Editorial

The Role of Biomathematics as a Scientific Discipline

O. Arino, S. Fleishman* and Z. Agur*, Pau University, France; * Institute for Medical BioMathematics (IMBM), Israel.

The perspective of the mathematician

Dear Z,

Attempting to answer your questions I find myself wondering why, after all, do we have a problem in defining biomaths, while there does not seem to be any problem in mathematical physics or theoretical physics?

And why do I, as a mathematician, find it difficult to be considered a biomathematician, while I would not care at all to be considered a physicomathematician? Is there anything to be compared between these two seemingly parallel issues, anything that could help us better understanding our role?

If I were to work in physicomathematics, I would have, for instance, dealt with the use of percolation theory in fluid dynamics, or some new models encountered in the theory of optics. I would never be worried about the physical significance of my mathematical findings and the community to which I belong would not penalize me for this.

It seems to me that Biomathematics is a double-edged sword**:**

Mathematicians do not seem to be interested in our mathematical results.
Why is it so? One possibility is that the role of a mathematician in biology is viewed as "technical", so that mathematical novelty is not expected in biomaths literature. The fact that the mathematician tends to underestimate mathematical contributions in biomaths can be seen, for example, in the fact that you will not find transversal references (with respect to the mathematics) in biomaths papers. A guy who studies structured populations in the context of the theory of epidemics will not quote papers on structured populations in the context of cells, for example. This way, it is difficult to foresee any progress in the mathematics arising from biology.

On the other hand**, biological predictions** based on mathematical arguments are not even read by biologists, who seem totally paralyzed by the use of mathematics. That is not to say that they consider mathematics has nothing to do with biology. They would even be bolder than mathematicians in using some tools that mathematicians would be reluctant to introduce, because biologists feel free from the sort of constraints that mathematicians have. In fact, symmetrically, mathematicians do not sense all the subtleties of biology. These "naive" views that each has on the other's disciplinary field may create opportunities for the emergence of new ideas.

Of course, in order to use mathematics in the context of biology, it is necessary to describe biological processes or part of them in terms of mathematical entities. Mathematics is a language for building models. Mathematics is more than a language, it is a way of looking at things, going from qualitative to quantitative. It may influence biology in the sense that it forces the biologist to make further observations, or it may can help discover relationships between parameters or variables.

I believe we should make every effort to illustrate this potentiality.

What mathematics can get from biology is new problems. This is also an important feature of biomaths, since our ability to use mathematics as a tool in biology will increase proportionally with our ability to solve mathematical issues arising from this field of application.

The perspective of the biomathematician

Dear O.,
Let me open by restating the Problem:

While the science of biomathematics is expected to bridge the gap between the qualitative attributes of biology and the quantitative analysis of mathematics, in practice it is often considered a no man's land for both empirical biologists and theoretical mathematicians. Despite its many developments and successes, biologists or mathematicians seldom refer to works in the biomaths field as a source of inspiration for their own work. Mathematical biology thus misses its purpose as a complementary view on biological problems and its capacity as a unifying, interdisciplinary force within the world of biology.

An entire spectrum of opinions exists regarding the role of biomathematics. Some may think of it as a means for mathematicians to find challenging new problems to analyze. Others may view it as a field that complements experimental biology in the sense that it considers the same challenges with an analytic methodology, thus gaining quantitative insight into problems that were only described phenomenologically.

In my opinion the ultimate goal of biomaths is to create the *theory of biology*. This is essential for turning biology from a descriptive science into a mature science, where experiments are performed to verify a theory. The short-range goal of biomaths. is to describe the *dynamics* of given biological systems, a task that can hardly be achieved in experimental biology. This is done in an iterative process in which the biomathematician chooses the appropriate mathematical model(s) for the biological problem at hand and subjects it to analysis. The biomathematician must also provide the biological interpretation of the model. Seeing it this way, I believe that it is essential that biologists will recognize the important contribution of biomathematics to their domain.

How to convince experimental biologists that the role of the biomathematician is indispensable in biology?

The key to alleviating the problem of applicability of biomathematics to biology is the understanding that biologists often see biomathematical work as impenetrable, in the sense that it is formulated in overly mathematical terminology. It would be unwise to blame this on biologists' ignorance, however. This is first and foremost our problem, wishing our work to be considered as participating and influential within the scientific framework.

Moreover, I think that, currently, our field suffers from a confusion between the role of the *mathematician* in the field and that of the *biomathematician*. I would like to suggest that the role of the *mathematician* is restricted to model analysis, with possible but not essential, mathematical novelties. In contrast the *biomathematicians* are commited to the biological problems at hand. Therefore the biomathematician is required to gain a very good understanding of the details of the biology and to produce results that are relevant to the biologists. I believe that the assimilation of these perceptions will aid biomathematicians in getting a wider acceptance. One practical suuggestion towards achieving the latter goal is suggested below.

The perspective of a young biomathematician

The problem of biomathematics lies in its generally bad communications with experimental biology, it should be the endeavour of a European society to create media that will facilitate such communication. In a field as dynamic as biology where work is deemed outdated astonishingly fast, offers of new periodical media are probably the best means of bridging the communication gap. I will deal here with one such idea, though many others may be put forth and implemented.

In my opinion, a heterogeneous field such as biomathematics cannot be 'overhauled' by virtue of a decision from a central board. The most the board of a society can do to channel developments in the field coherently is to offer resources and specific media for these developments to take place.

The idea is taken from the field of behavioural science in psychology. A prominent journal in the field is Brain and Behavioural Sciences (BBS). The format of the journal is very different from most other publications: every article is followed by a large section of 'open peer commentary' in which researchers in the relevant field give their views of the article in question. These commentaries may take the form of harsh criticism, sarcastic remarks or commendations. This section in turn is followed by the author's response to the commentaries.

It may be argued that such format is only legitimate in a field such as psychology, where no certain methodology is prevalent, and many of the works still have the status of competing schools of thought rather than firmly established paradigms, and that it would be inappropriate for a scientific journal. This type of format, if properly adapted, could however serve some useful purpose in biomathematics.

My suggestion is to establish a journal where each edition would carry a relatively small number of articles. The articles will follow closely the formulation of experimental works, with as little mathematics as possible (preferably none). However, the mathematics will not be neglected, but rather it will be thoroughly dealt with in an appendix. The articles will be followed by commentaries from prominent biologists and mathematical biologists of the field. Writers in the commentary section will be given full scientific freedom, within the constraints of space, and will be encouraged to comment on the work's applicability. The final comment will be a reply by the authors of the article to the commentary.

The separation between the biologically relevant results and the mathematics will allow even the biologist who is not versed in mathematics to read the article and understand its merits completely, without feeling lost in the mathematical treatment. Biomathematical work that is formulated in clear biological terms and is commented on by prominent biologists will be much more attractive for empirical biologists. On the other hand, the openness to criticism will induce biomathematicians to work on biologically relevant issues, thereby also creating an incentive for closer cooperation between empirical biologists and biomathematicians.

The journal will not be dedicated to any single field in biology, but would rather capitalize on one of the important merits of biomathematics – its capacity to bring together seemingly disparate fields, such as population dynamics and cell development – by deliberately including reviews by people who have insight into the matter, even though they may not be considered active in the given field.

It should be stressed that this proposal is by no means a criticism of currently active journals of biomathematics or a call to replace them, but rather a suggestion to complement the existing media with one that is more effective in facilitating communication between biologists and mathematical biologists, as well as communications within the biomathematical community.

Note by the Editors: it has seemed nice to offer the editorial space to members of the Board of ESMTB, to express, in an informal but enticing way, general concerns of the biomathematics community.

---

*The **closing date** for submissions to the next issue COMMUNICATIONS # 4 will be **May 30th, 2002**. Please send, preferably by e-mail, information, scientific reports and other material to one of the editors:*
Wolfgang Alt & Edith Geigant, Abteilung Theoretische Biologie, Universitat Bonn, Kirschallee 1, D-53115 Bonn, Germany, `wolf.alt@uni-bonn.de, edith.geigant@uni-bonn.de`
Andrea De Gaetano, CNR IASI Laboratorio di Biomatematica, UCSC - L.go A. Gemelli 8, 00168 Roma, Italia, `biomath@tin.it`
Hans (J.A.P.) Heesterbeek, Quantitative Veterinary Epidemiology Group, Faculty of Veterinary Medicine, P.O. box 80151, 3508 TD Utrecht, The Netherlands, `J.A.P.Heesterbeek@vet.uu.nl`

Society News

Call for Annual ESMTB Membership Fees Year 2002

The annual fee is Pounds Sterling (GBP) 25.00 or Euro (€) 40.00 (full member), and GBP 15.00 or € 20 (student member). Members from Eastern European countries should pay the student rate of GBP 15.00 or € 20. The methods of payment are given below:

(1) By CASH (either pounds sterling or your own currency to the correct value of GBP 25 or GBP 15). If you are sending cash, please use the following procedure: (a) Send the treasurer an e-mail informing him that you are sending cash so that he knows to expect it. (b) Put the cash in a sealed envelope and send this in another envelope to the address below. (c) Send the letter by registered post.

(2) By CHEQUE. If paying by cheque, please make the cheque payable to "ESMTB".

(3) By BANK DRAFT TRANSFER. Payment may be made directly to the ESMTB account, details of which are

Bank: The Royal Bank of Scotland, Balfour Street, Dundee, Dundee University Branch
Account Name: ESMTB
Sort Code: 83 18 38
Account Number: 00 145 384

Mark Chaplain, ESMTB *Secretary and Treasurer*, Dept. of Mathematics, University of Dundee, Dundee DD1 4HN, UK, `chaplain@mcs.dundee.ac.uk`

The ESMTB Hompage is located at

`http://www.esmtb.org/`

The e-mail address for questions and suggestions is
`esmtb@mis.mpg.de`

We will try to arrange for a preprint server where new results can be downloaded. Related information will be available on the web-page as soon as this service is working.

Permanent request for information!

Please send an e-mail to `esmtb@mis.mpg.de` if you
(i) Want to announce an upcoming conference,
(ii) Want the homepage of your working group to be included into the list we just started to build up,
(iii) Want to announce open positions.
Angela Stevens, Max-Planck-Institute for Mathematics in the Sciences (MIS), Inselstr. 22-26, D-04103 Leipzig, Germany, `stevens@mis.mpg.de`

Letter from the President of ESMTB

This is my third (and may be also the last one) letter as President of ESMTB. I wish to report about recent events related to the current state of our Society. According to the aims of ESMTB, a lot of promotion has been done by many members and by the Board in general, to extend the awareness of the relevance of the role of Mathematics in the Life Sciences in the scientific community. I will report in particular about the meeting organized by the European Mathematical Society (EMS) in Berlingen (Switzerland) in May to discuss the role that EMS may play in supporting applied Mhematics in Europe. ESMTB was invited and represented by Mats Gyllenberg as our delegate in the Council of EMS, and by myself as President. Apart from the typical but still anachronistic and even sterile dispute between the so called pure mathematics (I would better say pure mathematicians) and Applied, everybody realized the importance of the recent developments of Mathematical methods for Biology and Medicine. This recognition was made much more evident at the first EMS-SIAM joint Conference on Applied Mathematics in our Changing World which was held in Berlin during September 2-6,2001; as part of the Programme Committee it was possible for me to emphasize, among the focus topics of the conference, applications of Mathematics and Scientific Computing to Medicine, and to Biotechnology (there even was a general lecture on visualization of the cardiocirculatory system, in addition to a variety of minisymposia).

