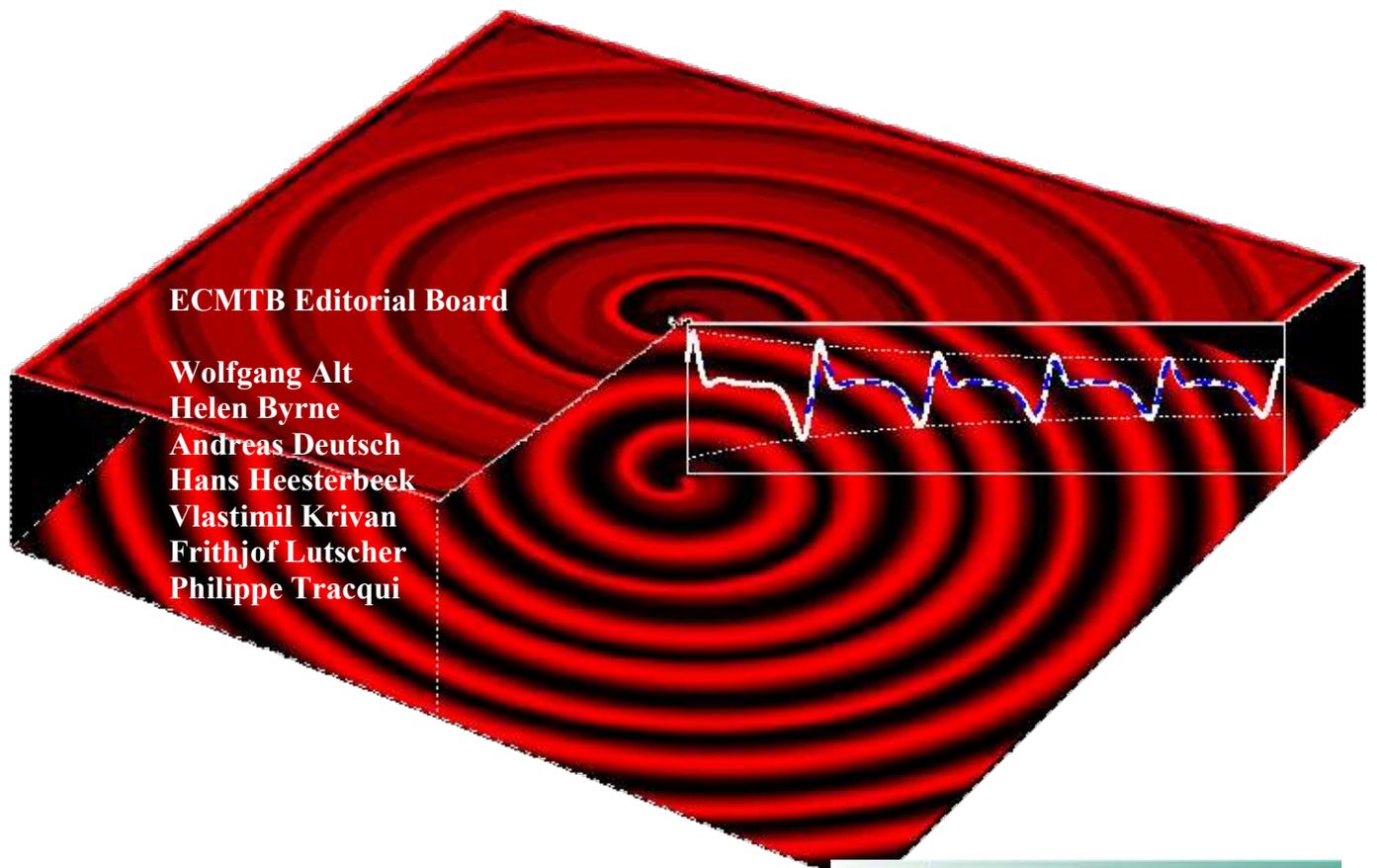


European Communications in Mathematical and Theoretical Biology
March 2004, No. 6

ECMTB Communications

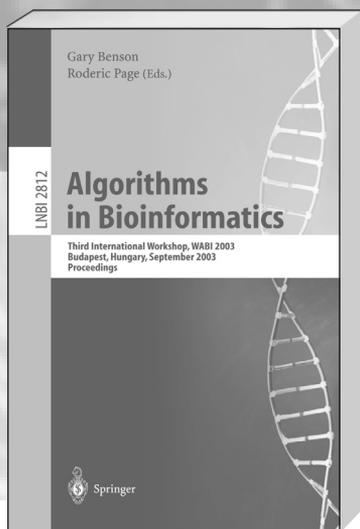


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A European Forum for Information, Presentation and Exchange
Official Communication Bulletin of the ESMTB:
European Society for Mathematical and Theoretical Biology



G. Benson, The Mount Sinai School of Medicine, New York, NY, USA; **R. Page**, University of Glasgow, UK (Eds.)

Algorithms in Bioinformatics

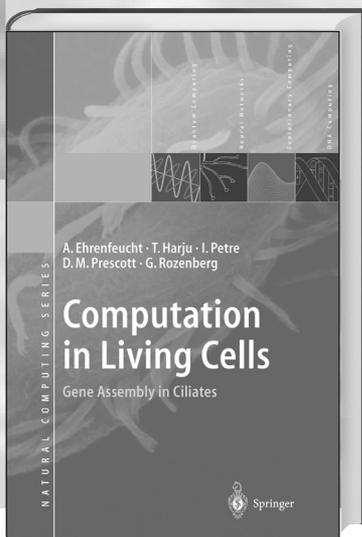
Third International Workshop, WABI 2003, Budapest, Hungary, September 15-20, 2003, Proceedings

This book constitutes the refereed proceedings of the Third International Workshop on Algorithms in Bioinformatics, WABI 2003, held in Budapest, Hungary, in September 2003. The 36 revised full papers presented were carefully reviewed and selected from 78 submissions. The papers are organized in topical sections on comparative genomics, database searching, gene finding and expression, genome mapping, pattern and motif discovery, phylogenetic analysis, polymorphism, protein structure, sequence alignment, and string algorithms.

Lecture Notes in Bioinformatics. Vol. 2812
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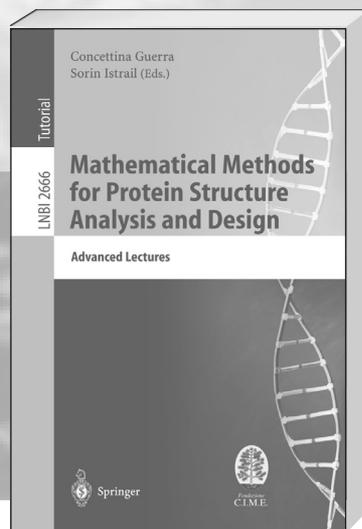
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Lecture Notes in Bioinformatics. Vol. 2666
2003. XI, 157 p. Also available online. Softcover
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The figure on the front cover shows a snapshot from numerical simulations of a two-dimensional nonlinear oscillatory system. The two layers depict the rotating spiral waves of the local phase (bottom) and the local amplitude (top) of the oscillations, respectively.

The spiral core is moving along a small circle and the emitted waves therefore acquire a modulation (shown in inset) that approaches a unique spatial profile.

For details see Brusch et al. (2003) "Doppler effect of nonlinear waves and superspirals in oscillatory media". Phys. Rev. Lett. 91, 108302 (2003).

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Editorial

Dear readers.

Mathematical and Theoretical Biology – what we are exploring together, concerns quantitative modeling and understanding of principles and varieties of life and – naturally and fatefully – also of death! One among us, namely *Ovide Orino (1947 – 2003)*, has very sadly and suddenly concluded his grateful life that he had devoted to Biomathematics and Population Dynamics, giving us and the coming generations his seminal expertise of teaching and organizing interdisciplinary research within theoretical and mathematical biosciences. Let us keep him in our mind and in our joint efforts to continue his ideas and plans (see the obituary on page 3).

One of the actions which our Society further promotes, is the organization of summer/winter schools and workshops on various central topics in modeling, simulation and analysis of biological structures and processes. Currently, Andrea de Gaetano and Rafael Bravo are preparing a proposal of a workshop program to the *European Commission Marie Curie FP6 Program* for the years 2005 – 2008. More information on this will be available in the next issue of these Communications. You find a currently valid list of **Forthcoming Events** at the end, pointing to this year's Summer School (June 7 – 18 in Croatia) as well as further conferences and workshops in Europe and overseas (see page 31).

Our European Society has now entered its 13th year of existence, and we are happy to register a steadily increasing number of members, particularly among younger scientists. With the coming extension of the European Union this year, we expect an enhancement of activities in the East-European countries and more responses by biomathematicians and theoretical biologists from there. The fact, that the next *European Conference on Mathematical and Theoretical Biology (ECMTB05), June 18 – 22, 2005* (see the announcement on page 36) will be held in Dresden, East-Germany, might be a sign towards further facilitating exchange of ideas and fruitful collaboration between Western and Eastern parts of Europe. We continue to take only half membership fees for all scientists from Eastern Europe as well as from developing countries in Africa, Near-East or other areas. Also, for members of national or sister societies we offer 20% reduced membership fees, reflecting an increasing amount of coordination and organization of joint events with these societies. Currently there are the

- SFBT: Soci t  Francophone de Biologie Th orique
- NVTB: Nederlandse Vereniging voor Theoretische Biologie
- ISTMB: Israelean Society for Theoretical and Mathematical Biology
- JSMB: Japanese Society for Mathematical Biology

and, last but not least, the international sister society

- SMB: Society for Mathematical Biology

with which our close connections (see the Report of the Dundee Conference on page 17) will continue to induce synergetic actions, e.g. by again combining our triennial conference *ECMTB05* in Dresden with the Annual Meeting of the SMB.

Indeed, that Mathematical Biology plays a more and more important role can be seen from the recently launched special activity of *Science Magazine* “to explore one of the hottest interdisciplinary collaborations in science today: ***the interface between mathematics and biology***”. In particular, in *Science's Next Wave* during the last months are presented the careers of a series of mathematicians engaged in biology and vice versa. For more details see page 31.

We begin the series **New Journals and Books** (on page 27) with the refreshed Journal of the Institute for Mathematics and its Applications, Oxford (IMA), now slightly renamed as ***Mathematics in Medicine and Biology***. For the first **6 months** of this year, all *ESMTB members will have free access* to the electronic issues of this journal and, if they want to continue for the whole year 2004, the reduced price will be 59 British Pounds (ca. 75 Euro).

Moreover, the traditional section on **History of Mathematical and Theoretical Biology** this time is devoted to illustrate life and work of the zoologist and theoretician *Jakob von Uexküll* who, almost 100 years ago, started to formulate basic modeling concepts characteristic for biological systems, such as '*feedback loop*' and '*functional cycle*', the latter in connection with his seminal introduction of the term '*Umwelt*', which by each organism is 'created' as a combination of its '*Merkwelt*' and '*Wirkwelt*' (see page 11).

We wish you an enjoyable reading of these 'Communications' and hope that this can support further communication between us biomathematicians and theoretical biologists. Moreover, you are welcome to send any suggestions or critical remarks to one of the editors (see addresses below) and, hopefully, participate in this *European Forum for Information, Presentation and Exchange* by sending us your own contribution for one of the next issues.

The editors: Wolfgang Alt, Hans Heesterbeek, Vlastimil Krivan, Frithjof Lutscher

*The closing date for submissions to the next issue COMMUNICATIONS # 7 will be **September 31st, 2004**. Please send, preferably by e-mail, information, scientific reports and other material to one of the editors:*

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Frithjof Lutscher, *Center for Mathematical Biology, Department of Mathematical and Statistical Sciences University of Alberta, Edmonton, AB T6G 2G1, Canada, flutscher@math.ualberta.ca*

Those who are interested in the Society or want to have more information, please use the Society web site:

<http://www.esmtb.org/>

The new ESMTB website describes goals and advantages of the Society, the procedure for membership application, ESMTB activities (conferences, schools) and a download option, in particular for this and other issues of the 'Communications'. The email address for questions and suggestions is

esmtb@zhr.tu-dresden.de

*A form for paying the 2004 membership fees you can easily find on our web site
or in this issue
on page 4 below*

Credit Card Payment now possible with PayPal

Information on **PayPal**:

PayPal enables any individual or business with an email address to securely, easily and quickly send and receive payments online. *PayPal's* service builds on the existing financial infrastructure of bank accounts and credit cards and utilizes the world's most advanced proprietary fraud prevention systems to create a safe, global, real-time payment solution.

Obituary OVIDE ARINO (24.4.1947 – 29.9.2003)



Ovide Arino was born in Toulouse (France) on April, 24, 1947. He studied Mathematics at the Université de Nice (France) with high profile French mathematicians such as Dieudonné, Boutet de Monvel and Grisvard. In 1972, he graduated from Nice, and in 1980, he obtained his PhD from the Université de Bordeaux (France) with a thesis entitled *Contributions à l'étude des comportements des solutions d'équations différentielles à retard par des méthodes de monotonie et bifurcation*.

In 1988, he became Professor of Mathematics at l'Université de Pau et des Oays de l'Adour (France), where he had been teaching courses mainly in partial differential equations as well as dynamical systems since 1973. From 1999 on he was First Class Research Director in I.R.D. (Institut pour la Recherche et le Développement), Paris-Bondy (France).

He held the position of a Visiting Professor at Brigham Young University (Provo), Memphis State University (Memphis), and Rice University (Houston) as well as a tenure-track position at the University of Mississippi (Oxford). He participated as plenary speaker, invited speaker, member of the scientific committee, member of the organizing committee, and organizer of special sessions in a countless number of conferences, seminars and workshops.

Ovide was a tireless propagator of the field of Biomathematics, and made great efforts to put students in contact with experts. Due to his scientific reputation, almost everyone followed his invitation to conferences or summer schools that he was organizing. During the last 10 years, he led the organization of more than 20 such events. Along with Profs. D. Axelrod (Rutgers) and M. Kimmel (Rice), he was the instigator of the series of International Conferences on Mathematical Population Dynamics.

He was reviewer of Zentralblatt, Math. Reviews of A.M.S, and SIAM Review and referee for the leading Applied Mathematics journals such as J. Math. Anal. Appl., J. Math. Biology, Proc. Royal Soc. of London, SIAM Analysis, JDE, Proc. A.M.S., Math. Biosciences, J. Theor. Biology, Nonlinear Analysis T.M.A.

During the last 10 years, he obtained sponsorship and financing for research projects from international public institutions such as CNRS-CNR (Morocco-France), PICASSO (Spain-France), POLONIUM (Poland-France), IFREMER (France), MedCampus (E.U.), DGXIV (E.U.)

Over the last 20 years, he was able to direct more than 60 theses (PhD., Thèses d'Etat, Thèses du 3^{ème} cycle), dedicating a great amount of his time to his students, almost to the level of a guru for their future development.

This enormous ability for organizing and encouraging students was backed by his great scientific capacity, imagination and deep knowledge of mathematics that became known through a long list of over 150 publications in prestigious scientific journals, inter alia SIAM Review, Nonlinear Analysis T.M.A., J. Diff. Equations, J. Math. Biology, J. Theor. Biology, J. Math. Anal. and Applications, Math. Biosciences.

His research developed along two different and complementary lines: works with mathematical aim and modeling in population dynamics. His results in the field of delay differential equations stand out: oscillations, functional differential equations in infinite dimensional spaces, state-dependent delay differential equations. His interest in population dynamics developed fundamentally in two large areas: cell proliferation models and fisheries. Some of the problems involved obtaining asymptotic properties of the solutions, in the framework of the theory of semigroups of positive operators as well as the application of aggregation of variables methods to models formulated with two time scales.

Ovide is survived by his wife Elizabeth, three sons Julien, Emilien and Lucien, one daughter Lisa and one grandson Samuel. Not even the brilliance of his professional life can be compared with his human quality. Ovide was much more than a great scientist: he was very much a family man, extremely generous, always ready to lend a helping hand and a great conversationalist. Ovide has left a significant imprint on our lives. The memory of those shared happy moment will stay forever in our hearts.

Rest in peace.

*Eva Sanchez, Pierre Auger, Rafael Bravo, Hassan Hbid
with additions from Elizabeth and Julien Arino.*

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a. The **Individual Annual Membership Fee** is:

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Minutes of the ESMTB Board Meeting

Bonn, September 19, 2003

Meeting starts 10.30 am

Present: Mats Gyllenberg (chair), Marcelle Kaufman, Vlastimil Krivan, Rafael Bravo de la Parra, Andreas Deutsch, Luigi Preziosi, Wolfgang Alt, Hans Heesterbeek (minutes).

Absent with apology: Helen Byrne, Philippe Tracqui

Adoption of the agenda

Two items are added to the agenda: Discussion on Curricula and date/place of next board meeting.

1. Minutes of the previous board meeting (Turku, February 21st, 2003)

The minutes of the board meeting as printed in the 5th issue of the Communications were approved. HH and MG remark that this is not the correct order of affairs (first make public then approve), but that we also do not want to have a delay of one year. In future the minutes will be circulated (almost) directly after the meeting and they will be corrected and afterwards approved by unanimous e-mail.

The points of action for the various board members, to be found in the minutes of the Turku meeting have almost all been dealt with. Most will be mentioned at appropriate places in the minutes below. The other points of action were: the new statutes and composition of the board were formally deposited at Grenoble (PT and HH); overview of EU-funding possibilities for mathematical and theoretical biology was published in issue 5 of the Communications (LP); discussion between MG and O. Arino about future financial benefit for the ESMTB from ESMTB summer schools (to be done).

2. Report from the President

- MG was invited to attend the ICIAM meeting in Australia to represent the ESMTB, but could not attend.
- V. Capasso (our past president) has contacted MG to inform him about the positive balance of 4000 Euro as a result of the 5th ESMTB tri-annual conference in Milan. Capasso and MG agreed upon the following: the money is the property of ESMTB. It can only be used according to decisions by the board. It is kept in a Milanese bank account for practical reasons (e.g. to avoid bank transfer charges).

After some discussion the board approved this arrangement.

