatiotemporal oscillations and chaos can arise in predator-prey interactions.

James Sneyd:

Models of calcium wave propagation

I present models of propagating calcium waves in two experimental systems: intracellular waves in the Xenopus oocyte, and intercellular waves in epithelial cell cultures.

Intracellular spiral waves of calcium in Xenopus may be modelled by a reaction-diffusion system, involving only a single intracellular calcium pool, and modulation of the IP_3 receptor by calcium in a biphasic fashion. The model gives specific experimental predictions which are in the process of being investigated.

The model for intercellular wave propagation uses a similar reaction-diffusion system and predicts that the observed intercellular wave may be the result of passive diffusion of IP_3 from the stimulated cell, only if the intercellular permeability is approximately $2\mu ms^{-1}$.

Horst R. Thieme:

An alternative explanation of sustained oscillations in childhood disease models (thesis of Zhilan Feng)

The multi-annual outbreaks of measles and other childhood diseases have previously been explained by an interaction of intrinsic epidemiologic forces which generate dampened oscillations and of seasonal or/and stochastic excitation. We show that isolation (i.e., sick individuals stay at home and have a reduced infective impact) can create self-sustained oscillations provided that the number of per capita contacts is largely independent of the number of individuals present which seems realistic as long as this number is sufficiently large. This means that the bilinear mass action term for disease incidence is modified by dividing it by the number of non-isolated individuals.

Carla Wofsy:

Modeling receptor aggregation

The aggregation of cell surface receptors, induced by the binding of hormones, interleukins, antigens and other extracellular signaling molecules, is essential for triggering diverse cellular responses. Mathematical models that include aggregation are required for the accurate interpretation of binding and dose-response data. Further, predictions of models reflecting different possible mechanisms of receptor aggregation and signal transduction suggest new ways to distinguish the mechanisms experimentally. We develop a model to analyze binding and aggregation kinetics when bivalent ligands aggregate cell surface antibodies into chains and small rings. We also model and analyze spatial point patterns from electron micrographs reflecting stages in the aggregation process.

Berichterstatter: Johannes Müller

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