A call for minisymposia has been launched by the organizers of the ICIAM conference to be held during July 2003 in Sidney; again as society members of ICIAM we are invited to organize minisymposia on various topics of interest for our community. We need to be prepared for the coming calls within the Sixth Framework Programme of the European Union, that will surely leave a large space, in terms of financial resources, to Biotechnology and Medicine. I recommend that members of the Society start immediately a coordination of different groups working on related topics, by establishing Activity Groups, so to be ready for the calls that are expected during 2002-2003. Coordination is very important since the idea of the planners of the Sixth FP is to support only large groups in order to favour synergy instead of competition.

As an example, within the EU Network of Excellence named MACSI (please visit the web site **macsinet.org**) a European Working Group has been recently approved on "Shape and Size in Biotechnology and Medicine"; I have included a first list of centres actively involved in real applications, as shown explicitly by the long list of private industries and public institutions that participate in this WG. A series of workshops have been planned in various European countries during 2002-2003; all interested people are welcome to participate. Another successful coordination carried out within the current EU Fifth Framework Programme is the Network on Mathematical Models for Tumor Growth and the Immune System, that is organizing regularly annual summerschools (**http://calvino.polito.it/**~biomat/school.html).

I wish to encourage all members to circulate information about other existing networks on relevant topics by means of the ECommunicationsMTB. We have already had two sessions of the ESMTB Summer Schools, supported by the EU, the first one was held in Martina Franca (Italy) during 2000, and the second one in Siguenza (Spain) during 2001.

This summer the third edition will be held in Urbino (Italy) after the 5th Conference of the Society in Milano. Please refer to this issue of ECommunicationsMTB for further information, and anyway to our web site www.esmtb.org. Also via the web site or directly via the specific web site **ecmtb.mat.unimi.it,** you may find continuously updated information about our 5th Conference to be held in Milano during July 2-6, 2002. It is a great pleasure for me to inform the reader that about all invited speakers, as proposed by an International Scientific Committee appointed by the Board of the Society, have already confirmed their participation. We also have a set of about 25 minisymposia (half of them invited by the ISC) on the different topics of the Conference; we welcome also contributed papers and posters. Young researchers are warmly invited to participate (many of them can be supported thanks to the generous contribution by the EU). Some funds have been made available by the Local Committee to support also senior researchers from Central and Eastern Europe, and from less favoured regions, who do not have access to sufficient financial support. Please note that members of the Society during 2002 may register at a reduced rate.

The Board is putting a lot of effort in establishing an official journal of the Society; contacts with:

Journal of Mathematical Biology, Journal of Biological Systems, and Acta Biotheoretica are under way, and we hope to give soon a successful answer to all members. In the meanwhile all members of the Society will receive a free copy of the ECommunicationsMTB, and may subscribe for the above Journals at reduced rates.

To conclude I wish to thank the Board and individual members of the Society that have invested a lot of their time in promoting initiatives tending to establish and/or to reinforce relevant activities favouring further development of our scientific community. We may give a significant contribution in establishing a common European Research Area. One of the strength of Europe is based on its diversity, which becomes richness if we emphasize a cooperative attitude instead of a competitive one among the various centres. From my experience it is evident that no one centre in Europe possesses all the skills and competence needed to face a real problem, for which we may need deterministic and stochastic modelling, analysis of inverse problems and statistics, numerical simulation and soft computing, visualization techniques, etc.

I am convinced that we have a lot to share for the benefit of all, and in particular of our students. The Society is now well organized, with a Board and various Coordinating Committees.

I wish that soon we can shift from the volunteered action of few enthusiastic occasional friends, to a permanent and solid structure coordinated in a professional way. For this we need many and active members. I take the

pride of having been among the first few volunteers and call to the action a new generation!

Prof. Vincenzo Capasso

ESMTB Secretary and Treasurer's Report

a) The membership is steadily growing, currently around 215; this is a very positive sign; however there are still members who have not yet paid their 2001 annual subscriptions.

b) The current balance is around 2000 pounds; this is after all payments (journals, annual membership fees to SIAM and EMS, payment to Andrea De Gaetano for the 2 issues of the ECMTB, payment of the student travel grants).

c) One student travel award of 250 pounds had been made.

No formal responsibility on the treasurer's report was taken by the Board. The treasurer was invited according to A9.3 to provide the budget in a formal manner to the Board. After the approval by the Board the budget will be published in the newsletter and submitted to final approval by the general assembly at Milan in 2002. The budget for 2001 and the preliminary budget for 2002 should also be presented. The budget should be closed at the end of each year. The financial accounts should always be open and accessible.

The regulation of the travel funds of ESMTB should be modified. Special attention should be given to countries which have less funding available. The subcommittee should inform the Board about its decisions. A clear advertisement for these funds should be put on the societies web page and in the newsletter. Philippe Tracqui volunteered to provide a file with details.

For the next Board meeting new statuses should be prepared and approved. These should be presented during the general assembly in Milan. Every member should receive the new statuses in advance to decide upon in Milan.

Prof. M.A.J. Chaplain
ESMTB Secretary and Treasurer
Department of Mathematics, University of Dundee
Dundee DD1 4HN
Scotland, UK

Minutes of the ESMTB Board Meeting
Friday 8th June 2001.
Max-Planck-Institute for Mathematics in the Sciences. Inselstr. 22-26, D-04103 Leipzig, Germany.

Present:
Z. Agur, O. Arino, V. Capasso, M. Gyllenberg, V. Krivan, A. Stevens, P. Tracqui.
Before the official meeting, the managing Director of the MPI MIS welcomed the participants, and confirmed the support of the Institute in Leipzig for research activities in the areas of mathematical and theoretical biology.

1) Apologies for absence:
M. Chaplain, H. Heesterbeek, M. Kaufmann.

2) Minutes of the previous meeting:
In point 6) Journals, change:
…and the Board would hopefully then be in a position to vote on adopting a journal for the Society. ...
into .... the Board will vote on adopting a journal for the Society. ...
With this change the Board members who were present at the last meeting approved the minutes

4) President's report:
Andrea DeGaetano had sent the report about the budget used for the production and distribution of the ECMTB. The ECMTB should become a registered Journal in Italy. The necessary amount of 500 Euro once and then 50 Euro per year will be paid by the Society; under these conditions we expect that expenses for mailing the Journal to members will be taken care of by funds raised by the local Editor Andrea DeGaetano.
Brought forward:

5) Report on the current status on the forthcoming ESMTB conference:
The preliminary budget for the conference is 150000 Euro. The EU, to support the participation of young researchers, has approved a financial support of 37.5K euro. The International Scientific Committee, that has been enlarged to include M. Mimura as a Liaison for JSMB and A. Hastings as a Liaison for SMB, is actively working under the coordination of V. Capasso, to identify invited speakers and invited minisymposia. S. Tavare could not join the ISC and Petr Lansky was included. The poster for the meeting was approved by the Board. Any other detail will appear soon on the Conferences homepage:
http://www.esmtb.org/ECMTB2002/

5.1) Report on summer schools:
This time mostly own grants support the summer school in Siguenza. Support for 30 people will be provided. Participants: 40 students + 30 speakers and workshop participants.
Forthcoming summer schools:
2002: Urbino - Mathematical Physiology
The application for support is out
2003: Corsika - Mathematical Ecology
Suggestion for a new summer school: Intracellular pathways. The next Board meeting will take place on January 18th, 2002.
Zvia Agur offered to host the meeting in Israel.
The Board thanked A. Stevens and the managing Director of the MPI MIS for the warm hospitality at the Institute in Leipzig.

7) Vice President's report:
ESMTB is accepted as EMS member organization. The ECMTB should be sent to the president and to the secretary of ICIAM. More initiatives should be proposed

to ICIAM. Proposals for minisymposia for ICIAM (Sydney) should be sent to Vincenzo Capasso.

8) "brand name" ESMTB:
Companies should be asked to propose their problems at ECMBM meetings in special sessions and contribute to sponsoring the meetings. Contact names will be sent by Zvia Agur.

10) Journal discussion:
The Board identified the following requirements to be proposed to the publishers for a final decision:
- The Society should be able to influence the scientific direction of the Journal and the choice of the Editor in chief in case he/she changes.

- The editorial board should also represent emerging scientific areas of interest.
- Associated editors should be nominated by the Society in order to take this into account.
- The price for the Journal should be much cheaper for Society members when compared to others.
- The printed and the electronic version (cheaper) should on average be comparable with the price of BMB.
The Board voted to approach the following Journals in the following priority:
1) JMB. 2) JBS. 3) Acta Biotheoretica
The possibility to change the name: JMB into JMTB, and JBS into EJMTB. It should be discussed with the respective publishers.

Scientific Articles

Two-dimensional simulations of tumour induced angiogenesis as a reinforced random walk.

[1]Wallis, I.P. and Sleeman, B.D.
School of Mathematics, University of Leeds, Leeds, LS2 9JT, UK.
Amtiw@amsta.leeds.ac.uk, bds@amsta.leeds.ac.uk
3 July, 2002

Abstract

An avascular tumour has no active transport mechanism for nutrients and waste products, and grows to a limiting size. In contrast, a vascular tumour has an effective transport mechanism for nutrients and waste products and is able to sustain its growth. The development of a network of capillary blood vessels (angiogenesis) provides the bridge between these states. In this paper, we examine the migration of endothelial cells from an existing capillary towards a solid tumour, in response to chemical gradients, thereby initiating the growth of new capillaries. The migration of individual cells is modelled using the theory of reinforced random walks. The results we obtain agree well with experimental observations.

1. Introduction

Angiogenesis, the process of generating new capillary blood vessels [FA] leading to vascularisation, takes place in several physiological and pathological situations, including embryogenesis [R]. cancer and rheumatoid diseases [FB].

In the 1960s and 1970s Folkman showed that solid tumours are dependent on vascularisation for their growth [FA]. A solid tumour grows to a certain small size (*1-3 mm* diameter) [BM] but the transport of nutrients and waste products is by diffusion alone, and the tumour cannot sustain further growth. In 1971, Folkman et al. [FMAW] isolated a factor responsible for initiating angiogenesis. They showed that this factor is secreted by the tumour colony and is transported, via diffusion, to nearby capillaries. It was later shown that this is not a single enzyme but a whole family of enzymes. It is now accepted [FK, PK] that some of this group of enzymes are pro- and some are anti-angiogenic [CJ]. Together these chemicals are known as Tumour Angiogenesis Factors (TAF). Collectively, their function is to initiate the formation of a capillary transport mechanism for nutrients and waste products [FK, PK, YDGRWH]. Individually, each has a subtly distinct role to play in the process.

A second substrate, fibronectin [BS, PK], is also relevant to our discussion of angiogenesis. It acts as an adhesive protein necessary for cell adhesion. Fibronectin is an integral part of the extracellular matrix.