- Professor Capasso has informed MG that the ESMTB has copyright on the Proceedings of the Milano ESMTB conference in 2002 and all royalties will be forwarded to the Society. The Proceedings have already been published in book form in record time. The board thanks V. Capasso for his hard work in bringing the book to print.
- The European Commission organizes a meeting for presidents of European scientific societies to discuss NEST (New and Emerging Science and Technology). MG will attend the meeting and report at the next board meeting.
- MK remarks in reaction to the above that there was a recent meeting at the EU in Brussels about "Systems Biology". Funding for activities under this new heading are becoming apparent in many places world wide. This is a new trend, for now with a more molecular focus (but expanding), in which computer scientists seem to be more successfully involved as yet than mathematicians. MK will enquire about the meeting and report on this new trend.
- At the Board meeting in Turku, Rafael Bravo de la Parra was asked to investigate the possibility of organizing the sixth ECMTB in Alcala in 2005 and to give his final answer by March 21, 2003. In a letter of March 18, 2003 addressed to the Board he declined to organize the congress. After that MG approached Wolfgang Alt (Bonn), Mark Chaplain (Dundee), Andreas Deutsch (Dresden) and Peter Jagers (Gothenburg) and asked them whether they would be willing to organize the congress and if so, submit a proposal by April 7, 2003. By the deadline one proposal, namely by Andreas Deutsch, was received. By email voting that took place during April 8-9, 2003 the Board unanimously (with the exception of AD who quite naturally abstained from expressing his view) decided that the 6th ECMTB 2005 will be arranged in Dresden during the period July 18-22, 2005 with Andreas Deutsch as responsible leader and Chairman of the Organizing Committee.

3. Report from the Treasurer

- A new bank account has been set-up in Dresden and everyone on the membership list has received an e-mail requesting payment of fees for 2003.

- Credit card payments will come into operation in 2004, and will then also be available for handling the conference fees in 2005. This will greatly simplify the payment of dues for many members and it is expected that the effort in setting this up will be rewarded with a substantial increase in payments.
- At the moment about 60 members have paid the 2003 fees, out of the ca. 300 members that received an e-mail, but payments are continuing to arrive.
- The balance (29-8-2003) is: 10.142 Euro. Out of this the following payments still have to be made: 10.000 Euro to Springer for the official journal of the ESMTB, the *Journal of Mathematical Biology*; 1533 Euro for the Communications and 200 Euro for the design of the ESMTB logo. AD has received a letter from Springer asking whether the society has to pay VAT. HH will find out and take up this matter with Springer. It is clear that without payments by members coming in, the society has no funds available for activities.
- Over the previous months, several board members discussed the goals and strategies of the society and the benefits for its members (AD, WA, HB, PT, VK). -- See the *Communications # 5* -- This has resulted in a very nice brochure that AD has produced for attracting new members. In addition a colour flyer was produced. Both can also be found on the ESMTB web-site. The board is very happy to extend heartfelt thanks to the employer of AD, the *Centre for High Performance Computing* of the Technical University Dresden, for taking care of the costs involved in producing these brochures. The same center also graciously pays for the upkeep of the ESMTB web-site.
- AD urges everyone to approach institutions and organizations for Institutional Membership. He will send out notices to several in Germany. WA remarks the fact that our next conference is near Eastern Europe, it might attract more scientists from Eastern European countries. It might be a good idea to also approach Eastern European institutions for membership. WA will look into this. WA suggests to again directly contact all 300 members who joined the society between one and three years ago and who still had received a copy of the Communications. In future only paying members will receive the Communications. WA will take care of that.
- HH raises the point that new negotiations with Springer for the JMB contract should start soon. Clearly the current contract is not to the benefit of our society in that it costs a large amount of money. It does provide our

members with access to the JMB as official journal of the ESMTB, but this access is only electronical and HH wonders how many members actually make use of this link. Many members have electronic access through their employer as part of a large package of scientific journals. As part of the contract, Springer should provide the board insight into the use of the service by members. HH will enquire with Springer whether these numbers can be obtained quickly. Clearly renegotiation of the contract is in order if this use is only small and paid membership remains below 200 members.

- To the text of the flyer will be added that members not only receive substantial discounts on the fees of ESMTB conferences and schools, but increasingly also for other conferences. This month for example there was a discount of 40 Euro on the fee for the *2nd Alcala Conference in Mathematical Ecology* and next year there is an equal reduction for the *Destobio-MPD* conference in Trento.
- The board expresses many thanks to AD for his activities.

4. Joint membership with SMB

WA and AD have attended the 2003-SMB conference in Dundee. WA participated in the SMB board meeting when it discussed the ESMTB proposal for reciprocal membership. The SMB has approved this with the same conditions that the ESMTB has adopted at the previous board meeting. This means that ESMTB members receive a 20% discount on the SMB membership fees (\$40 instead of \$50). The SMB will also instate student memberships (reciprocal \$20 instead of \$25). The SMB does not recognize a special fee for members from Eastern Europe. Eastern European members of the ESMTB do therefore only qualify for the reduced fee of \$40. The SMB does have a reduced fee for members from developing countries. WA proposes that we adopt the same. It is decided to extend the reduced-fee option to "developing countries". The treasurer will employ his wisdom in deciding which these countries are.

5. ESMTB web site

The ESMTB web site (www.esmtb.org) is fully operational, it has moved from Leipzig to Dresden. The policy is that it only contains society-related matters. All information (meetings, jobs, books, announcements, ..) not directly related to the society will be placed on an extra site to which the ESMTB-site is linked.[changed by the editors for actuality]. VK proposes to publish a list on the web site of academic institutions in Europe in our field, together with contact information, intended for students. After some discussion this idea is abandoned because of the large amount of work involved in keeping it up to date and completing such a list. Students have substantial opportunity to find contacts in their desired sub-fields by using internet search engines.

6. Report on the Communications

Thanks to VK, the printing and distribution of the Communications has moved from Rome to the Czech Republic. Many thanks go to VK to organize this.

WA mentions that the issue is not as good on content as usual. One example is the book section, for which HH is responsible. Other reasons are linked to the time pressure in releasing the issue on time, where the previous issues were much delayed. HH remarks that one of the problems was that it is unclear what the relation with the proposed content of the JMB pages is.

The costs of the issue can be lowered by printing the advertisements directly in the issue, instead of printing them separately and inserting them before mailing. This will be handled as it was before from the next issue. A fixed price will be charged per page. WA, PT and VK will work this out. Proof reading should also be improved to its old standard. Now that the editorial board has expanded, tasks can be more easily spread, but someone should now take charge as managing editor to make sure all tasks are performed. WA will take on this task.

7. Report on the JMB pages

HH remarks that one of the problems with the two pages that the society is allotted for society-related news in the JMB pages, is that any new information directly competes with the Communications. Since the Communications are the most visible and most-used “product” of the society, we should put our effort predominantly in that publication. It is also unclear who will read the JMB pages, since they will probably not appear on the Springer Web-site for JMB. HH has not found the existing pages from other societies that have Springer journals as their official journal. These societies, however, all obtain hard copies of the journal for their members. HH will enquire at Springer. WA remarks that the idea of having “perspectives” on our field written by specialists could draw mathematicians to the field. However, these mathematicians are already interested since otherwise they would not read JMB and the question is how many people are reached in this way that could not simply be directed to our web-site and the Communications. It is better to provide more space for perspectives in the Communications in future. It is decided to print a revised version of AD’s flyer in the JMB pages to start with. AD will provide this once HH mails him the Springer guidelines for contributions to JMB.

The board approves of the way Springer has displayed the new ESMTB logo on the proposed new cover of the journal and suggests to add “Official Journal of the ESMTB”, as was agreed by contract. HH will correspond this to Springer.

8. Summer schools

It is recalled that the school on Cell Biology and Mathematical Modelling to be held at Island of Hvar (Croatia), June 07-19 2004, organized by Branka Cajavec

(Managing director), A. Gandolfi, H. Herzel and M. Kimmel was accepted to carry the label of the society in the Turku meeting. Furthermore, WA will contact the Theoretical Biology group at the Humboldt-University Berlin to discuss potential summer schools in the following years.

9. ESMTB Dresden conference 2005

As mentioned above, the conference will take place from 18 to 22 July, 2005 in Dresden. The idea of the organizing committee is to have scientific sessions on pre-arranged key topics (10-15), rather than a meeting with a wild collection of mini-symposia to be proposed by anybody. For each topic, people will be chosen in the scientific committee, who would then have the responsibility for reviewing contributions and filling allotted time slots in the program. The scientific committee also should comment on and propose names for the list of invited speakers. All board members are asked to send topics and names to AD. AD will then draw up a list of topics, scientific committee members and invited speaker suggestions for the next board meeting. At that meeting the list of topics and scientific committee members will be finalized. The scientific committee then has to be instated quickly for them to comment on the preliminary list of invited speakers before the deadline for EU-funding applications (20 April 2004). AD will send the discussion lists to the board members before February 2nd, 2004 (two weeks before the board meeting).

The poster and 1st announcement of the conference will be available in the summer of 2004.

The SMB has asked the ESMTB conference to also host the annual SMB meeting for 2005 (as in the 4th ESMTB conference in Amsterdam). The board agrees to this and MG will contact the SMB president L. Gross to work out the details.

MG raises the point that we should already think about the 2008 conference. If we want to announce the 2008 meeting at the end of the Dresden meeting, we should be able to decide in early 2005 where this meeting will take place. MG is in favour of allowing several groups to submit proposals to the board, from which we can then choose. HH remarks that we then need a format, which does not force people to do a large amount of work, and criteria for deciding. MG will write down what he has in mind for the next board meeting.

10. Advisors for the board

Because lack of time this topic is shifted to the following board meeting.

11. European funding

LP has reviewed the funding possibilities at the EU where the board could apply for the Society, e.g. for a series of meetings. The possibilities exist, but it is clear that the EU

is not funding Marie Curie Research Training Networks on broad topics (such as “Mathematical and theoretical biology and medicine”), but aims for small, focussed topics.

His suggestion is that ESMTB should write one combined proposal for “Series of Events” (deadline April 20, 2004) which would include four summer schools (in the years 2005 – 2008) and other events like the “Mathematics in Medicine Study Group” in Nottingham. This is approved and will be initiated by HB and RB with further hints provided by LP.

Further proposals for “Research Training Networks” (in addition to the current one sent in by the cancer research group) are not visible so far.

(Added for attention:) A message from VK to the board (e-mail 3 Sept. 2003) should be noted, in which he points towards possible multi-disciplinary proposals within the ESF Scientific Programmes (the deadline, however, is 31 October 2003 !)

12. Curriculum

WA informs the board that Markus Kirkilionis (Univ. of Warwick) will not continue to work out possible modules for European curricula in “Biomathematics” or “Mathematical Biology” (which he had started for Germany within the MTBio network initiative).

Instead, LP presents a first draft of a list of curricula and corresponding places in Europe, which he gained from searching the net for key-words as “Bio-Medicine, -Engineering, -Statistics, -Mathematics ...”. It is agreed to complement and revise this list under the idea to give a survey on all European Study Programmes (and corresponding exams and degrees) that are related to research topics within our society. Currently on the list are only the degrees of bachelor (BS), master (MS) and doctor (PhD) – supplementary degrees are the diploma (DP) or others used in Europe.

LP is awaiting input from the other board members from their country ranges and areas of interest **until end of October, 2003 !**. These inputs (preferentially using the same format under EXCEL) will then be put into an updated EXCEL file, which then will be sent to all board members for revision or comments.

One important aim of this initiative is to foster the connections (in teaching and research) to neighbouring communities, not only to biology and statistics, but also to engineering and information sciences.

13. Next meeting

PT has kindly offered to organise the next board meeting in his new office in Grenoble. Since we wish to set a definite date and PT is absent we suggest to take PT up on his offer for the autumn 2004 meeting and to organise the spring meeting in Utrecht. The meeting will take place on Monday February 16th, 2004 at the Veterinary Faculty in Utrecht.

MG thanks Wolfgang Alt for hosting the meeting in Bonn and ends the board meeting at 16.30 pm.

The ESMTB and the Journal of Mathematical Biology

Report by the President and the Secretary

As all members know, the board of the ESMTB signed a contract with the publisher Springer-Verlag in early 2002, allowing the society to adopt the Journal of Mathematical Biology as its official journal. This gives the board a logo and name on the cover, two pages for society related news in each issue of the journal and, not unimportantly, the right to influence the direction of the journal by way of choosing managing editors, suggesting members of the editorial board and discussing future changes in content. In addition, the agreement gave every member full electronic access to the journal. The price to be paid for the latter service was about 30 Euro per member per year (this is market-conform price).

In 2003 it became clear that two mistakes were made in this marriage between the ESMTB and Springer. The current board takes full responsibility for these and is at the moment acting to right these wrongs. The first mistake was that, at the time of signing the contract, the membership of the ESMTB was taken to stand at about 300. Consequently, the contract asked for a lump sum of 10.000 Euro per year for the electronic access. The year 2002 was to be free from dues; payment would start from 2003. We had, however, at the time only about 100 members who actually paid their dues! The second mistake was that the board overestimated the value that electronic access through ESMTB would have for its members. It has become clear that most members already have electronic access at their workplace to many journals, including JMB. We of course debated this point at the meeting with Springer, but it turned out to be impossible to persuade them to provide a paper copy for that price, and the board was not experienced enough in negotiations with a commercial partner to be at an equal level.

Already at the time the board also knew of course that 10.000 Euro is a very large sum of money for our society (even with 300 members in mind). Fortunately the agreement contained an escape clause, which gave the ESMTB the right to cancel the present agreement by December 31st, 2003 if “its balance of accounts for the calendar year 2003 appears so precarious as to warrant freezing of all major expenditure”. During the board meeting in Bonn in September 2003 the board came to the conclusion that the situation was dangerous for our assets and that action needed to be taken (see minutes of that meeting in this issue of the Communications). As secretary, Hans Heesterbeek was asked to come up with a solution and he corresponded at length with Springer about our problems.

It became clear to both the ESMTB and Springer, with our bank balance standing at slightly more than 10.000 Euro before the 2003 payment, that it would be irresponsible of this board to not act when acting is still possible. From the point of view of sound financial management and

responsible governing, we therefore had no other option than to formally invoke the escape clause and to cancel the initial agreement. This was done by e-mail and with a formal letter before Christmas 2003.

Springer-Verlag has been very understanding to our problems and has taken a very positive attitude in providing suggestions and help. At the board meeting in Utrecht in February 2004, the board decided that talks with Springer should immediately start to negotiate a new contact that better reflects our needs and current size, but that at the same time guarantees the continued association between ESMTB and JMB, valued by both parties. At the

meeting the basis for these negotiations was formed and a strategy adopted. The president, the treasurer and the secretary have taken on the task of setting up a new agreement. In issue 7 of the Communications, the details of the final new agreement will hopefully be given. In the meantime Springer has offered to let the old situation continue and we have gratefully accepted.

Mats Gyllenberg & Hans Heesterbeek

New Research Projects

BISON: Biology-Inspired techniques for Self-Organization in dynamic Networks

BISON is a three-year Shared-Cost RTD Project (IST-2001-38923) funded by the Future & Emerging Technologies initiative of the Information Society Technologies Programme of the European Commission.

The project runs until December 2005.

Partners:

1. University of Bologna,
Department of Computer Science (Italy)
2. Telenor Communication AS,
Research and Development (Norway)
3. Technical University of Dresden,
Center for High Performance Computing (Germany)
4. Istituto Dalle Molle di Studi sull'Intelligenza Artificiale
(Switzerland)
5. Santa Fe Institute (USA)

Objective:

The complexity of modern Network Information Systems (NIS) has reached a level that puts them beyond our ability to deploy, manage and keep functioning correctly through traditional techniques. Part of the problem is due to the sheer size that these systems may reach with millions of users and millions of interconnected devices. The other aspect of the problem is due to the extremely complex interactions that may result among components even when their numbers are modest. Our current understanding of these systems is such that minor perturbations in some remote corner of the system will often have unforeseen, and at times catastrophic, global repercussions. In addition to being fragile, many situations arising from the highly dynamic environment in which they are deployed require manual intervention to keep NIS functioning.

What is required is a paradigm shift in confronting the complexity explosion problem to enable building robust NIS that are self-organizing and self-repairing. BISON proposes to draw inspiration from biological processes and develop techniques and tools for building robust, self-organizing and self-repairing NIS as ensembles of autonomous agents that mimic the behavior of social insects and immune networks. What renders this approach particularly attractive from a dynamic network perspective is that global properties like adaptation, self-organization and robustness are achieved without explicitly programming them into the individual artificial agents. Yet, given large enough colonies of agents, the global behavior is surprisingly adaptive and can cope with arbitrary initial conditions, unforeseen scenarios, variations in the environment or presence of deviant agents. This represents a radical shift from traditional algorithmic techniques to that of obtaining the desired system properties as a result of emergent behavior that often involves evolution, adaptation, or learning.

BISON will explore the use of ideas derived from complex adaptive systems (CAS) to enable the construction of robust and self-organizing information systems for deployment in highly dynamic network environments. BISON will cast solutions to important problems arising in Ad-Hoc and Virtual networks, P2P and Grid computing systems as desirable global properties that systems should exhibit.

Project coordinator:

Prof. Ozalp Babaoglu
University of Bologna, Department of Computer Science
(Italy)

Further information:

<http://www.cs.unibo.it/bison/>

Announcement of new Quantitative Biology (q-bio) archive

In recent years, an increasing number of researchers from mathematics, computer science, and the physical sciences have been joining biologists in the ongoing revolution in biology. In a variety of ways, these researchers are contributing towards making biology a quantitative science. With this letter, we announce the formation of the q-bio archive (<http://arXiv.org/archive/q-bio>, see also <http://arXiv.org/new/q-bio.html>), which aims to serve the need of this emerging community. If you and your colleagues have active interest in quantitative biology (including but not limited to *biological physics*, *computational biology*, *neural science*, *systems biology*, *bioinformatics*, *mathematical biology*, and *theoretical biology*), we urge you to subscribe to the archive and submit (p)reprints to it. Both theoretical and experimental contributions are welcome, and subscription is freely accessible over the internet to all members of the scientific community. Instructions for registration, submission and subscription to the archive can be found at

<http://arXiv.org/help/registerhelp>,
<http://arXiv.org/help/uploads>,
and
<http://arXiv.org/help/subscribe>.

The q-bio archive has grown out of a well-established series of e-Print archives accessible at <http://arxiv.org/>. The number of biology-related submissions to these archives has risen steadily over the last several years, and is averaging over 40/month so far in 2003. Unfortunately, these submissions are currently scattered across a number of sub-archives (including physics, cond-mat, nonlinear science, math, etc.), reflecting mostly the "home field" of the contributors rather than the subject matters of their submissions.