The first event to occur in angiogenesis is that TAF is transported across the tissue and reaches an existing capillary. Molecules of TAF are able to penetrate the capillary wall, which is a monolayer of flattened endothelial cells (EC) supported by a basal lamina (BL) [PK]. Outside the BL is an extracellular matrix (ECM).

Certain molecules of TAF bind to EC, and release proteolytic enzyme (protease) [PK], which degrades the BL. Movement induced by a gradient in the concentration of TAF, is known as chemotaxis (cells preferring to be in a stronger concentration of TAF) [PK]. When the BL has been degraded, EC are no longer supported by, or bound to the BL and migrate, under chemotaxis, into the ECM.

Some of the TAFs induce migration (movement) of EC [PK], and some induce mitosis (growth) of EC [FA]. The EC are able (via surface receptors [YDGRWH, YKF]) to sense concentration gradients in TAF and fibronectin and can move accordingly. Movement induced by a gradient in the concentration of fibronectin is known as haptotaxis (cells preferring to be in a stronger concentration of fibronectin) [PK].

Naturally occurring angiogenesis is difficult to observe, since it takes place in complex tissue structures. Therefore ways to observe *in vivo* tumour induced angiogenesis were created. Generally these involve implanting a tumour fragment in living tissue, and observing with light microscopy, the growth of a new capillary network.

Since angiogenesis is crucial to solid tumour growth [FA], developing an understanding of the processes controlling angiogenesis will provide valuable help in the formulation of diagnostic and therapeutic strategies. This paper presents a model for the migration of the lead EC, examining possible trajectories, which are influenced by chemical signals from TAF and fibronectin. In [SW] a similar model was proposed, assuming the TAF and fibronectin to be in pseudo-steady state. We assume here that the first stage of tumour angiogenesis has already taken place, i.e. the TAF has reached and penetrated a capillary, the BL has been degraded, and EC have entered the ECM and are ready to begin their migration. For a full discussion of these aspects, see [LSNA, LSNB, LPSN]. In these works, the authors focus on the biochemistry of the problem, and model angiogenesis on the basis of the throry reinforced random walks together with Michaelis-Menten mechanisms that view EC receptors as the catalysts for transforming TAF into proteolytic enzyme.

In §2 we consider EC migration as a reinforced random walk. In §3 we explain how the biology outlined above fits with the mathematical development in §2. In §4 we present results from two-dimensional numerical simulations, and §5 contains discussion and suggestions for future work.

2.   The mathematical model

The theory of reinforced random walks [D, LS, OS] provides the background for this model. For ease of presentation, this will first be considered in one space dimension.

Consider an EC on the spatial domain $x \in (0,1)$. This domain is split into N identical "units" each of width $h = 1/N$. If $n \in (0,N)$ describes the cell's position at time t, then at time $t + 1$, that individual EC will either a) remain at point n, b) move to point $n + 1$ or c) move to point $n - 1$. We apply no-flux boundary conditions, i. e. an EC cannot move to or from $x = 0$ or $x = 1$.

The functions $\hat{\tau}_n^\pm$ are rate functions that describe the probability rate of a transition starting at point n and moving to the right (+) or left (-) during one time step, and are functions of W, the substrate.

Let $P_n(t)$ be the probability density distribution for an EC at point n and time t. The rate of change of $P_n(t)$ is governed by the **master equation**

$$\frac{\partial P_n}{\partial t} = \hat{\tau}_{n-1}^+(W)P_{n-1} + \hat{\tau}_{n+1}^-(W)P_{n+1} - \hat{\tau}_n^+(W)P_n - \hat{\tau}_n^-(W)P_n .$$ (1)

That is, $P_n(t)$ will be increased by EC moving from $(n \pm 1)h$ to nh and diminished by EC moving from nh to $(n \pm 1)h$. The quantity $\left(\hat{\tau}_n^+(W) + \hat{\tau}_n^-(W)\right)^{-1}$ is the mean waiting time at site n.

It is convenient to think of the conditional probability $P_n(t)$ as the EC density. An EC at position $n = 20$ is in fact in the region $n \in (19.5, 20.5)$. In this model, cell locomotion is considered to be the result of chemoattraction at the outer edges of the cell, therefore we use the substrate densities at the mid-points between lattice points to calculate the transition probability rates $\hat{\tau}_n^\pm(W)$. The control substances W can be represented as a vector of components $W = (..., w_{n-1/2}, w_n, w_{n+1/2}, ...)$. $W(x,t)$ is a continuous function of the environment, but we only consider W at these discrete points.

While the basic model (1) can be exploited [OS] to describe many aspects of organism dynamics, it gives no restriction on the transition rates at a site and there is no distinction between the transition rates to the right or left.

Following Othmer and Stevens [OS], suppose that the decision of "where to move" is independent of the decision of "when to move". Then the mean waiting time of the process is constant across the lattice. Hence the transitions $\hat{\tau}_n^\pm(W)$ must be suitably scaled and normalised. Let them be normalised so that

$$\hat{\tau}_n^+(W) + \hat{\tau}_n^-(W) = 2\lambda$$ (2)

for some constant λ. Define the new jump process

$$\hat{\tau}_n^\pm = 2\lambda \frac{\tau(w_{n\pm1/2})}{\tau(w_{n+1/2}) + \tau(w_{n-1/2})} = 2\lambda N^\pm(W)$$ (3)

so that $\hat{\tau}_n^\pm(W)$ is only a function of $W(n \pm \frac{1}{2})$. This implies that these rates have no long-range dependency, but there is a distinction shown between transition rates to the left (-) and the right (+).

The master equation now reads

$$\frac{1}{2\lambda}\frac{\partial P_n}{\partial t} = N_{n-1}^+\left(w_{n-1/2}, w_{n-3/2}\right)P_{n-1} + N_{n+1}^-\left(w_{n+1/2}, w_{n+3/2}\right)P_{n+1}$$
$$- N_n^+\left(w_{n-1/2}, w_{n+1/2}\right)P_n - N_n^-\left(w_{n-1/2}, w_{n+1/2}\right)P_n$$ (4)

and is fundamental to our simulations.

As in Othmer and Stevens [OS], we can replace (4) by a continuum or macroscopic model by proceeding to the continuum limit in which $h \rightarrow 0$ and $\lambda \rightarrow \infty$ in such a way that

$$D = \lim_{h\rightarrow 0, \lambda\rightarrow\infty} \lambda h^2$$

exists giving the constant diffusion D. By performing this limiting process (4) tends to the equation

$$\frac{\partial P}{\partial t} = D\frac{\partial}{\partial x}\left(P\frac{\partial}{\partial x}\left(\ln\frac{P}{\tau(W)}\right)\right)$$ (5)

where P is now EC density.

This method can be extended [OS, SW] to EC movements in higher space dimensions, and this is done in §4.

3. The method of simulation

Although EC behaviour cannot be compared to diffusion in a physical sense, inhomogeneities in the ECM may cause some "random" movement [BM, BS]. For these purposes, this is equivalent to random diffusion. We refer to the coefficient of this movement as D, the concentration of TAF as v and the concentration of fibronectin as f. The chemotactic sensitivity is referred to as $\chi(v)$ and the haptotactic sensitivity as $\rho(f)$.

Suppose that $\tau = \tau(v,f) = \tau_1(v)\,\tau_2(f)$ i.e. it is a separable function of v and f, then (5) can be written as

$$\frac{\partial P}{\partial t} = D\frac{\partial^2 P}{\partial x^2} - D\frac{\partial}{\partial x}\left(P\frac{\tau_1'(v)}{\tau_1(v)}\frac{\partial v}{\partial x}\right) - D\frac{\partial}{\partial x}\left(P\frac{\tau_2'(f)}{\tau_2(f)}\frac{\partial f}{\partial x}\right). \qquad (6)$$

Chemotactic sensitivity is defined in [OS] as
$\chi(W) = D \ln(\tau(W))_W$
where W is a single chemoattractant. So we write

$$\chi(v) = D \ln(\tau_1(v))_v \text{ and } \rho(f) = D \ln(\tau_2(f))_f. \qquad (7)$$

Combining (6) and (7) results in

$$\frac{\partial P}{\partial t} = D\frac{\partial^2 P}{\partial x^2} - \frac{\partial}{\partial x}\left(\chi(v)P\frac{\partial v}{\partial x}\right) - \frac{\partial}{\partial x}\left(\rho(f)P\frac{\partial f}{\partial x}\right). \qquad (8)$$

Combining (5) and (8) gives, after rearrangement

$$\ln\tau = \frac{1}{D}\int\chi(v)dv + \frac{1}{D}\int\rho(f)df. \qquad (9)$$

Again, this can be extended to higher space dimensions.

Equation (8) may also be derived from mass conservation arguments as in [AC].

The technique we use is based on the one developed by Anderson et al. [ASYG] and exploited in Anderson and Chaplain [AC]. As in [SW], at each timestep, the particle at position n probes the local environment and measures $W(n \pm \frac{1}{2})$. Values of $\tau(W(n \pm \frac{1}{2}))$ are generated and normalised by (3) to define transition probability rates. These transition probability rates are then used to define the following confidence intervals;

$$R_0 = \left(0, 1-2\lambda k\right), k < 1/2\lambda,$$
$$R_1 = \left(1-2\lambda k, 1-2\lambda k N_n^-\right),$$
$$R_2 = \left(1-2\lambda k N_n^-, 1\right),$$

where k is the timestep and λ is taken to be D/h^2. We then generate a random number between 0 and 1 and depending on the range into which this number falls the particle under consideration will remain stationary (R_0) or move to the right (R_1) or move to the left (R_2). The longer a particular interval is, the greater the probability that such an interval will be selected. Each particle is thus restricted to move one step to the right or to the left or to remain stationary at each timestep.

4. Numerical simulations

The one-dimensional problem, while providing valuable guidance as to EC behaviour, is biologically unrealistic. The reader is referred to [SW] for full one-dimensional simulation. Here our attention is restricted to two space dimensions. In [SW] we also extend the simulations to three space dimensions.

Values for the biological constants are notoriously difficult to measure. For this reason, values have been chosen which highlight the important aspects of the underlying dynamics while retaining biological credibility. In this context, the approximate diameter of an EC is *0.005 cm* [SL].

For two-dimensional simulations, we consider an assay consisting of a square matrigel bed. The side length simulated is *1 cm* and therefore the system exists on an area of *1 cm^2*. Positions within the chamber are defined on a grid of *200 × 200* reference points. Each point is defined as *(n,m)* where n is an integer and *0 < n < 201*, m is an integer and *0 < m < 201*. *n = 0, m ∈ (0,201)* simulates the "capillary" (i.e. higher concentration of fibronectin), and a "tumour colony" (i.e. higher concentration of TAF), which is a disc of radius *1 mm*, is placed at *(200,100)*. This may be thought of as implanting a (large) solid tumour fragment in a gel dish (we note that this domain size is larger than those used for the corneal implant experiments). In these simulations, we assume that concentration gradients of TAF and fibronectin have been established at *t = 0*. Furthermore, we assume a line of EC placed at the side *(x = 0)*. We then use the method of §3 to track the lead EC initiated from the capillary. It is assumed that subsequent EC follow the trail laid down by the lead EC.

First of all we need a two-dimensional generalisation of the master equation (4). This is straightforward to achieve and in analogy with (4) the normalised transition probability rates are defined through the following steps.

Let $\hat{\tau}_{n,m}^{i\pm}$ be the transition probability rate of leaving site *(nh,mh)* and moving one step to the right/left when $i = h$ or up/down when $i = v$. In analogy with (2) we suppose the transition probability rates to be normalised so that

$$\hat{\tau}_{n,m}^{h+}(W) + \hat{\tau}_{n,m}^{h-}(W) + \hat{\tau}_{n,m}^{v+}(W) + \hat{\tau}_{n,m}^{v-}(W) = 4\lambda \tag{10}$$

for some constant λ, and define the new jump process via

$$\hat{\tau}_{n,m}^{h\pm} = 4\lambda \frac{\tau(w_{n\pm1/2,m})}{\tau(w_{n-1/2,m}) + \tau(w_{n+1/2,m}) + \tau(w_{n,m-1/2}) + \tau(w_{n,m+1/2})} \tag{11}$$
$$= 4\lambda N_{n,m}^{h\pm}(W)$$

$$\hat{\tau}_{n,m}^{v\pm} = 4\lambda \frac{\tau(w_{n,m\pm1/2})}{\tau(w_{n-1/2,m}) + \tau(w_{n+1/2,m}) + \tau(w_{n,m-1/2}) + \tau(w_{n,m+1/2})} \tag{12}$$
$$= 4\lambda N_{n,m}^{v\pm}(W),$$

so that $\hat{\tau}_{n,m}^{\pm}$ depends only on $w_{n+1/2,m}$, $w_{n-1/2,m}$, $w_{n,m+1/2}$, $w_{n,m-1/2}$.

Furthermore, no-flux boundary conditions are assumed to hold on the boundary of the square. In §4.1 and §4.2 we use classical chemotaxis ($\chi(v) \equiv \chi_0$) and classical haptotaxis ($\rho(f) \equiv \rho_0$). In §4.3 different forms for $\chi(v)$ and $\rho(f)$ are chosen. In all of the simulations in this section, $h = 0.005$, $k = 0.005$, $D = 0.001$.

In all of these simulations, the TAF distribution at $t = 0$ is given by
$v(x,y) = exp\,(aR + b), \quad R > 0.1,$
$v(x,y) = 1, \qquad\qquad R \leq 0.1,$ $\qquad\qquad\qquad\qquad$ (13)
where $R^2 = (1 - x)^2 + (0.5 - y)^2$, with $b = -ln\,(0.2)/11.5$, $a = -10b$,
and the fibronectin distribution at $t = 0$ is given by
$f(x,y) = 0.75\,exp\,(ax)$ $\qquad\qquad\qquad\qquad\qquad\qquad\qquad$ (14)
where $a = ln\,(0.2)$.

4.1. Preliminary modelling

In the first set of simulations, we define the substrate concentrations *a priori* using (13) and (14), and they are in pseudo-steady state. In accordance with [D], this is not a reinforced random walk but a biased random walk.

Here $\chi(v) \equiv \chi_0$ and $\rho(f) \equiv \rho_0$. Substituting these into equation (9), we see that

$$\tau(v,f) = exp\left(\frac{1}{D}(\chi_0 v + \rho_0 f)\right).$$

In figure *4a*, $\chi_0 = 0.75$, $\rho_0 = 0.1$ and it is observed that the capillaries migrate and focus towards the TAF source, together with some anastomosis. By increasing the haptotactic coefficient ρ_0 we can see in figure *4b* *($\rho_0 = 0.2$)* that there is increased networking near $x = 0$ corresponding to the high adhesive gradient of fibronectin. Migration is greatly impeded. This is consistent with observations in [BS].
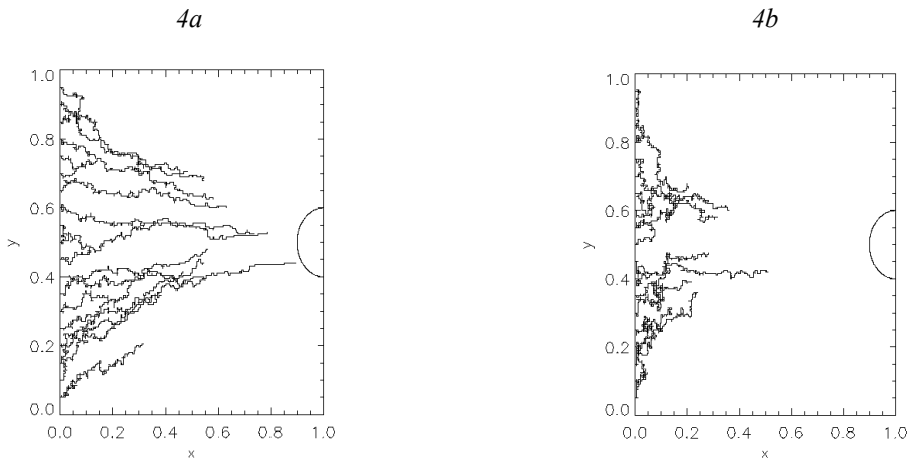

Figure 4a $\chi(v) = \chi_0 = 0.75$, $\rho(f) = \rho_0 = 0.1$, pseudo steady state substrate.
Figure 4b $\chi(v) = \chi_0 = 0.75$, $\rho(f) = \rho_0 = 0.2$, pseudo steady state substrate.

4.2. Substrate dynamics

To simulate the above problem with the addition of substrate dynamics, consider the following aspects of EC movement [PK]. As EC migrate in response to the gradients in TAF and fibronectin;

- EC are responsible for uptake and binding of TAF
- There is uptake and binding and degradation of fibronectin by EC
- Fibronectin is deposited by EC

We assume that the steady states of v and f have been established at $t = 0$. As EC migrate through the ECM, the three features above are modelled.

The parameter η relates to the uptake of TAF, the parameter γ relates to the uptake and degradation of fibronectin, and the parameter ψ to the deposit of fibronectin. When all of these observations are combined, the resulting equations for substrate dynamics are

$$\frac{\partial v}{\partial t} = -\eta P v,$$

$$\frac{\partial f}{\partial t} = \psi P - \gamma P f.$$

The reader is referred to [AC] for a complete derivation of these equations, and for a comparison of the results here with simulations based on a numerical discretisation of (8). At $t = 0$, the profile of TAF is given by (13) and the fibronectin is given by(14). The procedure outlined in §4.1 is used to track the lead EC. In all of these simulations, $\chi_0 = 0.75$, $\rho_0 = 0.1$.

If $\eta = \psi = \gamma = 0$, the results of §4.1 are repeated. However if η is large, this simulates enormous uptake of TAF and the resulting EC migration is more direct and rapid (figure *4c*). If γ is large, there is enormous uptake of fibronectin, and EC migration is again more directed (figure *4d*). Figure *4e* shows a possible evolution, when less exaggerated values of η, ψ and γ are used.

<div align="center">

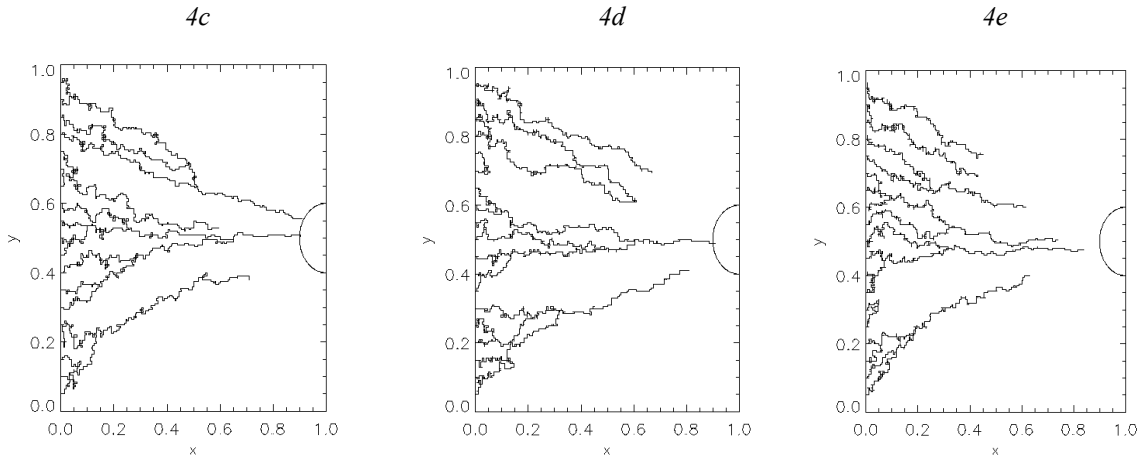*4c*   *4d*   *4e*

</div>

Figure 4c $\chi(v) = \chi_0 = 0.75$, $\rho(f) = \rho_0 = 0.1$, $\eta = 3.0$, $\psi = 0.3$, $\gamma = 0.2$
Figure 4d $\chi(v) = \chi_0 = 0.75$, $\rho(f) = \rho_0 = 0.1$, $\eta = 0.2$, $\psi = 0.3$, $\gamma = 3.0$
Figure 4e $\chi(v) = \chi_0 = 0.75$, $\rho(f) = \rho_0 = 0.1$, $\eta = 0.2$, $\psi = 0.3$, $\gamma = 0.2$

4.3. Sensitivity

If we take the function $\chi(v) \equiv \chi_0$, this describes *classical chemotaxis*. That is, the EC only sense the spatial gradient in chemoattractant. Cell locomotion is achieved through molecules of chemoattractant binding with surface receptors on the EC. If we consider that at high concentrations of v, the receptors become saturated, this can be modelled as follows. Suppose $\chi(v) = \chi_0(k_1/(k_1 + v)) = \chi_0/(1 + \alpha v)$ where k_1, α are constants. These sensitivity functions are of the type discussed in [AC, LSNA, LSNB]. This more accurately models the decrease in cell sensitivity as v increases. The parameter α may be viewed as a coefficient of sensitivity, where large values of α indicate greater desensitisation.

Response to fibronectin may be modelled in a similar way, so that $\rho(f) = \rho_0/(1 + \beta f)$ where β can be thought of as a sensitivity coefficient.
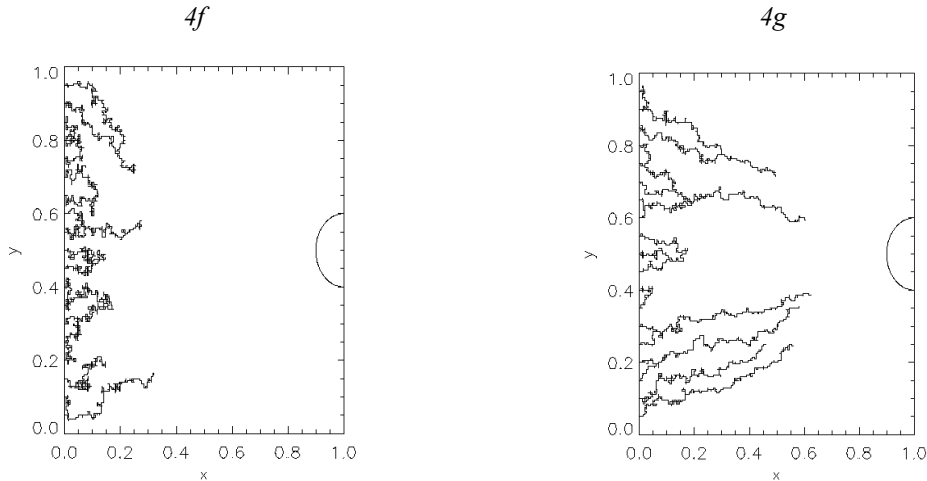
Using these expressions for $\chi(v)$ and $\rho(f)$, from (9) we see that $\tau(v, f) = (1 + \alpha v)^{\chi_0/\alpha D}(1 + \beta f)^{\rho_0/\beta D}$.