Many colleagues have expressed the desire to have a centralized archive to share their latest results, and to learn about related findings by others in this field. The q-bio archive is designed to address this problem. It is organized mainly according to different categories of biological processes and partitioned according to their scales in space and time. The categories <http://arXiv.org/new/q-bio.html> range from molecular and sub-cellular structures to tissues and organs, from the kinetics of molecules to population and evolutionary dynamics. In addition, a separate category is devoted to method-dominated contributions, including computational algorithms, experimental methods, as well as novel approaches to analyzing experimental data. All submissions are required to choose a primary category, with the option for one or more secondary categories.

Subscribers of the archive will receive by e-mail the title/abstracts of all submissions in their chosen categories on a regular basis. A large number of bio-related submissions to the e-Print archives during the past decade have already been identified and categorized according to the above scheme using an automated procedure. They can be accessed at <http://arxiv.org/archive/q-bio>.

Please note that the current list of categories is a compromise between the large number of active subject matters in biology and the areas of quantitative biology where the e-print archives have received significant contributions during the past several years. The subject list will undoubtedly be updated as the major active areas develop/shift in time. This continuous structuring of the archive is overseen by an advisory committee. It consists of a number of well-established biologists, [William F. Loomis](#) (UCSD), [Chuck Stevens](#) (Salk), [Gary Stormo](#) (WUSTL), [Diethard Tautz](#) (Cologne), together with a number of dedicated volunteers who will serve as "moderators" for each category listed at <http://arXiv.org/new/q-bio.html>. If you have suggestions to improve the q-bio archive, please contact the coordinators or the relevant moderators by e-mail.

It is our hope that the q-bio archive can eventually provide a greater community benefit than just a depository of (p) reprints. So far, there lacks a coherent forum devoted to quantitative issues in biology. Consequently, it has been difficult to follow progress in this discipline. We hope that the q-bio archive will serve as a virtual meeting point for all quantitative-minded scientists with serious interest in biology. Alternatively, the archive may be viewed as a virtual "half-way" house through which quantitative scientists can interact and support each other as they find their ways into the complex world of biological science. If successful, the open but focused environment provided by the q-bio archive may facilitate the maturation and self-organization of quantitative biology into a coherent field that contributes positively to both biology and the traditional quantitative sciences. Reaching this goal will require participation from every individual in this discipline. We look forward to meeting you at the archive. With best wishes,

The q-bio coordinators:

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History of Mathematical and Theoretical Biology

Jakob von Uexküll -- Theoretical Biology, Biocybernetics and Biosemiotics

Torsten Rüting, Universität Hamburg, Germany

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“As long as we use technical models in biology without being fully aware that by applying these models we just imply that nature performs according to the projected human requirements and guidelines, we are “blind for the significance (*bedeutungsblind*)” as Jakob von Uexküll expressed it. We are incapable of putting up questions about the origin and legitimacy of our own needs nor are we capable of asking for the origin and legitimacy of the needs of other living beings. We cannot investigate either, in which ways the needs of the different living beings on this planet are dependent on each other.” (transl. from Thure von Uexküll, 1980 : 42)

Introduction

The biologist Jakob von Uexküll (1864-1944) developed a theory of biology, which decisively contradicted the mainstream of biological thought in the 20th century. His main concepts summarized in his *Theoretische Biologie* (1920/1928) aimed at the re-introduction of the autonomous organism as subject into the focus of the life-sciences and at the same time, at making subjectivity the object of the scientific method. Uexküll was interpreted as vitalist, anti-evolutionist and mystic (Goldschmidt 1956). But scholars in different scientific and artistic fields like psychology, anthropology, philosophy, linguistics, architecture and literature, recognized the significance of his challenge.

Uexküll's approach became influential on the development of the *Organismic Biology* and *System Theory* of Ludwig von Bertalanffy (1901-1972) and the ethology of Konrad Lorenz (1903-1989) and Nico Tinbergen (1907-1988). Uexküll's concepts were mainly based on neuro-physiological studies of the movements of invertebrate animals and developed under the influence of Kant's philosophy. Already at the beginning of the 20th century Uexküll recognized the important role of negative feedback and reafferent control in organisms. He used the concept of the *Funktionskreis* (functional cycle) to illustrate behavior as a regulated process. Uexküll's models can be seen as predecessors of cybernetic models. Recently Uexküll has been discussed as a pioneer of cybernetics and Artificial Intelligence (Lagerspetz 2001, Emmeche 2001, Roepstorf 2001).

Interest in Uexküll revived, when he was internationally discovered as a pioneer of the semiotic approach in biology. Already in 1977 the hungaro-american linguist Thomas A. Sebeok (1920-2001) discovered Uexküll to be a “neglected figure in the history of semiotics” and celebrated Uexküll as one of the “masters of the sign” (Sebeok 1979). Accordingly Uexküll already at the beginning of the 20th century had recognized that the fascinating abilities and be-

havior of animals are based on sign processes – perception and transmission of signs to which meaning is marked on according to their significance. He had therefore introduced terms like *Merkzeichen*, *Wirkzeichen*, *Lokalzeichen*, *Momentzeichen*, *Merk – und Wirkmal*.



Fig. 1 Jakob von Uexküll in 1934

The actuality and interdisciplinarity of Uexküll's ideas was demonstrated on several conferences during the last decade. A special issue of the journal *Semiotica* (134/2001) compiled the contributions of scholars from linguistics to cybernetics and molecular biology, who explored the legacy of Uexküll in their fields of research. Alongside the “semiotic turn” the renewed interest in Uexküll's works was explained to coincide with a trend from temporal (evolutionary, genetic, “vertical”) biology towards spatial (organismic, genomic, “horizontal”) biology (Kull 2001 : 4). Uexküll's agenda is seen as “a main contribution to the 'developmental' or 'epigenetic' trend in the biology of the recent centuries; a lineage involving scholars like Karl Ernst von Baer, d'Arcy Thompson, Hans Spemann, Hans Driesch, Conrad Hal Waddington, Brian Goodwin, René Thom, Robert Rosen and Stuart Kauffman.” (Stjernfelt 2001:79)

In conclusion; acknowledging the contribution of Uexküll may help to fill a gap in the history of theoretical biology and “provides a link between Baer and Rosen”. (Kull 2001 : 4)

The life of an imaginative thinker

Jakob von Uexküll was born on the manor of Keblas in Estonia on the 8th of September in 1864. He was the fifth child in an aristocratic German-Baltic family. The mother Sophie von Hahn was from Kurland. The father Alexander von Uexküll, who within his young years as a geologist had made journeys to explore the natural history of the Ural, was later appointed honorary mayor of Reval (today Tallin). 1875-77 Uexküll attended the Gymnasium in Coburg (Germany). 1877 his family went back to the city of Reval (now Tallin). He was sent to the Domschule, whose rector was at that time the father of the future Gestalt-psychologist Wolfgang Köhler. 1884, on completing his Abitur, Uexküll studied zoology in Dorpat (now Tartu). He graduated with the academic degree "Kandidat der Zoologie" (candidate of zoology) and during his life never went through another academic examination. At first attracted by the materialistic and deterministic world view, Uexküll became critical to the simplistic explanations of the Darwinists. One of his teachers in Dorpat was Julius von Kennel (1852-1939), whose speculations about the ancestral lines of animals left Uexküll dissatisfied with the science of Biology. (Uexküll 1964 :35ff.)

As a "deserter" from biology Uexküll went to the University of Heidelberg in 1890 to study physiology in the laboratory of Wilhelm Kühne (1837-1900). Uexküll thought that physiology had stayed away from speculations and that its developed experimental methods could serve to renew biology. He specialized himself in the field of muscle- and neuro-physiology and from 1892 to 1903 he regularly spent many months of the year in the famous Zoological Station of Anton Dohrn in Naples.

Uexküll adapted the methods developed by Kühne for frogs to marine animals. He aimed at revealing principles underlying the muscular movements and reflexes of sea-urchins, brittle-stars, peanut-worms and octopuses. He designed several devices for the observation and recording of the physiology and behavior of animals (Mislin 1978). In 1899 he went to Paris to study in the laboratory of the physiologist Etienne Jules Marey (1830-1904), the master of the "graphical method" for the recording of body-movements and one of the pioneers of the cinema. Marey had constructed a camera for *chronophotography*, that produced the first short "movies" of moving animals. Uexküll bought one of them and used the *chronophotographic method* for studying the details of the movements e.g. of starfish and the flight of butterflies. Together with his colleagues in Naples, Albrecht Bethe and Theodor Beer, Uexküll produced an influential paper (Beer, Bethe, Uexküll 1999), that attacked the use of anthropomorphic terminology in sensory physiology and proposed a new more "objective" terminology, substituting e.g. *seeing* by *photoreception* or *smelling* with *stiboreception*. This paper turned out to have a broad impact on the development of behaviorism in the US and on the reflex concepts of Pavlov and Behterev in Russia. (Harrington 1996 : 42)

After a conflict with Dohrn in 1903, Uexküll went to marine research laboratories in Berck sur mer, Monaco, Roscoff and Biarritz. He married Gudrun von Schwerin, their daughter Dana and the sons Thure and Gösta were born in 1904, 1905 and 1909.

In 1907 Uexküll was given the honorary doctorate by the

University of Heidelberg for his studies in the field of muscular physiology, especially his discovery, that excitation is facilitated to flow towards the stretched muscle (Uexküll 1904a, 1904b). This finding, known as *Uexkülls law*, became useful in orthopedics (Kull 2001 : 5). In 1913 Uexküll applied for the post as head of the newly founded *Kaiser- Wilhelm-Institute for Biology*, but he was rejected by most of the biologists (Sucker 2002 : 136-151).

Only at the age of sixty Uexküll got his first paid position and headed his own laboratory. He was employed as "wissenschaftlicher Hilfsarbeiter" at the young University of Hamburg and became "Honorarprofessor" in 1926. Starting with a laboratory in the old aquarium, Uexküll managed to found the *Institut für Umweltforschung*. The institute flourished into a vital research center and within the first 10 years produced more than 100 papers under the direct supervision of its head. (Kühl 1965, Hünemörder 1979). Konrad Lorenz visited the institute in the 1930ies and dedicated his monograph "Der Kumpan in der *Umwelt des Vogels*" (Lorenz 1935) to Uexküll. Uexküll stayed director of the institute until 1940. He spent the evening of his life on the island of Capri, where he died in 1944.

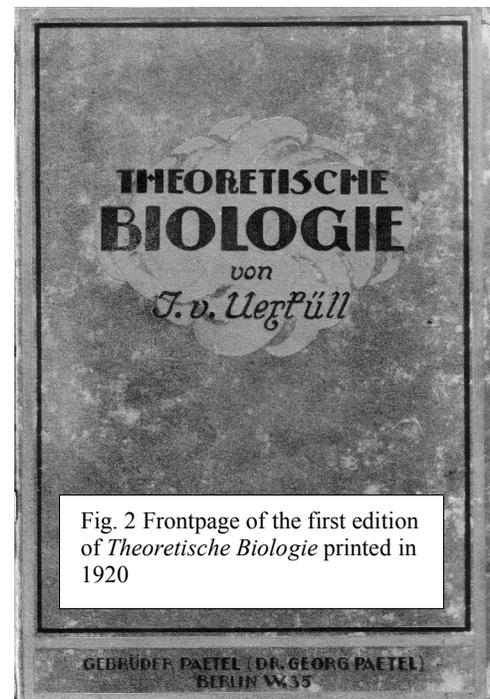


Fig. 2 Frontpage of the first edition of *Theoretische Biologie* printed in 1920

From Physiology to a theoretically renewed Biology

Already in his first monograph Uexküll (1905a) assigned different roles to physiology and biology. Physiology should organize the knowledge about organic systems by looking for causalities. Having preserved the advantage of the experimental method, physiology should help to renew biology. In distinction to physiology, biology has to use the scientific method to go beyond the investigation of causalities by exploring the laws that ensure the purposefulness (Zweckmäßigkeit) of living matter. Therefore biology should study organisms not as objects, but as active subjects, thus focusing on the organism's purposeful abilities that provide for the active integration into a complex environment. Biology therefore had to deal with holistic units and to maintain a broader scope than physiology in order to grasp the interactive unity of the organism and the world

sensed by it. For describing this unity Uexküll introduced the term *Umwelt* (Uexküll 1909).

Umweltforschung – exploring subjective worlds

Umwelt is the concept for which Uexküll is most frequently cited in the contemporary literature (Sutrop 2001). Central to Uexküll's work was the problem of how organisms subjectively perceive their environment and how this perception determines their behavior. In the book *Umwelt und Innenwelt der Tiere* (1909) he introduced the term *Umwelt* to denote the subjective world of an organism. For him *Umwelt* was the unique phenomenal world embracing each individual like a "soap bubble". He stressed, that that the individual organism is always *actively creating* it's *Umwelt*, but that this process is determined by the animal's design, it's activity, needs, etc. These interrelated factors that determine the process of the creation of *Umwelt* were the subjects of the scientific investigation of *Umweltforschung*.

Sensory physiology – basics for "Umweltforschung"

As Thure von Uexküll put it: "The approach of *Umweltforschung* aims to reconstruct creative nature's process of creation". It can be described as 'participatory observation'. "This method of observation, in the sense of Uexküll... means first of all ascertaining, which of those signs registered by the observer are also received by the living being

under observation" (Uexküll 1987:149). Sensory physiology had to pave the ground for further research into the problem, how the *Umwelt* of animals might look like. This basic research could reveal and illustrate the outline of the possible *Umwelt* of the animal. By investigating the animal's ability to perceive and discriminate different physical stimuli, one should get first indications of their significance to the animal's behavior - first ideas about the possible signs that constitute for the animal's *Umwelt*. For Uexküll this was basic methodology to analyze the "subjective space" (der subjektive Raum) of the animal (Uexküll und Brock 1927, Uexküll und Kriszat 1934/56).

Early ideas and schemes of negative feedback

In 1904 Uexküll formulated a law of neuro-motor regulation (1904a, 1904b, 1905a). *Uexküll's law*: 'nervous excitation always flows towards the stretched muscles', was widely acknowledged. It helped to explain muscular tone and position maintenance in animals and was useful in orthopedics (Haupt 1913; Wieser 1959). The finding that the activity of the nervous system facilitates the contraction of stretched muscle and thereby counteracts and regulates the stretching of muscles can be considered as a first formulation of the principle of negative feedback inside living organisms. In his *Theoretische Biologie* Uexküll developed these 'cybernetic' ideas and used little diagrams to illustrate them (Uexküll 1920: 201; 1928: 209).

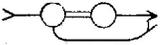
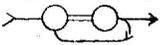
Viel häufiger findet die Kontrolle innerhalb des Körpers statt. Hier sind zwei Fälle zu unterscheiden: entweder wird die Bewegung der Effektoren-muskeln durch besondere sensible Nerven rezipiert, wie das beifolgende Schema zeigt.  Oder es wird die den effektorischen Nerven übertragene Erregung durch besondere zentrale Rezeptoren zum Teil aufgefangen und dem Merkorgan zugeführt.  Diese Rezeptoren bilden das zentrale Sinnesorgan von Helmholtz, das anatomisch noch völlig im Dunkeln liegt.

Fig.3: Little diagrams in the text illustrating a description of feedback and reafferent control (Uexküll 1920 : 201)

These figures already show the now familiar outline of feedback loops and may be seen as early graphical representation before the science of cybernetics had been developed. However, Norbert Wiener developed his ideas in the 1940s, when he was working on servomechanisms for anti-airplane guns and compared problems of automatic-steering mechanisms to problems of neuro-psychiatry to explain failures in goal directed movements which Arturo Rosenblueth had presented to him (Rosenblueth, Wiener, Bigelow 1943; Wiener 1948), (Lagerspetz 2001). As one can read in the text of Fig.3 Uexküll postulated that there are two ways that information of muscle movements is fed back into the afferent side of the nervous system: 1. from receptors for the movement of the muscles (hypothetical movement- or stretch-receptors) 2. from central receptors ("das zentrale Sinnesorgan" von Helmholtz) that take

up a part of the excitation sent to the efferent nerves and make it available to information processing in the afferent net of nerve cells. This second control principle was inaugurated by von Holst and Mittelstaedt at the end of the 1940ies as "*Reafferenzprinzip*" (Holst, Mittelstaedt 1950).

Functional cycles and reafferent feedback control

In the years after 1904 Uexküll had worked out a more general feedback concept introduced as functional cycle "Funktionskreis"(Uexküll 1920/28). By developing the functional cycle Uexküll tried to extend the concept of the reflex arc. In the second edition of *Umwelt und Innenwelt der Tiere*, Uexküll replaced the chapter on reflexes written in 1909 with a chapter on the functional cycle (Uexküll 1921). A section about "Die Funktionskreise" had already been included in the first edition of *Theoretische Biologie*

(Uexküll 1920). Here we find the first schemes of functional cycles (Uexküll 1920: 116-117, Fig. 3, 4). Interestingly, in these early schemes Uexküll also included and graphically represented (Fig. 4) the principle of refferent control. A second cycle, “*Neuer Kreis*”, stands for a connection within the nervous system, which ensures the direct flow of information from the *Handlungsorgan*, which generates the impulses for the effectors to the *Merkorgan*, which is processing it together with information from the sensory system. According to Uexküll this embodied mechanisms not only serves to control movements, but is a central prerequisite for a coherent perception of the world (Uexküll 1920 : 117). This idea has proven actuality in current concepts of cognition (Kelso 1995).

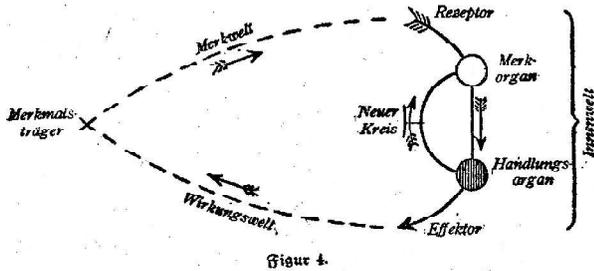


Fig. 4. Functional cycle with refferent cycle. (Uexküll 1920 : 117.)