Allowing $\alpha = \beta = 0$, the behaviour displayed is equivalent to §4.2 (i.e. $\chi(v) \equiv \chi_0$ and $\rho(f) \equiv \rho_0$), that is, no desensitisation is displayed to either v or f. If small but positive values of α and β are chosen, more realistic behaviour is shown by the EC.

Figure *4f* shows a situation where $\alpha = 3.0$ and $\beta = 0.5$. In this case, when the EC reach about $x = 0.3$ they are sufficiently desensitised to the TAF gradient to show no preference for a higher density of TAF. In figure *4g*, $\alpha = \beta = 0.5$ which shows a more realistic situation.

The initial conditions here are the same as in §4.1 and §4,2. In these simulations, we maintain the dynamic substrate. In each of these simulations, $\eta = \gamma = 0.2$, $\psi = 0.3$ and $\chi_0 = 0.75$, $\rho_0 = 0.1$.

Of course, other functional forms may be more appropriate for modelling $\chi(v)$ and $\rho(f)$ and therefore $\tau(v,f)$, and this will be explored in future work.

4f   *4g*

Here, $\chi(v) = \chi_0/(1 + \alpha v)$, $\chi_0 = 0.75$, $\rho(f) = \rho_0/(1 + \beta f)$, $\rho_0 = 0.1$, $\eta = 0.2$, $\psi = 0.3$, $\gamma = 0.2$

Figure 4f $\alpha = 3.0$, $\beta = 0.5$

Figure 4g $\alpha = 0.5$, $\beta = 0.5$

In each simulation in §4, the model runs until the tumour has been penetrated by two EC, or for 400 timesteps, whichever comes first.

5.   Discussion

A fundamental feature of cancer progression is the process of angiogenesis whereby new capillaries are induced to grow out of a pre-existing vasculature, responding to stimulation from a source of chemotactic factors secreted by the tumour source. In this investigation we have modelled the migration of EC as a reinforced random walk. That is, the EC are governed by a master equation in which the direction of EC movement depends on probability transition rates. In turn these transition rates are modelled to depend on the secreted TAF as well as fibronectin, a major component of the tissue ECM, which provides an adhesive gradient. This gives a directional stimulus to the EC.

Importantly, this model is robust to widely varying parameters, and individual features can be highlighted without changing the system's underlying properties. The idea of using a reinforced random walk model has the advantage of capturing the micro-cellular features of angiogenesis by appropriate modelling of the probability transition rates. While their precise form is difficult to determine at this level, our knowledge of the limiting continuum model provides important clues. Indeed, by using the properties of the continuum PDE (8) (i.e. macro-cellular model) and experimental evidence we are able to deduce reasonable models for the transition rates.

Even under the above simplifications, our simulations show how elementary networks can be formed. In particular, we have observed structures suggestive of the formation of anastomoses due to the relative roles of chemotaxis and haptotaxis in the formation of such networks. Our results may be experimentally tested, at least *in vitro*.

This work develops and exploits a strong link between reinforced random walk theory and tumour induced angiogenesis, and opens up several new avenues for research.

At this initial step we have not taken account of branching of capillaries or EC proliferation. This will be covered in future work. Furthermore, we have not modelled the structure of the ECM. This can be modelled at the macro-cellular level as a viscoelastic medium [HS] or possibly as a porous medium. This will be pursued in future work.

Finally we emphasise that modelling angiogenesis as a reinforced random walk provides a possible bridge (via the probability transition rates) between micro- and macro-cellular events and as such may aid our understanding of tumour development and its control.

References

[AC] ANDERSON, A. R. A. AND CHAPLAIN, M. A. J. (1998) Continuous and discrete mathematical models of tumour-induced angiogenesis. *Bull. Math. Biol.* **60**: 857-899.

[ASYG] ANDERSON, A. R. A., SLEEMAN, B. D. S., YOUNG, I. M. AND GRIFFITHS, B. S. (1997) Nemat ode movement along a chemical gradient in a structurally heterogeneous environment: II. Theory. *Fundam. Appl. Nematol.* **20**: 165-172.

[BM] BALDING, D. AND MCELWAIN, D.L.S. (1985) A mathematical model of tumour-induced capillary growth. *J. theor. Biol.* **114**: 53-73.

[BS] BOWERSOX, J.C. AND SORGENTE, N. (1982) Chemotaxis of aortic endothelial cells in response to fibronectin. *Cancer Res.* **42**: 2547-2551.

[CJ] CARMELIET, P. AND JAIN, R. K. (2000) Angiogenesis in cancer and other diseases. *Nature* **407**: 249-257.

[D] DAVIS, B. (1990) Reinforced Random Walks. *Prob. Th. Rel. Fields* **84**: 203-229.

[Fa] FOLKMAN, J. (1985) Tumor Angiogenesis. *Adv. Cancer Res.* **43**: 175-203.

[Fb] FOLKMAN, J. (1995) Angiogenesis in cancer, vascular, rheumatoid and other diseases *Nature Medicine* **1**: 27-31.

[FK] FOLKMAN, J. AND KLAGSBRUN, M. (1987) Angiogenic factors. *Science* **235**: 442-447.

[FMAW] FOLKMAN, J., MERLER, E., ABERTHANY, C. AND WILLIAMS, G. (1971) Isolation of a tumor factor responsible for angiogenesis. *J. Exp. Med.* **133**: 275-288.

[HS] HOLMES, M.J. AND SLEEMAN, B.D. (2000) A mathematical model of tumour angiogenesis incorporating cellular traction and viscoelastic effects. *J. Theor. Biol.* **202**: 95-112.

[LS] LEVINE, H. A. AND SLEEMAN, B. D. (1997) A system of reaction diffusion equations arising in the theory of reinforced random walks. *SIAM J. Appl. Math.* **57**: 683-730.

[LSNa] LEVINE, H.A., SLEEMAN, B.D. AND NILSEN-HAMILTON, M. (2000) A mathematical model for the role of pericytes and macrophages in the onset of angiogenesis: I. The role of protease inhibitors in preventing angiogenesis. *Mathematical Biosciences* **168**: 77-115.

[LSNB] LEVINE, H.A., SLEEMAN, B.D. AND NILSEN-HAMILTON, M. (2001) Mathematical modeling of the onset of capillary formation initiating angiogenesis. *J. Math. Biol.* **42**: 195-238.

[LPSN] LEVINE, H.A., PAMUK, S., SLEEMAN, B.D. AND NILSEN-HAMILTON, M. (2000) Mathematical modeling of capillary formation and development in tumor angiogenesis. *Bull. Math. Biol.* (in press).

[OS] OTHMER, H. AND STEVENS, A. (1997) Aggregation, blowup, and collapse: the ABCs of taxis and reinforced random walks. *SIAM J. Appl. Math.* **57**: 1044-1081.

[PK] PAWELETZ, N. AND KNIERIM, M. (1989) Tumor-related angiogenesis. *Critical Reviews in Oncology/Hematology* **9**: 197-242.

[R] RISAU, W. (1997) Mechanisms of Angiogenesis. *Nature* **386**: 671-674.

[SW] SLEEMAN, B. D. AND WALLIS, I. P. Tumour Induced angiogenesis as a Reinforced Random Walk: modelling capillary network formation without endothelial cell proliferation. *Mathematical and computer modelling* (In press).

[SL] STOKES, C.L. AND LAUFFENBURGER, D.A. (1991) Analysis of the roles of microvessel endothelial cell random motility and chemotaxis in angiogenesis. *J. Theor. Biol.* **152**: 377-403.

[YDGRWH] Yancopoulos, G.D., Davis, S., Gale, N.W., Rudge, J.S., Wiegand, S.J. and Holash, J. (2000) Vascular-Specific growth factors and blood vessel formation. *Nature* **407**: 242-248.

[YKF] YANCOPOULOS, G.D., KLAGSBRUN, M. AND FOLKMAN, J. (1998) Vasculogenesis, Angiogenesis and Growth Factors: Ephrins Enter the Fray at the Border. *Cell* **19 3**: 661-664.

Instructions to authors

The section *Scientific Articles* is a forum for publications by young scientists in mathematical and theoretical biology and medicine. The aim is to present new results, approaches or perspectives in a certain field as a brief scientific paper. Papers should be accessible to a wide audience of mathematical and theoretical biologists and the subject matter should be of broad interest to the community. Papers should achieve a good balance between biology/medicine and mathematics and the focus should be on ideas and concepts rather than on technical details only of interest to more specialist audiences. Papers should preferably start with a brief description of the research area and explain how the main problem that is addressed is relevant to that area. Papers are allowed to present the main ideas involved in a research program in progress.

Articles should be no more than 6 printed pages in length (about 10 A4 typewritten pages) including figures. The use of illustrations is encouraged. The standard format is: Title, abstract (25 words or less), introduction, results, discussion,

references, figure legends, tables, figures. Figures, legends and tables may also already be an integrated part of the manuscript. The style of references to literature should conform to the *Journal of Mathematical Biology* or the *Bulletin of Mathematical Biology*. The corresponding author must be clearly identified on the first page.

Two independent referees, knowledgeable in the particular area that is addressed, review all manuscripts. The editors, however, reserve the right to return manuscripts that in their opinion do not adhere to the general aims outlined above.

Manuscripts can be submitted throughout the year. Upon acceptance, the corresponding author will be required to send an electronic copy of the paper (including figures and tables) either by e-mail, ftp or diskette. Final versions of accepted papers must be in Word format.

Manuscripts should be sent in three copies to: Hans Heesterbeek, *Quantitative Veterinary Epidemiology Group, Faculty of Veterinary Medicine, P.O. box 80151, 3508 TD Utrecht, The Netherlands,* `J.A.P.Heesterbeek@vet.uu.nl`

Communications

MIRIAM
Milan Research Centre for Industrial and Applied Mathematics

The Centre was formally established in 1999, with the financial support of the University of Milano and a number of private companies. It has evolved from a long term experience in developing advanced mathematical methods motivated by real applications in Industry, Finance, Medicine, Biology, and in general to applied Sciences. The activity has increasingly involved researchers from both Academia and Industry.

Its distinctive characteristic is to operate on a European scale within networks of excellence; since 1991 it is a node of ECMI, the European Consortium for Mathematics in Industry and has been a founding node of the recently established European Network of Excellence MACSI-net, born with the scientific and organizational support of both ECMI and ECCOMAS.

MIRIAM is also a node of the Interuniversity Centre for Mathematics Applied to Environment, Biology, Medicine, etc. named CIMAB, including major academic institutions, from all over Italy.

Among the aims of MIRIAM we may list the following

Research:

-To promote the use of mathematical modelling in industry and applied sciences.