According to Uexküll the illustration of the functional cycle should help understanding all capacities of the central nervous system and the instinctive behavior of animals. It represents an animal organism as a subject integrating an object into its *Umwelt*: This process is depicted as a closed loop of interactions. A modern description of the ongoing process in English terms was tried by Figge (2001). The following attempt uses his terms and terminology introduced by Urmass Sutrop in Fig.5:

The organism’s nervous system is equipped with receptors and sense nets (*Merkorgane*), effectors and effect nets (*Wirkorgane*). The sense net is able to discriminate and represent particular features of the organism's *Umwelt*. The representation produced by a distinct receptor unit is called *Merkzeichen*, which is hardly to be translated as feature-sign. The effect net is tuned to produce muscle impulse patterns and stimulate effector cells producing an effector sign (*Wirkzeichen*). If a particular quality of an object in the organism's *Umwelt* stimulates the cells of the peripheral receptors, the corresponding sense net produces a feature cue (*Merkmal*) for the object, which is assigned to its original feature display on the object (*Merkmal-Träger*). The sensation e.g. of a green shade in the sense net is processed together with simultaneously produced feature-signs indicating space and time (*Lokalzeichen, Momentzeichen*) and recognized as a perceptual cue, which is assigned to a plant or meadow outside. The effect net is connected with specific peripheral effectors. The activation of specific cells of the effect net orchestrates the cells of peripheral effectors, and when this effector acts upon an object, then the effect sign (*Wirkmal*) as a functional cue is displayed on or by the object (*Wirkmal-Träger*). The functional cue effected on the object transforms the state of perception of this opposite structure, thus erasing the original cue. This change

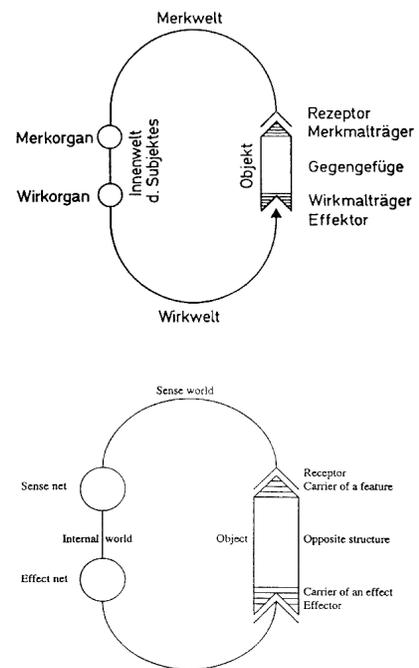


Fig. 5 Funktionskreis or functional cycle with German and English terms (Uexküll 1921 and Kull 2001, translated terms by Urmass Sutrop)

leads to the perception of a new cue which starts a new cycle of sign production, which is attuned according to feedback and refferent or other signs within the internal world of the organism.

Uexküll used the interaction of the female tick with a mammal to exemplify the description of behavior as a pre-designed chain of interconnected functional cycles (Uexküll 1936:7). The glands on the skin of mammals are carriers of the feature (*Merkmalsträger*), butyric acid, which stimulates the receptor-cells. The corresponding sense net produces a feature-sign (*Merkzeichen*), which is used as a cue (*Merkmal*), assigned to the mammal. The central processing in the sense net induces (and Uexküll stressed that it was not known how) the corresponding structures of the effect net, innervating the muscles of the tick's legs: The tick detaches herself from the twig she hang on and lands on the mammal, thereby putting an effector cue onto the hairs she is touching and that are thus carrying the feature for the next cue repected and turned into the feature cue of hairiness, which is assigned to the mammal and at the same time has erased the olfactory sign, so that a new cycle has started. The cue of hairiness induces the effect web to orchestrate the movements for crawling through the mammal's hair until the tick reaches bare skin, which erases the cue of hairiness and leads to the perception of the thermic cue of body temperature which induces the movements of drilling into the skin, where blood is the cue for the next cycle of sucking. Internal receptors produce signs of saturation that induce the tick to leave the skin, to drop, and to lay her eggs.

The example of the tick was chosen because just a few cycles are needed to describe the ticks behavior and because experiments had revealed that the cues butyric acid, hair, and body temperature were sufficient to induce the corresponding behavior and link one cycle to another. Uexküll said that the *Umwelt* of the tick was simple or “poor” in

comparison with the *Umwelt* of mammals, but “poverty” of the *Umwelt* is a condition for the safety of the success of the ticks behavior (Uexküll 1934 :8).

An early model for pattern recognition

In order to describe the design of the nervous system as unity and prerequisite for coordinated cognition and behavior within the functional cycle, Uexküll presented a model of recognition and coordination that can be compared to models used for the construction of artificial neural networks much later. In a scheme in the second edition of *Theoretische Biologie* (Uexküll 1928 : 106), he depicts interconnected networks of neural elements, see Fig.6. Lagerspetz (2000) identified in this figure an early model of the conditions of pattern recognition in biological systems, which “clearly shows the idea of parallel elements with interconnections”. He remarked that “it took thirty years before Rosenblatt (1958) used the same idea in his design of ‘perceptron’, which has been throwing light on the problem of pattern recognition. *Perceptron* is a practical example of the use of cybernetics in the modeling of mechanisms used by living organisms. It took yet another thirty years before these ideas were used in computers in the 1980s” (Lagerspetz (2000 : 650).

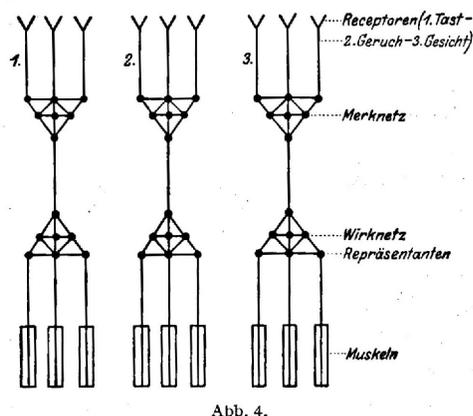


Fig. 6: Scheme of networks of neurons (Uexküll 1928 : 106)

Machine metaphors and semiotics

In his attempt to substantiate Kant's philosophy in biology, Uexküll preceded the cybernetic approach, the biosemiotic explanation and later conceptions of cognitive psychology. Uexküll had developed his ideas directly from research in the physiology of movements and the observation of behavior. His agenda had been to demonstrate the difference between the living organism's autonomous organization and the predetermined mechanisms of machines of his age. In contrast to Norbert Wiener who was fascinated to describe biological functions in mathematical terms, Uexküll avoided mathematics and discovered a semiotic language appropriate to embody Kantian philosophy with observations in biology. So Uexküll's approach preceded the cybernetic approach and, since it was developed to explain the fantastic regulation of animal movement and behavior, it was fruitful in ethology. It prepared Uexküll and his readers to envision a multitude of different functional cycles corresponding and suspending the animal within its

Umwelt, relating it to prey organisms, to enemies, to sexual partners, to different objects and media. But it also paved the way for a cybernetic view. With new techniques of computing and the wonderful automatic machines the acceptance of technical metaphors in biology increased. The emerging image of multiple types of different and interrelated closed-control-loops could explain body movements and also induced new ways of imagining, illustrating and calculating the complexity of interrelations of organisms and their environment in modern ethology and ecology (Lagerspetz 2001). But it seems that thereby a main aspect and advantage of Uexküll's theoretical thinking was left behind – the semiotic description and analyses of life.

Uexküll – the first biosemiotician

A special issue of the journal *Semiotica* dedicated to Jakob von Uexküll in 2001 termed Uexküll “a starter and pioneer of the semiotic approach in biology in the twentieth century” (Kull 2001 : 1). The editor stressed the fact that decades before semiotics was applied to biology Uexküll had commenced studying organisms as subjects in the center of sign processes (Kull 2001, 1999). Uexküll was recognized by Semioticians after his death. Thomas A. Sebeok from Bloomington University called Jakob von Uexküll a “crypto-semiotician” (Sebeok 1979). After meeting with Sebeok, Uexküll's son Thure von Uexküll, a famous physician, who had inaugurated psycho-somatic medicine in Germany, started to explain his father's biology in a semiotic conception (Uexküll 1979, 1980, 1981). He stated, that “one can truly understand his (Jakob's) terms only, if one sees them on the background of a theory of sign-processes and makes clear to oneself, that *Umweltlehre* is a science of signs sent and received by living beings” (Uexküll 1980 : 292). The recognition of the semiotic character of Uexküll's approach implies the fact that a biologist, who was not familiar with linguistics, Peircean, Saussurian or any other semiotic approach, was able to develop an elaborated terminology and conception for studying sign systems in the animal world. The historical perspective considers that Uexküll developed his approach as an alternative to the mechanistic and reductionistic trends in biology at the beginning of the 20th century (Uexküll 1913).

Uexküll's significance today

According to Uexküll, biology should focus on the organisms abilities to integrate itself into a complex environment, of which it is a part and which is constantly created by it. The study of the communicative unity of the organism and the world sensed by it, he called “*Umweltforschung*”. His ideas, terms and models became influential and innovative in the development of modern ethology, ecology, psychology, philosophy, etc. Thure von Uexküll's (Uexküll 1980) interpretation of Uexküll in semiotic terms shows convincingly how the new concept could make biology a meaningful (bedeutungsvolle) science, able to serve as a unifying paradigm for other sciences, like medicine, psychology, economy, ecology and sociology. The significance of Uexküll's quest for an alternative to reductionism in all approaches to life is appreciated today.

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Past Activities

SMB03: “The View from Dundee” International Conference on Mathematical Biology (Annual Meeting of the SMB)

August 6 – 9, 2004, University of Dundee, Scotland

The SMB03 International Conference on Mathematical Biology took place from 6-9 August 2003 and was attended by around 230 participants from all over the world. The conference programme was carefully coordinated through the International Scientific Committee with help from friends and colleagues in ESMTB, SMB and the Japanese Society for Mathematical Biology (JSMB). Special thanks on behalf of the Local Organising Committee go to W. Alt, N. Bellomo, V. Capasso, M. Lewis, P. Maini, M. Mimura, H. Othmer and N. Shigesada.

From a local perspective, the conference began in earnest in late June 2003 with the production of all the conference material such as the book of abstracts, the programme and timetable and the delegates' welcome packs (conference bag, mouse mat and extra-special “WOW!”-mug). All material was designed by the Dundee University Design Studio following the basic ideas and images given by the Local Organising Committee, reflecting the research carried out by the Mathbiology Research Group at Dundee. The underlying theme of the meeting was “social aggregation” as witnessed by the images of *Dictyostelium* amoebae streaming and endothelial cell migration to sources of attracting chemicals (cAMP, TAF, VEGF). Over the course of the conference (6-9 August) replace amoebae and cells by conference participants and cAMP, TAF, VEGF by Côtes-du-Rhone, Shiraz, Chardonnay and a picture of how the meeting ran begins to emerge...

Again from our local perspective, the meeting began in real earnest on Tuesday 5th August, with registration from 2-5pm in the foyer of the West Park Conference Centre. After a hard afternoon handing out 225 delegate packs, badges, bags and mugs (more about the mugs later) everyone was ready for something a little more formal – cue the Civic Reception hosted by Dundee City Council on board the RSS Discovery, the sailing ship built in Dundee in the 1890s that took Captain Robert Scott on his voyage to the South Pole. Thankfully the weather was more Barbados than Baltic and the Deputy Lord Provost of Dundee, Councillor Charles Farquhar, welcomed the conference participants with the traditional Gaelic mantra “*Cead Mile Failte!*” - one hundred thousand welcomes. Further social aggregation took place before the return to West Park Centre.

The following morning, Wednesday 6th August, after a short welcome to all delegates by Professor David Boxer, Vice-Principal of Dundee University, the conference began

in scientific earnest at 9am with an opening lecture by Professor Leah Edelstein Keshet. The high quality of the opening presentation in style and content was subsequently maintained throughout the week as delegates were treated to a mathbiology feast of 5 further Plenary Talks, the 2003 Okubo Prize lecture (Prof. J.A. Sherratt), 9 Minisymposia (3 talks per Minisymposium), 101 contributed talks in the parallel sessions and 50 posters (displayed throughout the meeting and with a dedicated poster session during the afternoon of Thursday 7th August). Throughout the week the 4 local organisers (MacAnderson, MacChaplain, MacDavidson and MacVasiev), easily visible in conference T-shirt and kilt, were on hand to field questions on a wide range of topics from bio-resource management (“what’s on the menu this evening?”), through bio-fluid dynamics (“where’s the nearest pub?”), pattern formation (“what tartan is your kilt?”), bio-informatics (“do you have e-mail facilities?”), computational biology (“how much is a T-shirt?”) to complex interacting particle systems (“where’s the SMB Board Meeting being held?”).

Now that the scientific programme was in full swing, care had to be taken not to forget to maintain the social aggregation theme of the meeting. With a wine reception provided by Springer Verlag on the Wednesday evening, the afternoon of Friday devoted to organised excursions (or a free afternoon) and a sherry reception prior to the conference dinner on Friday evening, all was well.

The social highlight of the week was very definitely the Conference Dinner on Friday evening. After another splendid meal laid on by the West Park staff, out-going SMB-President Mark Lewis handed over the Presidential Stole to in-coming President Lou Gross. After a few words from President Gross we were into the final phase of the evening – the award of the prizes. Having made the Springer poster prize awards to P. Namy, R. Salinas and A. Matzavinos, it was time for the final event of the evening, “The D’Arcy Thompson Look-a-Like Competition”. With such a high quality field of entrants, the panel of judges had a very difficult task in choosing the winners. However, in a closely fought contest and after much debate the top three places went to:

- 3rd place: Prof. P. Maini
- 2nd place: Dr. Nick Britton
- 1st place: Prof. J.D. Murray

After the presentations of the prizes there was time for one last round of social aggregation...

In summing up we would like to thank everyone for their participation and helping make the conference a success – even the weather was good!! Finally, special thanks go to the main sponsors of the meeting: the Engineering and Physical Sciences Research Council of the UK (EPSRC), Scottish Enterprise and GlaxoSmithKline (particularly

Frank Tobin). The success of the conference reflects the growing bonds of genuine collaboration and friendship that exist within the international mathematical biology community, bonds which will no doubt be strengthened even more with the joint ESMTB-SMB meeting in Dresden in 2005.

Haste Ye Back!

*The Conference Organisers SMB03
(A. Anderson, M. Chaplain et al.)*

Alcalá 2nd International Conference on Mathematical Ecology

September 5-9, 2003. Alcalá de Henares (Madrid), Spain

<http://euromedbiomath.aicme.free.fr>

The 2nd AICME was a follow-up of the very successful first conference held in September 1998. It was preceded by the Summer School "Scales in Mathematical and Theoretical Ecology (From Individuals to Ecosystems)" held in Sigüenza. The mastermind of the concept, planning and organization of these meetings was the late Ovide Arino, a tireless workaholic, a man of vision and generosity, who influenced the professional lives of many young (and not so young) people.

The conference took place in the beautiful historical town of Alcalá de Henares near Madrid, birthplace of Miguel de Cervantes. It brought to the ancient Colegio Mayor de San Ildefonso more than 250 participants from all over the world, representing all major fields of contemporary mathematical ecology in more than 230 lectures and posters. The program included 50 minutes plenary lectures, 21 specialized sessions, and posters.

The conference started with an opening lecture *Ecological Orbits. How planets move and populations grow*, delivered by Lev Ginsburg, who presented his theory that species cyclicity can be explained by the "transfer of quality from mothers to daughters".

Warmed up by the starting lecture and a welcoming glass of wine after it, the participants plunged in the proceedings. One or two plenary lectures in the morning and the afternoon were followed by 5 parallel sessions.

The plenary talks represented a well-planned balance between theory and applications. The list of the plenary talks titles demonstrates the diversity of topics discussed: *Why do plankton cells aggregate: a view from superprocesses* (Robert Adler); *Diversity: future challenge for modelling in fisheries oceanography* (Philippe Cury); *Spatial control in ecology: turning theory into practice for natural system management* (Louis Gross); *Synchronized reproduction of trees in the forests* (Yoh Iwasa); *Understanding local structure in epidemics: networks and pair-wise approximations* (Matthew Keeling); *Food web models as dynamical systems* (Bob Kooi); *Structured*

population dynamics problems with spatial migration: applications to heterogeneous insular populations (Michel Langlais); *The influence of size-dependent life history traits on the structure and dynamics of populations and communities* (André de Roos); *Modelling ecological effects of climate fluctuations through the statistical modelling of long-term time series data* (Nils C. Stenseth); *Modelling infectious diseases of livestock* (Mark Woolhouse).

The sessions covered most aspects of contemporary mathematical ecology: from individuals to populations and complex ecological systems, from molecules to complex biochemical systems, from classical functional models to individual-based simulation models.

The sessions and their organizers were: *Behavior-mediated population dynamics* (Vlastimil Krivan); *Bifurcation and singularities in models of biosystems* (Faina Berezovtsovskaya); *Control and optimization in ecological problems* (Jean-Luc Gouzé); *Demography and dispersal: integrating spatial movement and the life cycle* (Hal Caswell, Michael Neubert); *Dynamic Energy Budget theory for metabolic organization* (S.A.L.M. Kooijman); *Ecological applications of theoretical and simulation studies of branching stochastic processes* (Marusia Slatchova-Bojkova, Manuel Molina); *From individuals to populations and communities* (Eva Sánchez, Pierre Auger); *Individual-based spatial simulations of ecological systems* (Tanya Kostova); *Life history problems and structured populations* (Àngel Calsina, Joan Saldaña); *Mathematical aspects of fragmentation and coagulation models with application to ecology* (Ovide Arino, Ryszard Rudnicki); *Mathematical modeling and computer simulations in the context of the management of renewable resources* (Hassan Hbid, Omar Ettahiri); *Mathematical modelling of population dynamics involving delay differential equations* (Paolo Fergola); *Matrix models of population dynamics: straightforward applications and inspiring mathematics* (Hal Caswell, Dmitrii O. Logofet); *Modelling the spread of diseases in animal populations* (Suzanne Touzeau); *Molecular Ecology* (Marek Kimmel); *Pattern and process in terrestrial plant communities: integrating empirical and theoretical approaches* (Miguel Ángel Zavala); *Pattern formation, spatio-temporal chaos and noise in theoretical population dynamics* (Horst Malchow, Alexander Medvinsky); *Small and mesoscale processes in the ocean and their impact on the marine ecosystem* (Henning Wehde, Corinna Schrum); *Spatio-temporal complexity in population dynamics* (Shigui Ruan); *Stochastic versus deterministic modeling in population biology* (Shay Gueron); *Theory and observations of invasion processes* (Sergei Petrovskii, Horst Malchow).

The variety of topics discussed at the conference talks demonstrated that mathematical ecology is a fast developing, lively field. Apart from studies on more classical ecological problems at the level of populations of organisms, contemporary mathematical ecology includes research at the cellular and molecular level. The conference also showed that mathematical ecology plays an important role in tackling practical problems such as

elucidating and quantifying the factors for the survival and extinction of specific species.

Some of the papers based on the conference talks will be published, after peer review, in one of 5 journals: *Ecological Modelling*, *Mathematical Biosciences*, *Comptes Rendues de l'Academie des Sciences de Paris: Biologies*, *Nonlinear Analysis: Real World Applications* and *Ecological Complexity*.

The format and location of the conference provided many opportunities for personal contacts and professional exchange. The ancient building of Colegio Mayor de San Ildefonso surrounds a sunny square yard where conference participants would gather between and after lectures to exchange ideas. The social program also contributed to this end. A warm reception, a magnificent banquet and several excursions were organized, including trips to Toledo, Madrid, or Segovia.

The conference web-site was well supported and updated regularly. Interested readers can find on it the scientific program and all conference details, including photos taken during the days of the meeting.

We believe that most participants would agree that both the place and the work of the organizing committee led by the always good-humored Rafael Bravo de la Parra were of excellent quality and that they look forward to the 3rd Alcalá Conference on Mathematical Ecology.

T. Kostova and V. Krivan

International Conference "Linking mathematical and biological models in cancer research"

September 24-27, 2003, Magdeburg

The international conference on "Linking mathematical and biological models in cancer research" was hosted at the marvellous Herrenkrug Conference Hotel in Magdeburg. The chairman of the conference was Walter Schubert (Otto-von-Guericke University of Magdeburg, Institute of Medical Neurobiology and MelTec GmbH, Magdeburg, Germany).

The goal of this conference was to bring together and to discuss innovative approaches to the analysis of complex biological systems which promise to improve our knowledge on specific cancer mechanisms. Besides presenting highlights in this interdisciplinary field, special attention was given to presentations by young scientists, who, in the near future, are expected to strongly foster a new integrated form of cancer research. Key topics were biological model systems, new mathematical models and pattern recognition. Keynote speakers included nobel laureate Gerd Binnig (Munich). A round-table discussion with international experts on "Models and Reality in Cancer Research" complemented the conference. It was moderated by Christian Geinitz from the "Frankfurter Allgemeine Zeitung" (FAZ).

A well-composed social programme allowed to extend the scientific discussions and to get to know the conference location Magdeburg. A private tour through the Romanesque Cathedral of Magdeburg offered exciting in-

sights into the proud and famous city landmark that dominates the historical town centre. The conference dinner took place in the magnificent surrounding of the "Thousand Years Tower" and was accompanied by a reception and guided tour which allowed to perform experiments with many of the historical exhibits in the tower.

The conference integrated the final annual meeting of the FP5-EU training network "Mathematical modelling and computer simulation to improve cancer therapy" and the BMBF Proteomics Network CELLECT ("New efficient methods for functional proteomics research"). The conference was financially supported by the German Ministry for Science and Education (BMBF), the European Union within the framework 5, Otto-von-Guericke-University Magdeburg, and MelTec GmbH (Magdeburg).

Further information: <http://www.meltec.de/conference>

Andreas Deutsch

ITB Autumn School "Circadian Clocks"

October 14-18, 2003, Berlin

http://itb.biologie.hu-berlin.de/events/circadianclocks_2003.html

Theoreticians and experimentalists met from October 14-18, 2003 for a joint autumn school followed by a symposium on circadian rhythms in Berlin. It was organized by the Institute for Theoretical Biology at the Humboldt-University Berlin in cooperation with the Laboratory of Chronobiology of the Charite.

The focus of the autumn school was to promote the interaction between theoretical and experimental researchers of circadian rhythms. To achieve a common basis for discussions, the school started with two introductory tutorials. *Achim Kramer* (Charite) gave a short overview about the circadian rhythm in general. An overview of the mathematical tools that are used to investigate the underlying oscillations was given by *Hanspeter Herzel* (Humboldt-University). After this introduction 4 excellent speakers lead the audience in 3 successive days through the circadian field, starting with basics and ending with the state-of-the-art. *Ueli Schibler*, *Charles Czeisler* and *Russel Foster* spoke about the molecular mechanism of the circadian oscillator, the circadian rhythms in humans and the influence of light and the length of the day. *Albert Goldbeter* presented a series of mathematical models of the circadian oscillator in *Neurospora*, *Drosophila* and mammals. In the final symposium, 14 researchers reported about their current progress in experimental and theoretical studies. The diverse topics ranged from molecular processes in different species to the regulation of sleep in humans, from temperature compensation to circadian rhythm pathologies.

The combination of school and symposium has proven to be a very successful approach to keep the balance between established knowledge and recent developments and

thereby to reach a broad audience. The mixture of the different disciplines lead to a stimulating atmosphere, where both - experimentalists and theoreticians - had the chance to look at their projects from a different point of view. The very fruitful discussions did not stop with the talks, but proceeded during a joint dinner and self-organized parties in the evenings.

With this school a further step to a close cooperation between theoreticians and experimentalists was done. A series of schools organized by the Institute for Theoretical Biology was therefore successfully continued. Financial support came from the Deutsche Forschungsgemeinschaft (SFB 618).

Sabine Becker-Weimann

International Symposium: Signs and the Design of Life - Uexküll's significance today

January 9-10, 2004, University of Hamburg, Germany

On the occasion of the opening of the *Jakob von Uexküll-Archiv für Umweltforschung und Biosemiotik*, the Center for the History of Science at the University of Hamburg organized an international symposium in cooperation with the Jakob von Uexküll-Centre in Tartu. This conference and its international visitors demonstrated the significance of the work of the biologist Jakob von Uexküll (1864-1944), whose Institute für Umweltforschung had existed in Hamburg from 1926 to 1960. The symposium started with the film *Unbemerkte Wirklichkeit* about J.v.Uexküll, shown in a cinema and commented by the author Maximiliane Mainka. Afterwards, 170 international participants, guests and visitors, among them several members of the Uexküll-family, gathered in the Centre.

After the welcome by officials of the University and the *Joachim Jungius Gesellschaft der Wissenschaften*, the evening lectures started with a talk of Jakob von Uexküll Jr., the founder of the *The Right Livelihood Awards Foundation*, London. Uexküll jr., a fighter for the environment and human rights who donated the „alternative Nobelprice” and is just establishing a World Future Council in Hamburg, talked about „*Jakob von Uexküll and Right Livelyhood - The Current Actuality of*

his Weltanschauung“ . Torsten Rütting of the Center for the History of Science gave an overview on the history of *Jakob von Uexküll and his Institut für Umweltforschung in Hamburg*. Kalevi Kull of the Department of Semiotics and the Institute of Zoology and Botany of Tartu University in Estonia gave an account of the reception and significance of Uexküll in theoretical biology. Jesper Hoffmeyer (University of Copenhagen, Department of Biological Chemistry) explored the difference between Uexküll's *Umwelt* and the *Semiosphere*.

The opening of the archive was celebrated with a buffet and a party

On the 10th of January, a dense program of lectures was presented by, among others:

- John Deely (University of St. Thomas, Houston) on: *Semiosis and Jakob von Uexküll's Concept of Umwelt* .
- Anton Markos (Charles University Praha Faculty of Sciences. Department of Philosophy and History of Science) on: *Kauffman's biosphere and Lotman's semiosphere*
- Mathias Gutmann (Universität Marburg, Institut für Philosophie) on *Uexküll and modern biology*
- Andreas Weber (Humboldt-Universität, Berlin) on *Mimesis and Metaphor. The Biosemiotic Generation of meaning in Cassirer and Uexküll*
- Peter Klein (University of Hamburg, Institut für Didactics of Science) on: *The brain as a digital computer, what would be it's program? An Uexküllian perspective*

On the third day, a stroll through the Umwelten of Jakob von Uexküll in Hamburg was organized, leading the participants to places where Uexküll had lived and worked. In the afternoon the new Uexküll-archive was opened for visitors and research.

For further information about the archive and the symposium:

<http://math.uni-hamburg.de/home/rueting/projekte.htm>

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Recent Theses

Numerical Study of Size Structured Population Models

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Numerical and analytical research on continuous mathematical models that describe the dynamics of size-structured populations, constitute an important working

area due to its application on fields as Demography, Epidemiology, Ecology, etc. In the first models that we can find in the literature, the individual feature chosen to structure the population was age because they worked with human data. However, this variable has a limited practical value due to the fact that it is very difficult to measure experimentally in a large number of species. As an alternative, other physiological characteristics, which are not as difficult to measure as age (as length, weight, mass,

biomass, maturity, energy reserves, amount of foliage, etc.) are employed to model the dynamics of such species. They are grouped generically under the name of size. Besides, in many species, size is considered as one of the most important attributes of an individual to describe their ability to obtain the necessary resources to survive and reproduce. Thus, in the studies of the population dynamics for such species, size emerges as the most suitable parameter to structure the population. Then the circumstances previously described show that an (analytical and numerical) study the equations that describe the dynamics of a size-structured population is needed. Such study is still in an incipient state, especially in the numerical aspects.

In this PhD, I have approached the study of the numerical integration of one of these models that consists of the nonlinear integro-partial differential equation

$$u_t + (g(x, I_g, t)u)_x = -\mu(x, I_\mu, t)u$$

on the domain $0 < x < 1$, $t > 0$. The non-local boundary condition is given by

$$g(0, I_g, t)u(0, t) = \int_0^1 \alpha(x, I_\alpha, t)u(x, t)dx.$$

The functions I_n are given by

$$I_n(t) = \int_0^1 \gamma_n(x)u(x, t)dx.$$

In a general situation, this problem cannot be solved analytically, therefore its solution is performed by means of numerical techniques. This numerical solution is especially difficult since the vital functions (α , μ , and g) depend on a non-local functional of the population density and because the boundary condition is non-local and nonlinear.

The first part consist on a brief historical review of continuous models for size-structured population dynamics. Also, the details of the most important numerical methods that have been considered in the literature for the integration of such models are outlined. Finally, five numerical schemes are described. On the one hand, two schemes usually employed for the integration of hyperbolic conservation laws, suitably fitted to the model (Lax-Wendroff and Box methods). On the other hand different characteristics methods that have been developed originally in this work. We center our numerical study on these schemes. In the second part, a complete computational study of the considered numerical schemes is developed. Several theoretical test problems have been employed to reflect the complexity that could appear in this model. In general, the numerical experiment allows to conclude that there are different results although the selection grid nodes method is the best choice in all the situations. Also, at the end of this part and by means of the numerical experiment, a biological problem with real data is considered. Spurious oscillations appear when difference schemes are employed, and the characteristics methods shows best the cross-section of the theoretical solution. Finally, the selection grid nodes method has the best behaviour in a long-time integration and even with irregular data. In the last part, we

develop a complete convergence analysis of some of the numerical methods presented in the work. They are based on the properties of consistency and nonlinear stability. The methods analyzed are a characteristics method based on a natural grid for the autonomous model, the box method for the non-autonomous one and characteristics methods for the fully nonlinear problem. These studies are pioneer in each field.

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Synchronization Phenomena in Light-Controlled Oscillators

Gonzalo Marcelo Ramírez Ávila, Center for Nonlinear Phenomena and Complex Systems, Université Libre de Bruxelles, Belgium, February 2004

The aim of this work is to study both in experimental and theoretical ways the synchronous behavior in groups of light-controlled oscillators (LCOs) that are simple electronic devices that mimic firefly's behavior in the sense that these circuits interact such as fireflies do, i.e., by means of light-pulsatile coupling. At the same time, our LCOs constitute a good approach to study other systems that act as integrate-and-fire oscillators because an LCO is a typical relaxation oscillator with the presence of two time scales: a long charging stage and a very short discharging stage.

We performed several experimental measurements in order to understand the synchronization process in our LCOs. We found that synchronization is acquitted due to the effects (shortening of the charge or lengthening of the discharge) that are operated when a stimulus acts on it. The experimental work allows us to formulate a model that takes into account the effects mentioned above as well as the physics related to the LCO's circuit. We first used the model to characterize our LCO by means of the Phase Response Curve (PRC) that we have obtained analytically. The model has been validated by comparing the experimental measurements with the results obtained using the model. The fitting is excellent and the model reproduces even the bifurcation-like phenomenon observed in three LCOs in line due to the sensitivity to initial conditions that may lead the system to two different stable states. This fact enabled us to use the model for many different situations that are not easy to solve by experimental means.

We have analyzed two identical LCOs, and even for this simple case, we assumed some simplifications in order to find exact solutions. Depending on the initial conditions, we found two possible states for two identical coupled LCOs. The first one is the tendency towards synchronization in-phase and the second one is an anti-synchronous unstable state. We also found that the synchronization time scales with the coupling strength, i.e., with the distance between LCOs. We have built the Arnold tongues for two coupled LCOs founding regions with pure $n:m$ synchronization and regions in which synchronization and modulation overlap.

Numerically, we used uniform and Gaussian noise acting on the voltage source. We characterized the synchronous behavior of noisy LCOs using simple statistical parameters such as the mean value of the linear phase difference and the variance of the cyclic phase difference. We

demonstrated that noise does not only perturb synchronous states in LCOs but it may also enhance synchronization, especially for Gaussian noise with unequal variances.

We studied by statistical means the synchronization for locally coupled LCOs arranged in line, in ring and in lattice. We found that LCOs in rings exhibit more easily total synchronization. The synchronization time, however, is unpredictable. The analytical and numerical results suggest that total synchronization is the most probable phenomenon when the number of oscillators is not very large.

We studied static and mobile globally coupled LCOs. In both cases we found that synchronization is less probable when the number of LCOs increases. Considering a mean field approach, the synchronization time tends to decrease with the number of LCOs. For realistic cases in which the LCO's interaction depends on their distances, the determination of the synchronization time becomes unpredictable again. Finally, mobile LCOs may improve synchronization in certain cases. The latter could be useful in robotics.

Our system is closer to the reality than those considered in the literature because of its characteristics and its experimental basis. The obtained results could be applied to biological systems such as fireflies, cardiac cells, neurones, and so on but also to robotics, where the long distance communication by light and the emergence of synchronization patterns may be useful to conduct to specific tasks.

The content of this thesis has so far been published in the following papers:

Ramírez Ávila, G.M., Guisset J.L., Deneubourg, J.L. (2003), *Physica D* 182, 254-273.

Ramírez Ávila, G.M., Guisset J.L., Deneubourg, J.L. (2003), *Proceedings Nonlinear Dynamics of Electronic Systems*, Ed. R. Stoop, 11, 201-204.

Guisset J.L., Ramírez Ávila G.M., Deneubourg, J.L. (2001), *Revista Boliviana de Física* 7,102-114 (in Spanish). Available in English version in arXiv.nlin.AO/0206036.

Aggregation methods for linear discrete non-autonomous and stochastic systems

Angel Blasco, Department of Mathematics, University of Alcalá, Madrid, Spain, December 2002

Aggregation techniques allow us to reduce the dimension of some dynamical systems in order to simplify their analysis. The initial situation is that of a hierarchically structured system divided into subsystems that are slowly coupled but exhibiting a fast internal dynamics. The idea of aggregation is to choose a global variable, sometimes also called macrovariable, for each subsystem and to build up a reduced system for these global variables. The reduced system, or aggregated system, must reflect both dynamics, the one corresponding to the fast time scale and the one corresponding to the slow time scale. The slow dynamics of the general system, the initial complex one, usually corresponds to the dynamics of the reduced system, meanwhile the fast dynamics of the general system is reflected in the coefficients of the reduced one in such a way that it is possible to study influences between the different hierarchical levels.

This thesis is concerned with the application of approximate aggregation techniques to the analysis of some discrete dynamical systems that emerge in the modelling of population dynamics. These systems must incorporate the effect of two processes that act at different time scales; they will be called slow and fast process respectively. The projection interval of the original system must be that corresponding to the slow process and the fast process is assumed to act a large number of times throughout each of these intervals.

To be precise, the techniques developed in this work have been designed for dealing with three different kinds of systems:

1. Linear discrete non-autonomous systems. The aggregation of these systems had been developed before under a quite restrictive assumption: the parameters that determine the dynamics of the fast process were assumed to be constant along the entire projection interval. We present an aggregation method that eliminates this restriction allowing those parameters to change each time that the fast process acts. By means of the aggregated system we can detect the presence of ergodicity in the original system and obtain good approximations for the parameters that define its asymptotic behaviour: growth rate, stable structure, etc.
2. Linear discrete systems incorporating demographic stochasticity. In the study of the dynamics of small populations it becomes important to take into account the effect of the individual deviations from the vital rates. These random effects yield the so-called "demographic stochasticity" which has usually been modelled by means of certain stochastic processes called Multitype Galton-Watson Branching Processes. We provide an aggregation method that allows us to know the asymptotic behaviour of the original system by means of a lower dimensional one. The aggregated process gives us approximations for the growth rate of the expected population size, the extinction probability, the quasi-stationary expectation, etc.
3. Linear discrete systems incorporating environmental stochasticity. In most cases, the dynamics of real populations depend on environmental factors that are completely unpredictable, such as climatic conditions, interaction with other species, etc. This motivates the use of stochastic models where the vital rates affecting the population change randomly with time. One of the most useful features that reflect the asymptotic growth of the population is the "Stochastic Growth Rate" (SGR). We prove the convergence of the SGR of the original system to that of the aggregated system, which greatly increases the usefulness of the aggregation procedure.

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Blasco A., Sanz L., Auger P., Bravo de la Parra, R. (2002), Linear Discrete Population Models with Two Time Scales in Fast Changing Environments II: Non Autonomous Case, *Acta Biotheoretica*, **50**:15-38.

Blasco A., Sanz L., Bravo de la Parra, R. (2002), Approximate Reduction of Multiregional Birth-Death Models with Fast Migration, *Mathematical and Computer Modelling*, **36**:47-65.