-To develop fundamental research activity in the fields of Applied Mathematics which are relevant to problem solving in Industry, Finance and Commerce.

-To develop research experience and expertise in Applied Mathematics and to offer a centre of professional skills to public and private bodies which operate in Industry, Finance and Commerce, Biomedicine.

-To promote information and material exchange between researchers of the area. To act as a focus for these activities in Milan and Italy, also in collaboration with other centres, institutes and departments of the universities and of public research bodies, and to link with similar activities in Europe.

-To develop tools and methods of advanced scientific computing.

Training

-To promote and encourage, also in collaboration with public and private bodies, the training of applied mathematicians able to meet the growing need of mathematical skills, and be concerned with their continuing professional training.

In collaboration with MIRIAM, the Mathematics Department offers:

a) A PhD programme on Mathematics and Statistics for the Computational Sciences (three years).

b) A Master programme on Mathematics for Computational Science and Industry (one year).

c) Postdoctoral training and research is active within the European Research and Mobility Programmes.

Services

MIRIAM offers to industry:

Consulting on mathematical and statistical methods.

Participation to R&D activities.

Customized software production.

The main research areas of MIRIAM are:

Theory

Spatially structured dynamical systems, both deterministic and stochastic. Numerical methods for nonlinear PDE's. Nonlinear analysis Stochastic spatial patterns. Stochastic Geometry. Spatial statistics. Shape analysis. Signal analysis.

Applications

Material Science

Phase Change. Polymerization. Polymer crystallization

Medicine

Infectious diseases. Cancer. Genetic diseases. Signals and images. Artificial prostheses. Cardiovascular system.
Ecology.
Complex systems. Patterns. Behavior and organization of social insects. Environmental Pollution.
Economics And Finance
Reliability And Quality Control.
Insurance.
Within the Network of Excellence MACSI-net MIRIAM has recently organized a European Working Group on "Shape and Size in Biotechnology and Medicine" networking major European Academic and Industrial groups. A series of meetings and workshops have been planned, including minisymposia at next ESMTB Conference in Milano.
Anyone interested is welcome to participate.
Please visit the web site http://www.macsinet.org .

Free Directory For French-Speaking Scientists

With a **french-speaking biologist** group of postdocs we have developed a web site that provides a free directory for french-speaking scientists working all around the world in the field of life sciences:
http://www.ujf-grenoble.fr/biotoile/index_en.html (English version)
http://www.ujf-grenoble.fr/biotoile/index.html (French version).
If you are French-speaking please visit our web site. If you know French-speaking fellows around you (from Belgium, Canada, Marocco...) would you be so kind as to let them know about this web site?
La Toile des Biologistes - Biologist Network Réseau de Chercheurs Francophones en Sciences du Vivant
Adresse: http://www.ujf-grenoble.fr/biotoile
Email: worldpostdoc@hotmail.com

IBOY Newsletter

The DIVERSITAS - International Biodiversity Observation Year (IBOY) 2001 - 2002 is pleased to announce the first issue of the IBOY Newsletter.
The Newsletter contains information on upcoming activities of IBOY Core Network Projects and of the IBOY Secretariat including international meetings, significant publications and field courses.

It can be downloaded from
http://www.nrel.colostate.edu/iboy/news/septiboynews.pdf

Updated versions of scientific computing software

I am pleased to announce that we have just released updated versions of three of our scientific computing software packages:
SCIRun: A scientific computing problem solving environment.
BioPSE: A collection of modules for bioelectric field modeling, simulation, and visualization.
map3d: A stand alone surface-based visualization program.
You can download the software by clicking on the Software link on the SCI Institute web site:
www.sci.utah.edu
We encourage you to join our software users mailing lists:
http://software.sci.utah.edu/software/mailinglists.html
and to report any difficulties you may have in using the software:
http://software.sci.utah.edu/research/software/bugzilla/
  Chris Johnson
  Director,
  Scientific Computing and Imaging Institute
  University of Utah

A plant biologist (Johannes Reinke) and a mathematician (Karl Pearson) introduced the concepts and notions respectively of "Theoretical Biology" and "Biometrics".
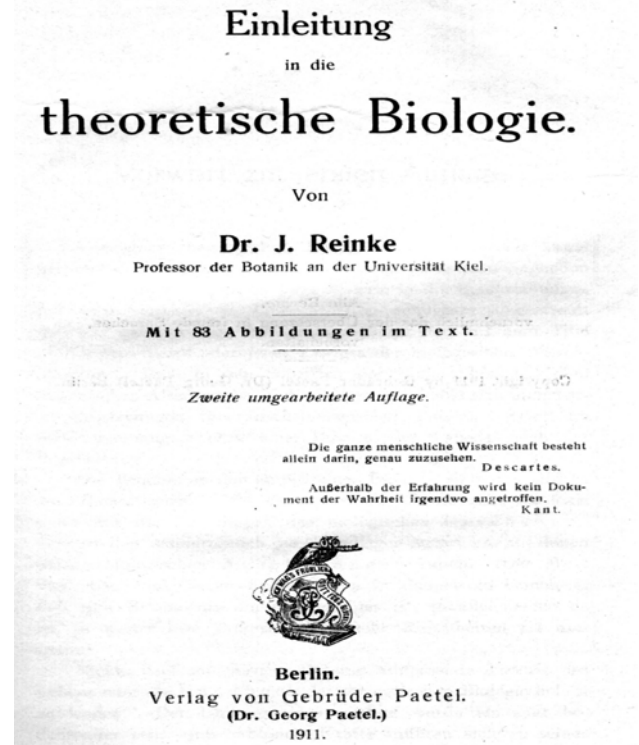

Johannes Reinke (1849 – 1931)

Karl Pearson (1857 – 1936)

In the preface to the first edition (in 1901) of his book, Johannes Reinke wrote:

"A theoretical biology has so far merely not yet been considered, at least not as a connected discipline", in contrast to the then already well established *theoretical physics*.

This might not surprise us, since it was only 100 years before that *biology* itself had grown up, from its adjutant role for medicine and agriculture, to become its own discipline: the botanist and zoologist Jean Baptiste de Lamark (1744 – 1825) at the Botanical Garden of London, and the professor for mathematics and medicine, **Gottfried Reinhold Treviranus**, who since 1797 was teaching at the g*ymnasium illustre* in Bremen, Northern Germany, and always was on search *for general laws of life*, first introduced the word **'*biology*'**: in 1802 Treviranus published the book "Biology, or Philosophy of the Vital Nature".

How can we imagine then, 100 years after its birth, the status of *biology* at the threshold of the 'modern'

20th century? It still appeared as a rather diffuse, methodologically dispersed and theoretically disordered empirical science, but with an enormously increasing input of new observations (e.g. from big expeditions into the colonial countries) and of experimental results (due to the new physical and chemical techniques), isn't there a striking analogy to the so-called 'post-genomic era' at the beginning of the new millenium?

Also 100 years ago, it was research at the medical faculty which, by fighting deadly epidemics and newly detected illnesses within the otherwise blooming national economies, most prominently stimulated scientific progress. Being part of medical research, *physiology* represented the

G.F. Treviranus (1776-1873)

trendy modern branch of 19th century natural science, first introduced by Johannes Müller and his great scholars, one of them being Hermann Helmholtz (see ECMTB #2).

They all were what we would call 'general natural scientists' in traditional sense, like, for example at the Royal Institute in London, the physician and natural historian Thomas Henry Huxley (1825 – 1895), who in his 'lectures on protoplasm' (1868) had written an assay about *"The physical basis of Life"*. However, already his successor as Fullerian professor for physiology, Michal Foster (1836 – 1907) complained in 1899 that *anatomists, zoologists, physiologists have ... become ... more and more estranged*. Indeed, at the end of 19th century the mentioned disciplines including botany had widely separated from each other and had become what they are today: more and more specialized.

In this situation though, somehow as a new 'nucleus' of theoretical thinking, *cell biology* had emerged as a central biological discipline. So **Max Verworn**, who studied philosophy and medicine in Berlin, became director of the Physiological Institute in Göttingen in 1901, could proclaim in his book "General Physiology" (1894): *If physiology wants to explain the elementary and general processes of life, it can do so only as cellular physiology.*

M. Verworn (1863-1921)

Indeed, the meanwile intensified research on structure and function of protoplasm, cell nucleus and cellular organelles brought the dispersed biological disciplines again together in the focussing question about the *elementary units of living organisms*: Do they exist in analogy to the atoms of physics and the molecules of chemistry? Can they even be totally reduced to purely chemical and physical processes?

F.F. Blackman (1866-1947)

Various hypotheses were offered like the theoretical concepts of *'pangenes'* by Hugo de Vries (1889; see picture below), *'plasomes'* by Julius Wiesner (1892), both plant physiologists, or *'biogenes'* by Max Verworn (1894).

They all tried to cope with the brand new discoveries of enzyme functions in **biochemistry**, a young science just in the process of being born out of medical and plant physiology and strongly influencing the theoretical discussions. For example, **Frederick Frost Blackman** (see picture), who studied medicine and became lecturer for botany at Cambridge in England, could later publish an article on *"Incipient Vitality"* (1906) where he
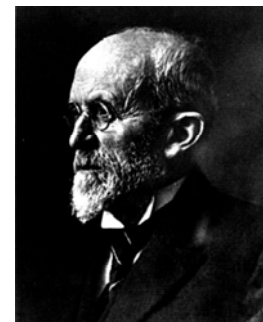
characterizes the protoplasm as *a complicated congeries of katalytic agents adapted to the metabolic work that the cell has to do*.

Also **neurobiology** was then still a young discipline, after the pathologist and anatomist Wilhelm Waldeyer (1836 – 1921) in Berlin had 1891 introduced the notion of a *'neuron'* characterizing it as the *anatomical, physiological,*
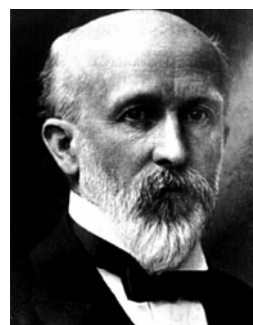

S. Ramon y Cajal (1852-1934)

metabolic and genetic (!) unit of the nerve system. However, this was not yet generally accepted as a doctrine, since there were still open questions about the mechanisms of synaptic transmission, although the up-to-now valid theory on signal uptake at the dendrites and transduction to the axons had already 1890 been formulated by two cooperating histologists, **Santiago Ramon y Cajal** (see picture) from Spain and A. van Gehuchten from Belgium as the *'law of dynamic polarisation'*.

R. Hertwig (1850-1929)

Finally, **protozoology** had turned out to become the provoking interdisciplinary field of biological research on developmental processes (may be analogous to today's molecular genetics and the research on stem cells). In the first issue of the new journal 'Archiv für Protistenkunde' (1902), founded by the young zoologist Friedrich Richard Schaudinn (1871 – 1906), who at the famous marine station Rovigno (in Croatia) was doing malaria research and thereby had invented the notion **'microbiology'**, there appeared a review article 'Die Protozoen und

O. Hertwig (1849-1922)

die Zelltheorie' by **Richard Hertwig** (see picture), who together with his older brother **Oscar Hertwig** (see picture) had been student and later assitant at the new Anatomical Institute of Max Schultze (1825 – 1874) in Bonn, the 'father' of protoplasm theory.