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Micromanipulation of living cells using AFM spectroscopy. Application to cancer

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Cell microrheological properties are investigated using a modified JKR technique [1], which gives access to the cell local elastic and adhesive properties. The experiments are based on the AFM technique and use a functionalized spherical bead glued onto the AFM cantilever [2]. The experiment is set on an inverted microscope equipped with Phase contrast, RICM and Fluorescence. Results related to the interaction between cancer cells and endothelial cells are presented. The levels of adherence are modified by forcing the cells to express ICAM-1 proteins at their surface. The attachment of ICAM-1 to the cytoskeleton can also be modified. Elastic moduli as well as surface energy values are measured and are found to be in agreement with those found in the literature. Different results are shown and discussed. Another way to measure adhesion is by pulling the bead away from the surface of the cell. In such a case, the time-dependent mechanical response of the cell is measured, together with the detachment of adhesion molecule clusters at the interface. The interpretation is based on the Evans-Ritchie's model [3]. Applications of such results in the context of cancer metastasis are discussed.

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Dwarfs and Giants: The Dynamic Interplay of Cannibalism and Competition

David Claessen, Institute for Biodiversity and Ecosystem Dynamics, University of Amsterdam, The Netherlands, 2003

This thesis is about the population dynamic consequences of the interplay between cannibalism and competition in size-structured populations. One aim is to obtain a better understanding of these consequences for population dynamics in general. A second aim is to obtain a better understanding of the dynamics of cannibalistic, size-structured populations of piscivorous fish, in particular Eurasian perch (*Perca fluviatilis*). In order to achieve these aims, size-structured population models are formulated, parameterised, and analysed to make testable predictions.

The predictions are then compared with empirical data on long-term population dynamics.

Cannibalism is an interaction between members of the same population which generally involves: (1) mortality of victims; (2) energy gain by cannibals; (3) size-dependent interactions; and (4) competition between victims and cannibals. Chapter 1 is a review of population dynamic literature on cannibalism, relating the predicted dynamic consequences of cannibalism to these four aspects.

In all models studied in this thesis, size-dependent competition emerges from the combination of size-dependent vital rates and a dynamic resource. If small individuals can sustain themselves at a lower resource density than large individuals then, in the absence of cannibalism, competition-induced generation cycles are predicted. In Chapter 2 we show that the interplay between size-dependent cannibalism and competition can result in either stabilisation of such competition-induced population cycles, or in population cycles in which the population size distribution is sharply bimodal, consisting of (mainly planktivorous) dwarfs and giant cannibals.

Chapter 3 studies the relation between the size-dependent nature of cannibalism and population dynamics. The range of victim sizes that a cannibal can capture is referred to as the cannibalism window. It appears that the lower limit of the cannibalism window determines the potential of cannibalism to stabilise competition-induced population cycles. The upper limit of the cannibalism window has less impact on dynamics but can drastically affect life history.

In Chapter 4 a simplified model is studied with a newly developed equilibrium continuation method. We found coexisting stable states, associated with two saddle-node bifurcations. For certain parameters, the population can either converge to a 'stunted' state with small individuals or a 'piscivorous' state with giants, depending on initial conditions. The driving force of the bistability, coined the "Hansel and Gretel effect", is based on the dependence of the mean yield of cannibalism on the size distribution of cannibals. Due to the cannibalism window, if cannibals are larger they have a larger gain from cannibalism because on average they consume victims when they are larger and contain hence more energy.

Chapter 5 investigates the evolutionary consequences of an ontogenetic niche shift with a population model in which the size at niche shift is a genetic trait. Although the actual diet depends on the densities of the two different resources, the gradual shift from exploitation of the first to the second resource is part of the definition of an individual life history. We found that the adaptive dynamics of a monomorphic population (i.e., all individuals have the same trait) always converge to a strategy which exploits both resources equally by switching to the second niche at an intermediate body size: an ontogenetic generalist. Once the generalist has established itself, it depends on the size-scaling of the functional response whether this strategy is evolutionarily stable or the population branches into two subpopulations, which diverge genetically from each other.

In that case, eventually two specialist populations result, each consuming only a single resource throughout its life.

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Study of dynamics and mechanisms of aggregation in *Lasius niger* (L.) and other ant species

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This thesis is dedicated to the study of the aggregative behaviour in the ant *Lasius niger* in order to characterize the phenomenon at the collective level by a study of the dynamic and the collective structure, and at the individual level to understand the mechanisms underlying the phenomenon. We demonstrated experimentally and verified by a model that aggregation is essentially due to an amplificatory phenomenon: the greater the ant numbers in a cluster, the greater the time spent by an ant inside this cluster. Our results indicate that the aggregation level and the form of the collective structure depend on different factors such as the density and the surface: for brood-tenders, an evolution of the aggregative structure is observed shifting from a large stable aggregate for low density-surface to several smaller clusters with a less pronounced hierarchical size for the greater density-surface. Aggregation is also influenced by the ethological caste of the ant: the brood-tenders aggregate in a big stable cluster and the foragers in some unstable clusters. This difference is explained by a smaller probability of foragers to stay inside the cluster. In mixed groups, ants keep their own characteristics, not appearing to be influenced by the caste of the individual encountered. Finally, aggregation is influenced by the ant species: our studies on *Crematogaster scutellaris*, *Atta sexdens-rubropilosa*, *Solenopsis invicta*, *Pheidole pallidula*, *Linepithema humile*, *Myrmica rubra* and *M. ruginodis* show us a large variety of responses, in the number and the size of the clusters, which is also a function of the caste of ants which is used. A constant result, nevertheless, appears in our results: brood-tenders seem to aggregate better than foragers. These results are discussed in term of their adaptive value for the colony and a possible link with the spatial distribution of ants inside the nest.

The content of this thesis has so far been published in the following papers:

- Depickère S., Fresneau, D. & Deneubourg, J.-L. (2004), *Insectes Sociaux* 51(1), In press.
Depickère S., Fresneau, D. & Deneubourg, J.-L. (2004), *Journal of Insect Behavior*, 17(1), In press.
Depickère S., Fresneau, D., Detrain, C. & Deneubourg, J.-L. (2004), *Insectes Sociaux*, In press.

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The interplay of migration and population dynamics in a patchy world

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One of the important issues in spatial ecology is how explicit considerations of space alter the prediction of population models. In this thesis we scrutinized some classical theories related to the issue via spatial population models derived mechanistically.

Incorporation of the behavioural details of individuals of species living in a patchy habitat into the population-level description naturally gives rise to cross-migration models in which the per-capita rate of migration of one species depends on the density of some other species.

We formulated and mathematically justified the idea in a general manner and gave a series of examples demonstrating the derivation of cross-migration models.

To look into the impact of the cross-migration factor on population dynamics we first studied a specific two-patch predator-prey cross-migration model while focusing on the hypothesis that space reduces predator-prey oscillations. We found that there are both qualitative and quantitative differences between the cross-migration model and the classical model. Having realized that cross-migration is an ubiquitous feature of multi-species systems we then investigated some general multi-patch multi-species cross-migration models while concentrating on the well-known theory of Turing Instability. We found that a cross-migration factor has crucial effects on Turing instability. Our results lead to new insights into the theoretical issues concerned.

The thesis is available at:

<http://www.library.uu.nl/digiarchief/dip/diss/2003-0709-122256/inhoud.htm>

Mathematical epidemiology and the control of classical swine fever virus

Don Klinkenberg, *University of Utrecht, The Netherlands, April, 2003*

The thesis describes epidemiological research carried out to improve the control of classical swine fever virus (CSFV) epidemics. The major part consists of research into control measures and strategies, so that quick and adequate action upon CSFV detection is possible. CSFV transmission experiments are described, as well as a mathematical model of CSFV transmission between herds. Both are used to assess the effectiveness of the E2 subunit marker vaccines with respect to CSFV transmission. Quantification of the effectiveness was done with the 'basic reproduction ratio' R_i (R_h), defined as the number of animals (herds) that are infected by one typical infectious animal (herd) in a completely susceptible population. R_i (R_h) has an important threshold property, as major outbreaks (epidemics) can only occur if R_i (R_h) is larger than 1.

Estimation of R_i from transmission experiments was done by assuming an SEIR model for virus transmission. In the SEIR model, susceptible animals (S) are infected by

infectious animals with a rate proportional to a transmission parameter β . After infection, the susceptible animal becomes exposed (E) and after some fixed time it becomes infectious (I) itself. Then it recovers from infection with a rate α , so that it is removed (R) from the transmission process. By regularly sampling animals during the experiments, it could be determined when the animals had been infectious, and when they had acquired infection. This information was used to estimate β and α , and also R_i , as $R_i = \beta / \alpha$ in this SEIR model.

The transmission experiments pointed out that R_i decreases to below the threshold value 1 as of three weeks after vaccination until at least six months after vaccination. It appeared that the presence of maternal antibodies at the time of vaccination may reduce the antibody levels at later age, but these lower levels still keep R_i below 1.

Aside from testing vaccines at the animal-to-animal level, various control strategies were tested in a mathematical model of CSFV transmission. The model was a two-type branching process of two types of infected herds, sow herds and finishing herds. Immediately after 'birth' of an infected herd, it can cause the 'birth' of new infected herds with a rate proportional to the number of infectious animals within the herd. Removal of infected herds also occurs with a rate proportional to the number of infectious animals. The number of infectious animals within herds was assumed to grow exponentially, with a random initial level to correct for stochastic fluctuations just after infection of the herd.

Model parameters were estimated from the Dutch CSFV epidemic of 1997/1998. Control strategies were considered effective if $R_h < 1$. Effective control strategies were compared with respect to the time to extinction of the epidemic branching process, and the cumulative number of infected herds, by carrying out stochastic simulations. It appeared that effective control requires that, in addition to the control measures prescribed by the European Union, at least half of the pigs should be vaccinated in the area of the epidemic. Increasing the effort however, can greatly reduce the time to extinction and the cumulative number of infected herds.

In addition to the investigation of control measures and strategies, a mathematical model was tested, which had been developed to analyse the effectiveness of the control strategy in an ongoing epidemic. The model, a two-type branching process of infected and detected herds, was designed to use data of an ongoing epidemic for estimation of R_h and the number of infected, yet undetected herds. The only data needed for the calculations are the numbers of detected herds in each week of the epidemic. Unfortunately, the only result the model could generate was whether R_h was smaller or larger than 1. Further research is needed to understand the shortcomings. Until then, some extra data need to be used, e.g. an estimate of the number of infected herds at the day of the first detection, or an estimate of the average time between infection of a herd and detection.

Infectious diseases among animals: combining models and data

Aline de Koeijer, Quantitative Veterinary Epidemiology, Wageningen University and Research Centre, The Netherlands, September 2003

To eradicate or control the spread of infectious diseases, knowledge on the spread of the infection between (groups of) animals is necessary. Models can include such information and can subsequently be used to observe the efficacy of various control measures in fighting the infection. Availability of information and data to build and quantify these models is essential for applying such models in real life. In this thesis, mathematical models for the spread of infectious diseases in animals are always combined with the analysis of data concerning the host, the infectious agent, their interactions and often also case data from epidemic or endemic disease situations. To do so, various infections presently circulating in the Netherlands are discussed.

For the *Phocine Distemper Virus* (PDV), data of the epidemic in 1988 show that clustering of animals has a strong influence on the transmission and survival of the animals. A previously applied model to analyse the seal situation did not fit the data very well. A model that incorporates the clustering of the animals on sand banks gave a better fit. Due to their clustering, the death rate was higher than could be expected from the first model.

About Infectious Bovine Rhinotracheitis (IBR) it is known that the persistence of the infection in previously infected animals may cause a delay in control and eradication. We have quantified the probability for such a virus to reactivate in the field, and combined that with a model that calculates the expected time to extinction. Thus, control measures in the eradication process can easily be compared for efficacy and a time frame can be defined.

The control of BSE was an important issue in the last decade, but due to limited data, exact advice was difficult to find. By quantifying the transmission parameters, the various control measures can be compared for efficacy. Now that more information is available concerning risks for humans and cattle, optimisation of the surveillance and control can be introduced based on such models. The age distribution of BSE cases offers information on the efficacy of BSE control in the past, but also concerning the prevalence of the infection in the future. Risk assessment and modelling are especially important for countries that would like to prove the absence of BSE in their country.

Monitoring of an animal disease situation may have many purposes, for instance to prove freedom from infection for a certain farm or country. In the last chapter of the thesis, we give an opening for extended modelling to quantify the risk of missing a new outbreak in a country that has the 'free from disease' status. An integrated approach of transmission models that specifically includes the frequency of sampling over time enables us to calculate the probability that an epidemic escapes from detection.

The thesis is available in pdf at

<http://www.library.uu.nl/digiarchief/dip/diss/2003-0918-123231/inhoud.htm>

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Dynamical Modeling of Hematopoietic Stem Cell Organization - Design and Validation of the New Concept of Within-Tissue Plasticity

Ingo Röder, Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig, December, 2002

This work presents a new, comprehensive concept of stem cell organization in the hematopoietic system. It introduces a fundamentally new perspective on processes underlying the regulation and control of proliferation and self-renewal. In contrast to previous concepts, "stemness" is not treated as an explicit cellular property, but as the result of a dynamic process based on self-organizing principles. The concept fulfills all criteria of the prevalent functional definition of tissue stem cells, and at the same time, it provides a consistent explanation of many experimentally and clinically observed phenomena. These include for example cell kinetic and functional stem cell heterogeneity, reversibility of cellular properties, system regeneration after disturbances, fluctuation and competition of cell clones, and the dependence of potential and functionality of stem cells on their actual growth environment.

The concept is based on the assumption that individual cells are able to use different options from their repertoire of possible functionalities depending on influences of the local growth environment. Cellular properties can reversibly change within a range of options. This potential reversibility is denoted as *within-tissue plasticity*. Stochastic switches between the growth environments introduce fluctuations in the cellular development and eventually generate the observed heterogeneity of the stem cell population.

Formalizing these aspects, leads to the following minimal set of model assumptions:

- Cells are able to reside in two different growth environments (GE-A, GE- Ω).
- Each cell is characterized by two properties, the cycling status and a property a which describes the affinity of cells to reside in GE-A.
- Cells can change from GE-A to GE- Ω and vice versa with transition intensities (probability per time interval) α and ω , respectively. These depend on the actual affinity a , the cycling status, and the cell numbers in the system.
- Residing in GE-A, a cell is assumed to be non-proliferating. In contrast, cells in GE- Ω proliferate with average turnover time τ_c . Due to the possibility of growth environment switches, the cycling status can reversibly change.
- Cellular development with respect to affinity a is reversible. Whereas cells in GE-A have the propensity to increase a , cells in GE- Ω tend to decrease a .
- If a has become critically small ($a < a_{min}$) the cell is considered to have lost the potential to stick to GE-A. These cells are called differentiated.

Referring to the hematopoietic system, these assumptions can be interpreted as follows: Two different growth environments in the bone marrow are considered where

stem cells can either be attached to (GE-A) or detached from (GE- Ω) specific stroma components. These different attachment states result in switches between several patterns of gene expression and activation of signal transduction pathways which induce different cellular developments. Differences in the cycling behavior of different stem cell subsets and the observation that stroma contact can prevent the loss of repopulating ability support this interpretation.

To validate this concept of stem cell organization using computer simulations, it is necessary to translate the model assumptions into a specific mathematical form. This is done using a single cell based stochastic Monte-Carlo approach. Herein, each cell is characterized by a set of properties and functionalities. At discrete time steps these are updated for all cells on the basis of predefined rules, which include stochastic decisions. This allows the analysis of processes on the level of cell populations and on the single cell level. Experimental influences and interventions (e.g. *in vitro* conditions, transplantations, application of cytotoxic drugs) are included into the analysis by a specific choice of model parameters and simulation sequences.

Simulation results are compared to data originating from a wide range of different experimental settings. It is demonstrated that the model is able to explain classic results, such as the observed heterogeneity of colony size and number in the CFU-S assay (colony-forming unit spleen assay: a specific murine cell colony assay) or the different repopulating potential of selected subpopulations of bone marrow cells, as well as recent experimental observations. The latter ones include time courses of cell kinetic parameters, the development of individually marked cell clones, and fluctuating contribution of different clones to blood production.

In addition to the above described single cell based stochastic approach, another mathematical representation of the concept, namely a system of partial differential equations, is investigated. Both mathematical models are compared with respect to their system properties. It is shown that both methods adequately reproduce the average behavior of large cell populations. However, for investigating populations comprising only small numbers of cells (e.g. in the analysis of clonal competition and fluctuation phenomena) the single cell based approach is more appropriate.

The major conclusions of this thesis can be formulated as follows:

- The presented concept of within-tissue plasticity suggests a fundamentally new perspective of tissue stem cell organization.
- It abandons the classical view of an one-directional differentiation hierarchy and dismisses the concept of stem cells being predefined entities with specific, but fixed properties and functionalities.
- Instead, stem cell organization is understood as a dynamic, functional process based on self-organizing principles. It uses the ability to reversibly change cellular properties within a

range of options and the stochastic switching between different growth environments as essential mechanisms to generate diversity in the functional potential of stem cells.

- The concept is fully consistent with the functional definition of tissue stem cells.
- It consistently explains a broad variety of macroscopic phenomena, observable in different *in vitro* and *in vivo* experiments, by a microscopic mechanism.
- The mathematical representation of this concept provides a comprehensive quantitative model of hematopoietic stem cell organization, which is able to describe dynamics on the population and the single cell level.
- It is the first model which covers an explanation of plasticity and reversibility of cellular properties/functionalities within a tissue or lineage, and it has the potential to serve as a

general approach to explain the phenomenon of tissue plasticity.

Several extensions of the model are planned for the future. These include the incorporation of feedback regulations from more mature cell stages and lineage specification processes, as well as the explanation of tissue plasticity phenomena.

Besides its substantial contribution to the formulation of a new theoretical framework for the understanding of tissue stem cell organization, also clinical applications of the proposed model are conceivable in different fields. For example, the model can be utilized to determine optimal sampling strategies for individual clone tracking experiments in gene therapeutic settings. Furthermore, it could contribute substantially to the optimization of current treatment strategies or to the design of new clinical trial settings for clonal disorders.

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New Journals and Books

Mathematical Medicine and Biology: A Journal of the IMA

Formerly the IMA Journal of Mathematics Applied in Medicine and Biology.

– See ***special offer mentioned in the editorial !***

Editors: Oliver E. Jensen, and John R. King (University of Nottingham) James P. Keener (University of Utah)

Mathematical Medicine and Biology publishes original articles with a significant mathematical content addressing topics in medicine and biology. Papers exploiting modern developments in applied mathematics are particularly welcome. The biomedical relevance of mathematical models should be demonstrated clearly and validation by comparison against experiment is strongly encouraged.

The journal welcomes contributions relevant to any area of the life sciences including:

Biomechanics, biophysics, cell biology, developmental biology, ecology and the environment, epidemiology, immunology, infectious diseases, neuroscience, pharmacology, physiology, and population biology.

Polymer and Cell Dynamics: multiscale modelling and numerical simulation

W. Alt, *University of Bonn*, **M. Chaplain**, *University of Dundee*, **M. Griebel**, *University of Bonn*, **J. Lenz**, *University of Bonn* (Eds.)

Birkhäuser, 2003, ISBN 3-7643-6924-8, 344 pp., EUR 88.

"Polymer and cell dynamics play an important role in processes like tumor growth, metastasis, embryogenesis, immune reactions and regeneration. This volume - based on an international workshop on numerical simulations of polymer and cell dynamics in Bad Honnef (Germany) in 2000 - provides an overview of the relevant mathematical and numerical methods, their applications and limits. The contributions are from the fields of applied and numerical mathematics, scientific computing, theoretical physics, molecular biophysics, cell and molecular biology as well as chemical and biomedical engineering."

Function and Regulation of Cellular Systems: experiments and models

A. Deutsch, *TU Dresden*, **J. Howard**, *MPI, Dresden*, **M. Falcke**, *FU Berlin*, **W. Zimmerman**, *University of Saarbrücken* (Eds.)

Birkhäuser, 2003, ISBN 3-7643-6925-6, 432 pp., EUR 88.

"Current biological research demands the extensive use of sophisticated mathematical methods and computer-aided analysis of experiments and data. This interdisciplinary volume focuses on structural, dynamical and functional aspects of cellular systems and presents corresponding experiments and mathematical models. Recent model approaches are presented with applications in cellular metabolism, intra- and intercellular signaling, cellular mechanics, network dynamics and pattern formation. In addition, applied issues such as tumor cell growth, dynamics of the immune system and biotechnology are included."

Data Mining: multimedia, soft computing and bioinformatics

S. Mitra, *Indian Statistical Institute Kolkata*, **T. Acharya**,
Arizona State University

Wiley, 2003, ISBN 0-47146054-0, 424 pp., USD 89.95.

"While the digital revolution has made huge volumes of high dimensional multimedia data available, it has also challenged users to extract the information they seek from heretofore unthinkable huge datasets. Traditional hard computing data mining techniques have concentrated on flat-file applications. Soft computing tools-such as fuzzy sets, artificial neural networks, genetic algorithms, and rough sets-however, offer the opportunity to apply a wide range of data types to a variety of vital functions by handling real-life uncertainty with low-cost solutions. This book aims to provide an accessible introduction to fundamental and advanced data mining technologies. Topics include application in mining biological databases."

Quantitative Methods in Population Health: Extensions of Ordinary Regression

M. Palta, *University of Wisconsin*

Wiley, 2003, ISBN: 0-471-45505-9, 311 pp., USD 89.95.

"The study of population health often involves the use of observational data from existing data sets, complex survey designs and longitudinal follow-up. Ordinary regression analysis, familiar to most researchers and practitioners is inadequate for analysing such data and answering important questions about the relationship of risk factors to health. Non-statisticians such as epidemiologists and health services researchers require a working knowledge of the sophisticated modelling techniques used by professional statisticians. Quantitative Methods in Population Health aims to provide an accessible guide for students in an applied statistics sequence as well as for practicing researchers and professionals."

Cancer Modelling and Simulation

L. Preziosi, *Politecnico di Torino (Ed.)*

Chapman & Hall/CRC, 2003, ISBN 1584883618, 456 pp., USD 129.95

"Tumour evolution is a complex process involving many different phenomena. Mathematical modelling and computer simulations can help us understand these phenomena, but their development requires a multidisciplinary background-one that includes an understanding of the biological phenomena involved and knowledge of the mathematical techniques used to obtain both qualitative and quantitative results.

Cancer Modelling and Simulation builds the requisite biological foundation and presents the mathematical models and methods useful for understanding the dynamics of tumour development and growth. In chapters contributed by an interdisciplinary team of researchers, this book addresses the entire modelling process, from phenomenological observation to simulation and

validation, through the development of mathematical models and their qualitative and quantitative study."

Data analysis tools for DNA microarrays

S. Draghici, *Wayne State University*

Chapman & Hall/CRC, 2003, ISBN 1-58488-315-4, 512 pp., USD 59.95

"Technology today allows the collection of biological information at an unprecedented level of detail and in increasingly vast quantities. To reap real knowledge from the mountains of data produced, however, requires interdisciplinary skills-a background not only in biology but also in computer science and the tools and techniques of data analysis. To help meet the challenges of DNA research, Data Analysis Tools for DNA Microarrays builds a foundation in the statistics and data analysis tools needed by biologists and provides the overview of microarrays needed by computer scientists. It first presents the basics of microarray technology and more importantly, the specific problems the technology poses from the data analysis perspective. It then introduces the fundamentals of statistics and the details of the techniques most commonly used to analyze microarray data. The final chapter focuses on commercial applications with sections exploring various software packages from BioDiscovery, Insightful, SAS, and Spotfire. The book is richly illustrated with more than 230 figures in full color and comes with a CD-ROM containing full-feature trial versions of software for image analysis (ImaGene, BioDiscovery Inc.) and data analysis (GeneSight, BioDiscovery Inc. and S-Plus Array Analyzer, Insightful Inc.)."

Differential Equations and Mathematical Biology

D.S. Jones, *University of Dundee*, **B.D. Sleeman**,
University of Leeds

Chapman & Hall/CRC, 2003, ISBN 1-58488-296-4, 408 pp., USD 79.95

"The conjoining of mathematics and biology has brought about significant advances in both areas, with mathematics providing a tool for modelling and understanding biological phenomena and biology stimulating developments in the theory of nonlinear differential equations. The continued application of mathematics to biology holds great promise and in fact may be the applied mathematics of the 21st century.

Differential Equations and Mathematical Biology provides a treatment of both ordinary and partial differential equations, techniques for their solution, and their use in a variety of biological applications. The presentation includes the fundamental techniques of nonlinear differential equations, bifurcation theory, and the impact of chaos on discrete time biological modelling. The authors address numerical techniques and a range of applications, including heart physiology, nerve pulse transmission, chemical reactions, tumour growth, and epidemics."

Modelling and Simulation of Capsules and Biological Cells

C. Pozrikidis, *University of California, La Jolla (Ed.)*

Chapman & Hall/CRC, 2003, ISBN 1-58488-359-6, 344 pp., USD 99.95

"In the past three decades, considerable progress has been made in the mathematical analysis, modelling, and simulation of the fluid dynamics of liquid capsules and biological cells. This book explores topics related to the modelling and numerical simulation of capsule fluid dynamics and cell biomechanics. The book covers the fundamentals of cell and membrane mechanics, modelling hydrodynamics under various flow conditions, and drop and bubble dynamics associated with temperature variations and surfactant transport."

Modelling Metabolism with Mathematica

P.W. Kuchel, P. Mulquiney, *University of Sydney*

CRC-press, 2003, ISBN 0849314682, 328 pp., USD 149.95

"The experimental and theoretical study of metabolism in mammalian cells has a long and fruitful history, but our understanding of cellular metabolism at the molecular level is far from complete. With the advent of sophisticated general programming environments like Mathematica, the task of developing new models of metabolism and visualizing their responses has become accessible to students of biochemistry and the life sciences in general. *Modelling Metabolism with Mathematica* presents the approaches, methods, tools, and algorithms for modelling the chemical-dynamics of metabolic pathways. The authors explain the concepts underpinning the deterministic theory of chemical and enzyme kinetics, present a graded series of computer models of metabolic pathways leading up to that of the human erythrocyte, and document a consistent set of rate equations and associated kinetic parameters."

Nonlinear Dynamics in Physiology and Medicine

A. Beuter, *Université de Montpellier*, **L. Glass**, *McGill University*, **M. C. Mackey**, *McGill University*, **M. S. Titcombe**, *McGill University* (Eds.)

Springer-Verlag, 2003, ISBN: 0-387-00449-1, 428pp., USD 69.95

"This book is divided roughly into two sections. The first part mainly introduces concepts from nonlinear dynamics using an almost exclusively biological setting for motivation. The second part consists of five in-depth examples of how the authors have used the concepts of the first part of the book in their research investigations of biological and physiological systems. Appendices highlight those techniques found most useful. The book emphasizes analytic and computer exercises throughout the book using XPP or Matlab. Introductions to both XPP or Matlab are included in the appendices."

Essential Mathematical Biology

N.F. Britton, *University of Bath*

Springer-Verlag, 2003, ISBN: 1-85233-536-X, 335pp., USD 34.95

"*Essential Mathematical Biology* is an introduction to the fast-growing field of mathematical biology, written for students with a mathematical background. It sets the subject in its historical context, but guides the reader towards questions of current research interest. A broad range of topics is covered, including: Population dynamics, Infectious diseases, Population genetics and evolution, Dispersal, Molecular and cellular biology, Pattern formation, and Cancer modelling. Particular attention is paid to situations where the simple assumptions of homogeneity made in early models break down, and the process of mathematical modelling is seen in action. A dedicated website at www.springer.co.uk/britton accompanies the book and provides further exercises and more detailed solutions to the exercises in the book."

Dynamical Systems in Population Biology

Xiao-Qiang Zhao, *Memorial University of Newfoundland*

Springer-Verlag, 2003, ISBN: 0-387-00308-8, 276 pp., USD 79.95

"The conjoining of nonlinear dynamics and biology has brought about significant advances in both areas, with nonlinear dynamics providing a tool for understanding biological phenomena and biology stimulating developments in the theory of dynamical systems. This research monograph provides an introduction to the theory of nonautonomous semiflows with applications to population dynamics. It develops dynamical system approaches to various evolutionary equations such as difference, ordinary, functional, and partial differential equations, and pays more attention to periodic and almost periodic phenomena. The presentation includes persistence theory, monotone dynamics, periodic and almost periodic semiflows, travelling waves, and global analysis of typical models in population biology."

Complex Population Dynamics: a theoretical/empirical synthesis

P. Turchin, *University of Connecticut*

Princeton University Press, 2003, ISBN 0-691-09021-1 (pb), 456 pp., USD 29.95

"Why do organisms become extremely abundant one year and then seem to disappear a few years later? Why do population outbreaks in particular species happen more or less regularly in certain locations, but only irregularly (or never at all) in other locations? Complex population dynamics have fascinated biologists for decades. By bringing together mathematical models, statistical analyses, and field experiments, this book offers a new synthesis of the theory of population oscillations."

Peter Turchin first reviews the conceptual tools that ecologists use to investigate population oscillations, introducing population modelling and the statistical analysis of time series data. He then provides a discussion of several case studies—including the larch budmoth, southern pine beetle, red grouse, voles and lemmings, snowshoe hare, and ungulates—to develop a new analysis of the mechanisms that drive population oscillations in nature. Through such work, the author argues, ecologists can develop general laws of population dynamics that will help turn ecology into a truly quantitative and predictive science."

Mathematics in Population Biology

H.R. Thieme, *Arizona State University*

Princeton University Press, 2003, ISBN 0-691-09291-5 (pb), 392 pp., USD 39.95

"The formulation, analysis, and re-evaluation of mathematical models in population biology has become a valuable source of insight to mathematicians and biologists alike. This book presents an overview and selected sample of these results and ideas, organized by biological theme rather than mathematical concept, with an emphasis on helping the reader develop appropriate modelling skills through use of examples.

Part I starts with unstructured single species population models, particularly in the framework of continuous time models, then adding the most rudimentary stage structure with variable stage duration. The theme of stage structure in an age-dependent context is developed in Part II, covering demographic concepts, such as life expectation and variance of life length, and their dynamic consequences. In Part III, the author considers the dynamic interplay of host and parasite populations, i.e., the epidemics and endemics of infectious diseases. The theme of stage structure continues here in the analysis of different stages of infection and of age-structure that is instrumental in optimising vaccination strategies. Each section concludes with exercises, some with solutions, and suggestions for further study."

Models in Ecosystem Science

C. D. Canham, J. J. Cole, *Institute of Ecosystem Studies*,
William K. Lauenroth, *Colorado State University*.

Princeton University Press, 2003, ISBN 0-691-09289-3 (pb), 504 pp., USD 35.00

"Quantitative models are crucial to almost every area of ecosystem science. They provide a logical structure that guides and informs empirical observations of ecosystem processes. They play a particularly crucial role in synthesizing and integrating our understanding of the immense diversity of ecosystem structure and function. Increasingly, models are being called on to predict the effects of human actions on natural ecosystems. Despite the widespread use of models, there exists intense debate

within the field over a wide range of practical and philosophical issues pertaining to quantitative modelling. This book—which grew out of a gathering of leading experts at the ninth Cary Conference—explores those issues. The book opens with an overview of the status and role of modelling in ecosystem science, including perspectives on the long-running debate over the appropriate level of complexity in models. This is followed by eight chapters that address the critical issue of evaluating ecosystem models, including methods of addressing uncertainty. Next come several case studies of the role of models in environmental policy and management. A section on the future of modelling in ecosystem science focuses on increasing the use of modelling in undergraduate education and the modelling skills of professionals within the field. The benefits and limitations of predictive (versus observational) models are also considered in detail."

Consumer Resource Dynamics

W.W. Murdoch, *University of California, Santa Barbara*,
C.J. Briggs, *University of California, Berkeley*, **R.M. Nisbet**, *University of California, Santa Barbara*

Princeton University Press, 2003, ISBN 0-691-00657-1 (pb), 456 pp., USD 35.00

"Despite often violent fluctuations in nature, species extinction is rare. California red scale, a potentially devastating pest of citrus, has been suppressed for fifty years in California to extremely low yet stable densities by its controlling parasitoid. Some larch budmoth populations undergo extreme cycles; others never cycle. In *Consumer-Resource Dynamics*, the authors use these and numerous other biological examples to lay the groundwork for a unifying theory applicable to predator-prey, parasitoid-host, and other consumer-resource interactions. Throughout, the focus is on how the properties of real organisms affect population dynamics. The core of the book synthesizes and extends the authors' own models involving insect parasitoids and their hosts, and explores in depth how consumer species compete for a dynamic resource. The emerging general consumer-resource theory accounts for how consumers respond to differences among individuals in the resource population. From here the authors move to other models of consumer-resource dynamics and population dynamics in general. Consideration of empirical examples, key concepts, and a necessary review of simple models is followed by examination of spatial processes affecting dynamics, and of implications for biological control of pest organisms. The book establishes the coherence and applicability of consumer-resource theory and connects it to single-species dynamics. It closes by stressing the theory's value as a hierarchy of models that allows both generality and testability in the field."

Mathematics in Nature: modelling patterns in the natural world

J.A. Adam, *Old Dominion University*
Princeton University Press, 2003, ISBN 0-691-11429-3,
448 pp., USD 39.50

"From rainbows, river meanders, and shadows to spider webs, honeycombs, and the markings on animal coats, the visible world is full of patterns that can be described mathematically. Examining such readily observable phenomena, this book introduces readers to the beauty of nature as revealed by mathematics and the beauty of mathematics as revealed in nature. Generously illustrated, written in an informal style, and replete with examples from everyday life, *Mathematics in Nature* is an introduction to the ideas and methods of mathematical modelling. It illustrates how mathematics can be used to formulate and solve puzzles observed in nature and to interpret the solutions. In the process, it teaches such topics as the art of estimation and the effects of scale, particularly what happens as things get bigger. Examples studied include such natural phenomena as cloud formations, halos and glories, tree heights and leaf patterns, butterfly and moth wings, and even puddles and mud cracks."



In a special collection of articles, published from February 2004 on, *Science Magazine* and its online companion sites team up to explore one of the hottest interdisciplinary collaborations in science today: the interface between mathematics and biology. In *Science*, News, Viewpoint, and Review articles cover how mathematics and computation are informing biology on a wide variety of fronts, the need for incorporating quantitative approaches into bioscience curricula, and some of the uses -- and abuses -- of mathematical models for biological systems. The [Signal Transduction Knowledge Environment](#) focuses on computational models of cell signaling, with Reviews, Protocols, and a special discussion forum. The [Science of Aging Knowledge Environment](#) looks at mathematical approaches to studying several issues of interest to the aging-research community. And [Science's Next Wave](#) offers a month-long series on careers at the math-biology interface. Notice therein the presentations by several ESMTB members such as *Thomas Hillen*, *Frithjof Lutscher* and *Andreas Deutsch*, the latter also describing our Society and particular European prospects.

Visit: <http://www.sciencemag.org/sciext/mathbio/>

Forthcoming Events

First French Society for Theoretical Biology International Conference

May 21 – 25, 2004, Marrakech, Morocco

La Société Française de Biologie Théorique ([SFBT](#)) a été fondée en 1984 à l'instigation de Pierre Delattre et de René Thom. Elle s'est ouverte à l'espace francophone en 2001 en devenant la **Société Francophone de Biologie Théorique**. Elle tient son séminaire annuel à St Flour et envisage d'organiser périodiquement une conférence francophone dans un pays autre que la France, dont la première aura lieu à Marrakech du 21 au 25 Mai 2004.

Objectifs

- Réunir des chercheurs travaillant dans les domaines liés à la biologie théorique : biologie, écologie, médecine, mathématiques, informatique, physique, chimie...
- Faire le point sur la recherche dans le domaine.
- Tracer des nouvelles perspectives d'action de la SFBT.

- Permettre à des jeunes chercheurs des pays francophones de se rencontrer et de présenter leurs travaux devant des spécialistes.
- Renforcer la recherche pluridisciplinaire.

Thèmes de la Conférence

- Ce seront principalement les thèmes classiquement abordés dans le cadre de la SFBT, à savoir
- Biologie et Ecologie Marine.
- Ecologie Théorique.
- Systèmes Dynamiques en Biologie.
- Approches Théoriques en Médecine.
- Approches Théoriques en Biologie au niveau cellulaire et sub-cellulaire.
- Cette liste n'est pas exhaustive, la conférence est ouverte à toute communication relevant de la biologie théorique ou mathématique.

Langue principale d'expression: Français

Actes de la Conférence:

Les travaux présentés à la conférence seront publiés, selon leur discipline, dans des numéros spéciaux des revues: Acta Biotheoretica, Ecological Modelling, Maths Biosciences, CRAS Biologies, selon les règles de publications de ces revues. Des discussions sont en cours avec la revue M3AS.