By that time, sea urchin eggs already were the international 'model organism' to study the role of recently detected protoplasm and nuclear *structures* like nucleoli, centrosomes or chromatin, and to generally understand the *construction of the living substance*. In his review article, Richard Hertwig refers to several leading German scientists in this field, as to the famous **Ernst Haeckel** (see picture), Julius Sachs or Thomas Boveri, but only to one french publication and two papers by the later famous American zoologist **Thomas Hunt Morgan** (see picture).

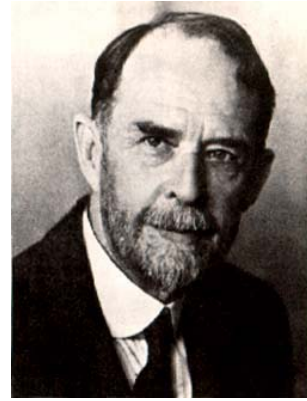As typical for international cooperation then a day,

E. Haeckel (1834-1919)

Morgan had undertaken trips to Europe each second year and had published the obtained results in various national journals. Indeed, biological (as other) research 100 years ago, was performed quite seperately within own national institutes or on congresses of own national societies; in those times, leading to the first world war, the big European nations were well prospering and strongly concurring. International congresses were still an exception.

Thus, it was on an annual meeting of the national society of 'German Natural Researchers and Physicians', 1900 in the old European capital Aachen, that the anatomist Oscar Hertwig (see picture above) gave a review talk about 'Biology in the 19th Century', in which he proclaimed that the ever ongoing fights between modern 'mechanists' and conservative 'vitalists' had now been overcome by new theoretical concepts. Though biology essentially needs and uses physics and chemistry, it has its own 'peculiar' aspects: *Life is based on a peculiar organisation of material* with which *are connected again peculiar processes and functions, how they never can be found in non-living nature*; and further: *With each of the infinite steps and forms of organisation there are produced new kind of effects ('Wirkungsweisen')*. This we might see as an early formulation of a nowadays-favored definition

of 'life' as a complicated adaptive, regulatory, dynamical system based on physico-chemical mechanisms.

Also Reinke's 'Theoretical Biology' (see picture above of the second edition in 1911) is essentially based on such a 'mechanistic' but not purely 'reductionistic' view. Indeed, during his one year stay at Bonn University (1872/3) the young plant physiologist

T. H. Morgan (1866-1945)

Johannes Reinke (see ECMTB #2 and picture above) had been in contact with the two Hertwig brothers as well as with a series of other natural scientists and philosophers. Thus, almost 30 years later, in 1901 with an age of 52, he also could present a talk at the next annual meeting of German natural researchers and physicians in Hamburg, with the title *"On forces being effective in organisms"*. Orienting on Helmhotz' definition of forces in theoretical pyhsics, he claims that in addition to these purely *'energetic forces'* executing the actual work (physical and chemical processes) and maintaining the substantial structures (molecules, cell compartments), there are so-called *'psychic forces'* being effective in the *configuration of living systems*, including mechanical, intentional or even imaginational forces. Here 'forces' means *'effectivity'('Wirksamkeit')* in a general sense, describing mutual influences in natural phenomena of the observed *'reality' ('Wirklichkeit')*. Using analogies from the theory of machines by Immanuel Kant (formulated in 1786), Reinke calls these (unconcious) psychic forces *'dominants'*, as they *determine and regulate the energetic actions that guarantee survival* – very similar to the (now computer, formerly engineering) programs of a machine that guarantee its *security*, and like 'governers', a term used almost 50 years later by Norbert Wiener to create the theory of *'Cybernetics'*. As most prominent examples for such 'dominants' Reinke sees the instincts (not only of animals but also of plants e.g. in geotropism), which he characterizes as *hereditary adaptations to master certain tasks of life*. What is transmitted to progenies by heredity of such 'dominants' (today's 'genetic programs'), Reinke and the other scientists 100 years ago did not know. (Do we know today?)

Yet Johannes Reinke until his death in 1931 insisted that it could not be only physico-chemical 'energies' or 'working substances' (as proteins) that are transmitted, rather the whole *system of psychic forces of an organisms* that regulate and depend on the organism's configuration, while giving the directives in its process of development and morphogenesis. (Did he anticipate a today desirable 'post-genomic' theory of complex genetic and epi-

genetic control systems?) Anyhow, Reinke emphasizes that the *possibilities of energetic*

H. Driesch (1867-1941)

(physico-chemical) *effects on the system of dominants of an organism enables the determination of its form as non-fixed but adaptable, thus providing diversity ('Mannigfaltigkeit') and variability of the living nature*.

Such concepts were quite common around 1900, when also the zoologist and only later 'neo-vitalist' **Hans Driesch** (see picture), who had been student of Ernst Haeckel and Oscar Hertwig, and already 1891 had published an assay on *"The mathematical-mechanical treatment of morphological problems in biology"*, became well-known for his 1894 formulated principle of a *'harmonic-equipotential system'* that determines the embryonic development of fertilized eggs. More than 20 years later it was picked up by Hans Spemann (1869 – 1941) with the notion 'Organisationszentrum' and later modified after the detection of morphogenetic gradients in the 1930th, henceforth guiding the principle ideas of spatio-temporally differentiated gene expression.

H. de Vries (1848-1935)

However, hundred years ago *genetics* had not yet been invented, although the 'Mendelian laws' had just (1900) been redetected by several botanists including **Hugo De VRIES** (see picture), professor at Leiden university and later on director of the botanical garden in Amsterdam, who 1901 published the first volume of his book on *"The Origin of Species by Mutation"*. This was only two years after **Ernst Haeckel** (see picture above), already since 30 years being the propagator of materialism and Darwinism, had published his central theoretical work "Die Welträthsel: Gemeinverständliche Studien über monistische Philosophie", which later was so often cited but also severely attacked, in particular by Johannes Reinke and the 'Kepler-Bund', founded 1907 in opposition to the 'Monisten-Bund'.

And it took several more years until the English biologist **William Bateson** (see picture) at Cambridge in 1905 introduced the notion *'genetics'* for the research on *Mendelian heredity of characters*, and finally the Danish pharmacist and botanist William Johannsen (1857 – 1927) at Kopenhagen in 1909 proposed the notion *'gene'* as *something in the gametes, by which the properties of the developing organism is or <u>can</u> be conditioned or <u>co</u>-determined*. Isn't this a provisionary, very carefully chosen terminology being worth to be reconsidered in the nowadays' fast progressing and too much simplifying usage of the notion 'gene'?

In a fertile communication between those experimental biologists and some applied mathematicians during this first decade of the 20th century, the foundations were laid for the soon florishing *population genetics* in the 1930th, thereby building the most important column for the later developing *biomathematics*. Namely, **Karl Pearson** (see picture at the top) and his active group at the Institute of Eugenics in London had so far been doing 'population statistics', mainly applied to anthropology and

socio-economic problems of demography (á la Quetelet and Galton). Now, after the foundation year 1901 of their new journal 'Biometrica' (see picture above) they became well known and wanted as *'biometricians'*, since they had started to investigate probabilistic and statistic formula that could explain the discrete 'Mendelian laws' and yet would be able to describe the continuous 'Darwinian change of characters' – at a time, where the distinction between 'geno-' and 'phenotypes' had not yet been found.

Particularly devoted to this difficult task was Pearson's student George Udny YULE (1871 – 1951), an English mathematician who (after additional studies of physics in Bonn) since 1896 was assistant professor for applied mathematics at the University College of London. Stimulated by his partially controversial papers and scientific discussions on a meeting of the Royal Society for Medicine in 1908, the British mathematician Godfrey Harald Hardy (1877 – 1947) could formulate the basic and famous Hardy Weinberg laws, so named because independently found by the German physician Wilhelm Robert Weinberg (1862 – 1937). Thus, I want to emphasize that Karl Pearson, who already in 1896 had written a series of articles about "Contributions to the mathematical theory of evolution, had originally initiated the development of the 'classical' population genetics and quantitative evolution theories*". His applications of now standard statistical techniques as probability curves and regression lines to genetic data then, in 1900, appeared (e.g. to a German custos at a zoological museum) even as *the first proof of a mathematical law for biological events*; whether true or not, it's impressive enough!

The question then remains, what happened to the idea of Johannes Reinke in 1901, to form a **theoretical biology**, whose task would be *not only to find out the origins of biological events, but also to check the basic assumptions of our biological thinking ('Anschauung' = Greek: theory)?*

Though a revised second edition of his book appeared in 1911, it was not before the end of World War I that the first continuous initiatives in this direction were undertaken. In particular, the zoologist and morphologist Julius Schaxel (1887 – 1943) in Jena (Germany), passionate fighter for the thoughts of his teacher Haeckel, founded a series of monographs entitled 'Theoretische Biologie'. Herein Hans Driesch published his assay "The concept of Organic Form" (1919), Johannes Reinke his last conceptional work "Foundations of Biodynamics" (1922) and, finally, the science philosopher **Ludwig von Bertalanffy** (see picture) one of his first publications "Critical theory of Morphogenesis" (1928).

L. von Bertalanffy (1901-1972)

The current year 2001 also celebrates Bertalanffy's 100th birthday, who became famous as a co-founder of 'General Systems Theory' after his permanent move to North America in 1949, but also for his well-kown book on *'Fließgleichgewicht' (flow equilibrium)*, a concept which, by the way, had already been introduced by the so-called **psycho-physicist** Gustav Theodor Fechner (1801-1887, see ECMTB #2), about whom Bertalanffy wrote his dissertation in 1926. Then in 1932, one year after Reinke's death, he published the first volume of his systematic book **'Theoretical Biology'**, 1942 followed by a second volume; a conceived third part never appeared as the manuscript was destroyed during the war.

However, we should not forget the early **environmentalists**, the most prominent one being the German zoologist Jakob von Uexküll (1864 - 1944), who already 1920 wrote his **'Theoretische Biologie'**, where he presents his seminal distinction

'Umwelt – Innenwelt – Außenwelt', embedded into a Kantian philosophy, similarly as Reinke. But there are also very important, though widely neglected roots of physiology and theoretical biology in Russian natural science: **Kliment Arkadjevich Timirjasev** (see picture), professor for anatomy and physiology at the Lomonossov University in Moscow, who 1894 had to quit his teaching job at the Agricultural Academy because of his opposition to the zaristic burocracy, gave 1903 a lecture at the Royal Society in London *"On the cosmic role of plants"*, where he developed his theoretical thoughts from biochemical processes in cells and nuclei over

K. A. Timirjassev (1843-1920)

the evolution of species up to the concept of *'biosphere'* and environmental protection. In the first years of the young Soviet Union he was the main constructor of modern Russian biology (before Lyssenko took over the scientific regime).

Thus, in 1935 the *Timirjasev-Institute for (Theoretical) Biology* in Moscow could publish a book 'Problems in Theoretical Biology', in which also the originally Hungarian biologist Erwin Bauer (1890 – 1942) published parts of his book *'Theoretical Biology'* that also appeared in 1935, though in Russian language. Based on an own kind of scientific historicism he reveals *intrinsic biological laws*, for example in the distinction of *interior and exterior work performed by organisms*, where the amount of the latter is increasing due to environmental and competitive conditions during the evolution.