Date limite d'envoi des résumés : 30 Mars 2004

Envoi des résumés à : sfbt@ucam.ac.ma

Date limite d'inscription : 21 Avril 2004.

Gordon Research Conference on Theoretical Biology & Biomathematics

June 6 – 11, 2004, Tilton, NH, USA

<http://www.grc.uri.edu/programs/2004/theobio.htm>

Chairs: Tim C. Elston & Raymond Mejia

Vice Chair: Paul C. Bressloff

This conference serves to introduce students and bring participants to the forefront of areas of investigation covered by Theoretical Biology & Biomathematics. This year the topics given below have been selected for discussion at the plenary sessions. Poster sessions will afford participants an opportunity to present and discuss work in all areas of Theoretical Biology & Biomathematics.

Topics for Discussion:

Emergent Species/Diseases and Invasion (Carlos Castillo-Chavez), Theoretical Ecology (Graciela Canziani), Immunology (Ramit Mehr), Neurobiology (Paul Bressloff), Motors and Motility (Ed Pate), Systems Biology/Molecular Regulatory Networks (John Tyson), Stochastic Effects in Gene Regulation and Signal Transduction (Jeff Hasty), Biofluids (Aaron Fogelson), The Future of Biomathematics and Theoretical Biology (Alan Hasting).

Summer School on Cell Biology and Mathematical Modelling

June 7 – 18, 2004, Island of Hvar, Croatia

<http://itb.biologie.hu-berlin.de/~school2004/>

The school is a follow-up of the Termoli school held in 1999, and the Siguenza school held in 2001. The school is intended mainly for PhD students but postdocs are also very welcome. Students from different fields, including biology, biochemistry, physics and mathematics are invited. The school will start with tutorials in biology and mathematics that will cover the basics needed to follow the course lectures.

Topics:

1. Cell cycle and tumorigenesis
2. Signalling Cascades and Gene Regulation
3. Circadian Rhythms: Experiments and Models
4. Ca²⁺ Dynamics
5. Genomic and Proteomic Techniques: From high throughput data to mathematical models

Tutorials:

1. Tutorial on Mathematical Modeling (Prof. H. Herzl and collaborators)
2. Tutorial on Molecular Cell Biology (Branka Cajavec and N.N.)

Lectures:

Each course is divided into 6 to 8 units of 40min. There will be ten days of classes, Monday through Friday, during two weeks. The instructors are

- * A. Bertuzzi (1)
- * A. Gandolfi (1)
- * A. Goldbeter (to be confirmed) (3,4)
- * H. Herzl's group (1,2,3,5)
- * T. Höfer (4)
- * N. Keith and Nedime Serakinci (1)
- * M. Kimmel(5)
 - M. Mackey (1,2)
 -

Free Boundary Problems in Biomathematics, Multiscaling, and Infinite-Dimensional Dynamical Systems

June 10 – 12, 2004, Montecatini Terme

Please visit the web page

<http://fbp2004.math.unifi.it/>

where you can register and apply for a short talk.

No registration fee is required.

Invited speakers:

Gregoire Allaire, Peter Bates, Juan Casado-Diaz, Alain Damlamian, Emmanuele DiBenedetto, Eduard Feireisl, Miguel Angel Herrero, Nobuyuki Kenmochi, Stephan Luckhaus, Masayasu Mimura, Francois Murat, Gabriel Nguetseng, Adelia Sequeira, Songmu Zheng

Free Boundary Problems.

These are boundary-value problems for differential equations, which are set in a domain whose boundary is a priori unknown, and is accordingly named a free boundary. Problems of this sort arise in a large number of phenomena of applicative interest, and have been the object of intense research in the last forty years. This conference is devoted to three topics that are certainly prominent for applications of free boundary problems.

Biomathematics.

Biology and medicine are becoming more and more important sources of interesting and stimulating mathematical problems. Cell populations, cancer growth and therapies, hemodynamics and other branches of physiology and biology are remarkable fields of application of P.D.E.'s with frequent inclusion of free boundaries.

Other subjects treated in the conference will be *Multiscaling* and *Infinite-Dimensional Dynamical Systems*.

Computational and Mathematical Population Dynamics

June 21 – 25, 2004, Trento, Italy

Joint Meeting of the Seventh International Conference on Mathematical Population Dynamics (MPD7) and the Third International Conference on "Deterministic and Stochastic Modeling of Biointeraction" (DESTOBIO 3)

Topics of the conference will be the use of mathematical models in different areas of biology, especially ecology (including epidemic spread), cell population dynamics (including immunology, tumour growth), and molecular biology (including molecular evolution and genetics, genomics).

The Conference will consist of plenary lectures, parallel sessions on some of the topics outlined above, plus contributed talks and posters. Everybody is invited to suggest proposals for sessions in related areas any time before January 1, 2004. A proposal form will be made available on the Web page www.science.unitn.it/~dbio-mpd

More information on the conference can be found on www.science.unitn.it/events/mpd/

SCIENTIFIC COMMITTEE:

Agur, Zvia (Institute for Medical BioMathematics, Israel), Axelrod, David (Rutgers), Bellomo, Nicola (Pol. Torino), Bertuzzi, Alessandro (CNR, Roma), Braumann, Carlos (Evora), Chakraborty, Ranajit (Cincinnati), Diekmann, Odo (Utrecht), Gatto, Marino (Pol. Milano), Gyllenberg, Mats (Turku), Herzog, Hanspeter (Humboldt, Berlin), Iwasa, Yoh (Kyushu), Willi Jäger (Heidelberg), Krivan,

Vlastimil (Czech Acad. Sci.), Langlais, Michel (Bordeaux), Levin, Simon (Princeton), Mackey, Michael (McGill), Mode, Charles (Drexel), Rudnicki, Ryszard (Silesian Univ.), Stevens, Angela (Max Planck Inst., Leipzig), Webb, Glenn (Vanderbilt)

Gordon Research Conference on Metabolic Basis of Ecology

July 4 – 9, 2004, Bates College, Lewiston, ME

Chairs: James H Brown & James Gillooly

This first of its kind Gordon Research Conference will bring together scientists from around the world who are working to relate ecological processes to fundamental laws of biology, chemistry and physics. Specifically, we will focus on fundamental constraints imposed by body size, temperature and stoichiometry (i.e., elemental composition). Recent integrative studies on the effects of body size, temperature, and stoichiometry have led us to conclude that these three factors are the primary determinants of rate processes in organisms, including the most fundamental biological process, metabolism. Since metabolic rate is the rate of transformation of energy and materials in an organism, many other biological rates are governed by metabolism. From the perspective of ecology, metabolism determines the rate of exchange of energy and materials with the environment, and the rate of allocation of these resources to all components of the life history: maintenance, growth and reproduction. The next important step is to quantify how the effects of body size, temperature and stoichiometry on metabolism constrain species' life histories, population dynamics, and their distribution and diversity. This, in turn, will help to better understand ecosystem level processes such as nutrient cycling and trophic dynamics. The next step here is to develop mechanistic explanations for these broader scale ecosystem and global patterns. From this perspective, it is now clear that much of ecology reflects the outcome of the same biological and physical processes. We will bring together a trans-disciplinary group of distinguished ecologists, physiologists, physical scientists and mathematicians to guarantee diverse perspectives. This will insure a dynamic exploration of this new frontier in biology, with a special emphasis on discussing future areas of research and collaboration.

Topics:

We will explore how basic principles constrain or optimize biological processes at all levels of biological organization, from individuals and populations to communities and ecosystems. Topics likely to be covered include: life history constraints, population dynamics, community structure and function, nutrient cycling, stoichiometry, and allometry.

<http://www.grc.uri.edu/programs/2004/metbasis.htm>

International Conference on Differential Equations and Applications in Mathematical Biology

July 18 – 23, 2004, Nanaimo, British Columbia, Canada

Topics:

Differential equations, Delay differential equations, Integro-differential equations, Difference equations, Mathematical biology, Mathematical ecology, Population Dynamics, Dynamical systems, Control and optimization

Abstract submission:

Authors are invited to submit abstracts of at most one page before March 20, 2004. There will soon be instructions for authors.

The notifications of acceptance are scheduled for April 15, 2004.

Important Note: Each submitted abstract must be prepared in accordance with AMS-Latex (see <http://www.ams.org/tex/>).

Contact: Elena Braverman

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Internet:

<http://web.mala.bc.ca/math/conference/default.htm>

Annual Meeting of The Society of Mathematical Biology (SMB)

July 25 – 28, 2004, University of Michigan, Ann Arbor, Michigan

www.smb.org/SMB-2004final.pdf

The University of Michigan is proud to be hosting this summer's Annual meeting for the Society for Mathematical Biology. We have put together hopefully a diverse and exciting program that includes plenary lectures to be given by

Bard Ermentrout,
Rakesh Jain,
Simon Levin,
Alan Perelson,
Charles Peskin,
Tamar Schlick,
James Sneyd, and
Michael Waterman

We also will be running numerous minisymposia and contributed sessions on the topics of

Neuroscience
Tumor growth and control
Ecology
Education
Immunology and Infectious Diseases
Mathematical Challenges in Biology
Developmental Biology
Molecular genetics and Computational Biology
Physiology and Cellular Biology.

Anyone interested in organizing a minisymposium or contributed sessions, i.e., a group of up to 6 talks of 15 minutes each on a focused subject, is encouraged to submit a proposal to the conference organizers through the conference website. We encourage proposals that include 6 speakers or less as many other people will want to contribute a talk and the organizers will place them accordingly.

Also, we are now accepting abstracts in poster or lecture format from anyone interested in participating in the conference. Please advise the organizers as to which you prefer and they will do their best to accommodate.

In case of questions and for further information, please see <http://www.math.lsa.umich.edu/SMB2004/SMBindex.html>

Algorithms for Macromolecular Modelling IV

August 18 – 21, 2004, University of Leicester, UK

The goal of this meeting is to assess the state of the art in the development of algorithmic tools for simulation of large molecules (especially biomolecules), and to help identify the most important directions for future research on this subject. Molecular simulation is now a standard tool in a vast plethora of chemical processes ranging from applications in nanotechnology to the identification and prediction of biomolecular structure and function. To date, many challenges have been addressed in an incomplete manner, and there is a continuing demand for high quality algorithms and supportive theory for high performance computations. Principal topics to be addressed at this meeting are algorithms for force evaluation, integration, and sampling; methods for structure prediction, reaction paths, free energy profiles and conformational dynamics; modelling of force fields and implicit solvents; and multiscale techniques for quantum-classical and classical-elastic models.

Scientific Committee:

Ben Leimkuhler (Chair), University of Leicester
Christophe Chipot, CNRS
Peter Deuffhard, Zuse Institute Berlin
Ron Elber, Cornell University
Alan Mark, University of Groningen
Sebastian Reich, Imperial College and Potsdam University
Tamar Schlick, New York University
Robert Skeel, University of Illinois at Urbana-Champaign (SIAM Rep)

Registration will be available here from the end of January 2004. For assistance or information, please contact the organizers by mail to organizers@am-3.org

This meeting is an official cooperative activity of the Society for Industrial and Applied (SIAM)

ISDA 2004: Fourth International Conference on Intelligent Systems Design and Applications

August 26 – 28, 2004, Budapest, Hungary

Intelligent Systems Design and Applications (ISDA 2004) is the fourth International conference that brings together international computational intelligence/ soft computing / artificial Intelligence researchers, developers, practitioners, and users. The aim of ISDA'04 is to serve as a forum to present current and future work as well as to exchange research ideas in this field.

ISDA'04 invites authors to submit their original and unpublished work that demonstrate current research in all areas of computational intelligence including design of artificial neural networks, fuzzy systems, evolutionary algorithms, hybrid computing systems, intelligent agents, and their applications in science, technology, business and commerce.

Important Deadlines:

Workshop/ sessions/ tutorial proposals: March 1, 2004

Paper submission (full paper) : April 1, 2004

Notification of acceptance: May 10, 2004

Camera ready papers and authors' registration : June 10, 2004

ECEM/EAML-04

ECEM-04: The Fourth European Conference on Ecological Modelling and, EAML-04: The Fourth International Workshop on Environmental Applications of Machine Learning

September 27 - October 1, 2004, Bled, Slovenia

The deadline for submitting two-page abstracts is March 20. More information on the events can be found at the web site.

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Internet: [http://www-](http://www-ai.ijs.si/SasoDzeroski/ECEMEAML04/)

[ai.ijs.si/SasoDzeroski/ECEMEAML04/](http://www-ai.ijs.si/SasoDzeroski/ECEMEAML04/)

5th International Conference on Systems Biology

October 9 – 13, 2004, Heidelberg, Germany

“Systems Biology - From Bioscience To Medicine”

The 5th International conference on Systems Biology 2004 continues an annual series of systems biology conferences that was initiated by Hiroaki Kitano 2000 in Japan. Since then the conference has been organised at Caltech in Pasadena and Karolinska Institute in Stockholm. In 2003 the ICSB was hosted by [Washington University in St. Louis](http://www.washington.edu), USA.

According to a well-accepted tradition, the ICSB 2004 programme committee has coined a motto for the conference in 2004: "Systems Biology - From Bioscience to Medicine".

Following this guideline session topics for the conference were chosen that encompass the understanding of metabolic and signal transduction systems, bacterial systems biology, hepatocytes and their implication for systems biology for medicine, and spatial models. We cordially invite the scientific community to submit abstracts to the organisers. For your information you can download the [Call for Papers](#) here.

The 5th International Conference on Systems Biology will be co-organised by the [German Federal Ministry of Education and Research](#), [DECHEMA e.V.](#), [Deutsches Krebsforschungszentrum](#), [European Molecular Biology Laboratory](#), and [European Media Laboratory](#). The conference will be hosted under the auspices of the German Federal Minister of Education and Research Mrs. Edelgard Bulmahn.

Organising Committee:

Jens Doutheil, DECHEMA e.V., Frankfurt

Roland Eils (Chair), DKFZ, Heidelberg

Karl Kuchler, University of Vienna

Ursula Kummer, EML, Heidelberg

Hans Westerhoff, BioCentrum, University of Amsterdam

Scientific Committee:

Uri Alon, Israel

Peer Bork, Germany

John Doyle, USA

Ernst D. Gilles, Germany

Reinhart Heinrich, Germany

Pedro Mendes, USA

Siegfried Neumann, Germany

Dieter Oesterhelt, Germany

Bernhard O. Palsson, USA

Klaus Prank, Germany

Bert Sakmann, Germany

Stefan Schuster, Germany

ACRI 2004 "From individual to collective behaviour" Sixth International conference on Cellular Automata for Research and Industry

October 25 – 28, 2004, University of Amsterdam, Science Park Amsterdam, The Netherlands

<http://www.science.uva.nl/research/scs/events/ACRI2004>

Scope of the conference:

Cellular Automata, in spite of their apparent simplicity, represent a very powerful approach to study spatio-temporal systems in which complex phenomena build up out of many simple local interactions. They often provide solutions to real problems for which other, conventional approaches fail.

John von Neumann, who is recognized as the father of cellular automata, would have been a hundred years old in 2004. ACRI 2004 wants to commemorate this important date by inviting researchers to submit contributions related to von Neumann's work or to the emergence of organisation in systems in which collaboration between components wins over the individual behaviour.

The goal of this conference is to collect contributions concerning Cellular Automata in various fields such as theory, implementations and applications.

Local organizing committee:

P.M.A. Sloot (University of Amsterdam)

sloot@science.uva.nl

B. Chopard (University of Geneva)

bastien.chopard@cui.unige.ch

Preliminary list of invited speakers:

- Prof. P. Hogeweg (Confirmed)
- Prof. J. Crutchfield (TBD)
- Prof. Toffoli (TBD) (in view of the von Neumann 100th anniversary memorial session)
- Prof. Andrew Adamatzky (TBD)
- Prof. Vollmar (TBD)
- Industrial (TBD)

Important dates:

Paper submission: April 9, 2004

Notification of acceptance: May 21, 2004

Camera ready version: July 1, 2004

Registration deadline: July 1, 2004

Participants are invited to submit a paper of no more than 8 pages A4. Further information on paper format, registration, travel and accommodation will be posted as soon as possible on the conference web site:

<http://www.science.uva.nl/research/scs/ACRI2004>.

Email address for the conference: acri2004@science.uva.nl

Conference themes:

We welcome contributions related to the following domains:

- Complex systems, emergent behaviour versus local behaviour
- Environment: (Pollution models, biomass evolution, desertification, erosion processes, landslides, etc)
- Biological systems: (ecological models, species evolution, immune systems, contamination processes, artificial life)
- Socio-economical models: (vehicular and pedestrian traffic, urbanism, social models, economical and financial processes, etc.)
- Tools and Theory: (new algorithms based on CA, theory of computation, CA environments, parallel cellular computing)
- Modelling of physical or chemical systems: (hydrodynamics, reaction diffusion systems, complex flows, etc)

2005

European Conference on Mathematical and Theoretical Biology, ECMTB 05

July 18 – 22, 2005, Dresden, Germany

The main goal of the conference is to show the enormous diversity and success of mathematical modelling approaches in the life sciences. The conference will demonstrate that application of mathematical methods and computer simulation are absolutely essential to solve key problems in current biology ranging from the organizational level of individual cells to the dynamics of organisms and populations. The conference consists of plenary lectures, a limited number of parallel sessions (contributed talks) and poster sessions on carefully selected key topics. Key topics include cell physiology and physics, development, neuroscience, immunology, biomedicine, innovative mathematical methods, biotechnology and -engineering as well as education in mathematical/theoretical biology. The conference will be accompanied by a mentoring programme for new-coming students and a company exhibition.

Application will be possible from June 2004.

Applications are welcome for contributed and poster presentations. In addition, application for the organization of a limited number of mini-symposia is possible.

The conference is organized by the European Society for Mathematical and Theoretical Biology (ESMTB) in cooperation with the Society for Mathematical Biology (SMB).

Dresden is a prime place for hosting ECMTB05. It offers a high quality infrastructure in a superb urban surrounding, rich in culture and natural beauties within easy reach. The atmosphere in the city is very supportive to all activities arranged in the interdisciplinary field between Biology/Medicine and Mathematics/Physics.

Contact: Andreas Deutsch

ECMTB05@zhr.tu-dresden.de