This year 1935 and the last decade before world war II apparently brought a world-wide 'harvest' of the seminal thoughts on 'theoretical biology' 100 years ago. Further activities to be mentioned are: a scientific foundation with international memberships at the Zoological Institute at Leiden University (Netherlands) which, besides other publications, started 1935 the still existing journal *'Acta Biotheoretica'* as well as, by Adolf Meyer-Abich in Hamburg, the foundation of a book series on Theoretical Biology named *'Bios'* and, finally, by Nicolas Rashevsky at Chigaco, the foundation in 1938 of an own "house journal" named *'Bulletin of Mathematical Biophysics'* which turned into the now important and well-known *'Bulletin of Mathematical Biology"*.

New journals and books

The General Theory of Evolution

James Patrick Brock, Horniman Museum and Gardens
Academic Press, 2000, ISBN: 0121347400, $99.95 (hbk)

"The data of evolutionary biology have changed in a very radical way in recent years, the most significant input to this revolution being the advances made in developmental genetics. Another recent development is a noticeable shift away from extreme specialization in evolutionary biology. In this, we are perhaps to be reminded of George Gaylord Simpson's comments: "evolution is an incredibly complex but at the same time integrated and unitary process." The main objective of this book is to illustrate how natural adaptive systems evolve as a unity--with the particular objective of identifying and merging several special theories of evolution within the framework of a single general theory. The book, written by a natural historian, provides an interdisciplinary overview of the general theory of evolution from the standpoint of the dynamic behaviour of natural adaptive systems."

Remote Sensing and Geographical Information System

Simon I. Hay, *Sarah E. Randolph* (eds.)**,** University of Oxford
Academic Press, 2000, ISBN 0123335604, $69.95, Advances in Parasitology, vol. 47

"Global problems require global information, and satellites are a key to providing this. With ever more sophisticated control methods being developed for infectious diseases, our ability to map spatial and temporal variation in risk is more important than ever. Only then may we plan control campaigns and deliver novel interventions and remedies where the need is greatest, and sustainable success is most likely.
This book is a guide to using methods of surveillance from satellites, to analysing spatial data within geographical information systems, to interpreting complex biological patterns, and to predicting risk both today and as it may change in the future. Of all infectious disease systems, those that involve free-living invertebrate vectors or intermediate hosts are most susceptible to changing environmental conditions, and have hitherto received most attention from the marriage of analytical biology with this new space technology. Accordingly, this volume presents detailed case studies on malaria, African trypanosomiasis (sleeping sickness), tick-borne infections and helminths (worms). For those who are unfamiliar with this science, and unsure how to start, the book ends with a chapter of practical advice on where to seek hands-on instruction."

Elements of Mathematical Ecology

Mark Kot,
Cambridge University Press, 2001, 464pp, ISBN: 0521001501, GBP 27.95 (pbk)

"Elements of Mathematical Ecology provides an introduction to classical and modern mathematical models, methods, and issues in population ecology. The first part of the book is devoted to simple, unstructured population models that ignore much of the variability found in natural populations for the sake of tractability. Topics covered include density dependence, bifurcations, demographic stochasticity, time delays, population interactions (predation, competition, and mutualism), and the application of optimal control theory to the management of renewable resources. The second part of this book is devoted to structured population models, covering spatially-structured population models (with a focus on reaction-diffusion models), age-structured models, and two-sex models. Intended for upper level students and beginning researchers in ecology, mathematical biology and applied mathematics, the volume includes numerous clear line diagrams that clarify the mathematics, relevant problems thoughout the text that aid understanding, and supplementary mathematical and historical material that enrich the main text."

Economics in Nature

Ronald Noë, Jan A. R. A. M. Van Hooff, Peter Hammerstein
Cambridge University Press, 2001, 288pp, ISBN: 0521650143, GBP 55.00 (hbk)

"Since the development of game theory, the analysis of animal behaviour using the theories of economics has become a growing field of biological research in which models of games and markets play an important role. Studies of sexual selection, interspecific mutualism and intraspecific cooperation show that individuals exchange commodities to their mutual benefit; the exchange values of commodities are a source of conflict, and behavioural mechanisms such as partner choice and contest between competitors determines the composition of trading pairs or groups. These "biological markets" can be examined to gain a better understanding of the underlying principles of evolutionary ecology. In this volume scientists from different disciplines combine insights from economics, evolutionary biology and the social sciences to look at comparative aspects of economic behaviour in humans and other animals. *Contributors*:
Peter Hammerstein, Elinor Ostrom, Charles L. Nunn, Rebecca J. Lewis, Jan A. R. A. M. van Hooff, Ronald Noe, Louise Barrett, Peter S. Henzi, Redouan Bshary,

Jason D. Hoeksema, Mark W. Schwartz, Boguslaw Pawlowski, Robin I. M. Dunbar, Andrew Pomiankowski, Yoh Iwasa, Geoffrey A. Parker, Mike A. Ball."

Mathematics of Genome Analysis

Jerome Percus
Cambridge University Press, Jan. 2002, 160pp., ISBN: 0521585171, GBP c. 37.50 (hbk)

"The massive research effort known as the Human Genome Project is an attempt to record the sequence of the three trillion nucleotides that make up the human genome and to identify individual genes within this sequence. While the basic effort is of course a biological one, the description and classification of sequences also lend themselves naturally to mathematical and statistical modelling. This short textbook on the mathematics of genome analysis presents a brief description of several ways in which mathematics and statistics are being used in genome analysis and sequencing."

The Geometry of Ecological Interactions: simplifying spatial complexity.

U. Dieckmann, IIASA, *R. L*aw, University of York, *J.A.J. Metz*, University of Leiden (eds.)
Cambridge Studies in Adaptive Dynamics, Vol. 1, Cambridge University Press, 2000, 564 pp., ISBN 0 521 64294 9 (hbk), 45 pound Sterling.

In this spacious book, the three editors have collected 23 chapters, written by carefully selected experts, covering a broad range of aspects of spatial ecology. A lot of thought by the editors has gone into selection of topics, the level of exposition, the ratio between attention paid to reviewing past developments, current developments and future problems, uniformity, references, cross-referencing and relationships between chapters. We, the readers, can be thankful to them for taking the word 'editor' very seriously indeed which adds tremendous value to the volume. The 23 chapters are arranged into four thematic parts with an increasing focus on and use of mathematics: (plant) field ecology; examples of spatial ecological modelling (most showing the difference that adding explicit space makes to the behaviour of particular systems); examples of applications of recent analytical techniques that express the hope of obtaining insight into mechanisms and processes behind some of the differences noted in part B; and finally several chapters discussing the major of these techniques themselves. Not a lot of aspects of spatial ecology are missing, but I found that a chapter devoted to metapopulation theory and applications might have been appropriate. Maybe the editors argued that several good volumes devoted to that topic alone already exist. But still, a 24th chapter could not have hurt.
Even given the final technically sophisticated part, the book is very much *not* a textbook to learn the mathematical techniques involved. The chapters do have boxes on techniques in many places, but these do not give enough details to know how to apply techniques to ones own problems. This non-technical nature has the advantage that most chapters are easily accessible and readers get a good impression of the value of some of the techniques for studying particular problems and the insight that can be obtained by using these techniques. Therefore, the reader can learn to appreciate some tools and developments for his/her own benefit (and turn to study them more in detail in other publications) and discard others as not immediately relevant. I think this is a strong, rather than a weak point.
If pressed to name at least one weak point I would have to agree with Steve Ellner in his review of the same volume in TREE. Almost none of the modelling chapters (so most of parts B, C and D) contain comparison of models with data and overall the evidence given for the importance of space is weak (apart from relevance to dynamics in grassland communities in part A). Not having lots of evidence from nature is not necessarily a criticism of the editors of authors, there simply is not a large number of empirical studies to demonstrate the importance of space. With budgets of research institutes and universities under pressure it will not be easy to generate sufficient funding for the kind of experiments or observational studies that are required. From models the evidence is very convincing, space matters a lot and increasingly sophisticated techniques come available that allow one to comprehend how processes involving space actually work. It would, however, be a bad development that when some of the modelling approaches reach the stage where they are applied to real-world problems in nature management (where decisions impacting on space are made every day) there are no data available to actually validate the models. A clear discussion in the book what would have to be done empirically to determine the influences of space in relation to phenomena observed in the analysis of models would have been valuable and is an opportunity missed.
Notwithstanding this (slight) criticism, I like the book very much. If you want an introduction to spatial ecology in (almost) all of its myriad aspects and want to be brought up to speed then this is certainly the volume for you. It is not to be missed for anyone interested in questions in population dynamics and ecology that involve spatial interaction or have a spatial dimension (and one could argue that any dimension is spatial).

Hans Heesterbeek
Centre for Biometry, Wageningen

Modelling and Quantitative Methods in Fisheries

Malcolm Haddon, University of Tasmania
Chapman & Hall/CRC, 2001, 424pp., ISBN: 1584881771, $ 69.95

"Quantitative methods and mathematical modelling are of critical importance to fishery science and management. The text is organized into three sections: an introduction to modelling in fisheries and ecology, a straight

methodology section covering a range of methods, and a section focusing on specific fields in fisheries science. This book also addresses a topic of recent debate in fisheries and ecology, describing and comparing the uses of Least Squares, Maximum Likelihood, and Bayesian quantitative methods. Designed as stand-alone units, each chapter provides examples from both classic and recent literature and comes with Excel spreadsheets to serve as active examples, which can be modified and customized and can be used as templates for analysing one's own data."

Chaos in Real Data: Analysis of Non-Linear Dynamics from Short Ecological Time Series

Joe N. Perry, Robert H. Smith, Ian P. Woiwod, David R. Morse (eds.)
Kluwer Academic Publishers, 2000, 236pp., ISBN 0-412-79690-2, $122.00 (hbk)

"*Chaos in Real Data* studies the range of data analytic techniques available to study nonlinear population dynamics for ecological time series. Several case studies are studied using typically short and noisy population data from field and laboratory. A range of modern approaches, such as response surface methodology and mechanistic mathematical modelling, are applied to several case studies. Experts honestly appraise how well these methods have performed on their data. The data remain available, as benchmarks for future study, on the worldwide web. *Contents and Contributors*: Forward; *W.M. Schaffer.* Preface; *J.N. Perry.* **1.** Defining chaos for real, noisy data: local Lyapunov exponents and sensitive response to perturbations; *S.P. Ellner.* **2.** Modelling time-series data; *P. Turchin, S.P. Ellner.* **3.** Measles as a testbed for characterising nonlinear behaviour in ecology; *B.T. Grenfell.* **4.** Population dynamics of small rodents in northern Fennoscandia; *H. Henttonen, I. Hanski.* **5.** Analysis of population fluctuations in the aphid *Hyperomyzus lactucae* and the moth *Perizoma alchemillata*; *I.P. Woiwod, P. Rothery, Xilong Zhou.* **6.** One, two and three-species time series from a host-pathogen-parasitoid systems; *M. Begon, S.M. Sait, D.J. Thompson, Xilong Zhou, E.D. Bell.* **7.** Blowflies as a case study in non-linear population dynamics; *R.H. Smith, S. Daniels, K. Simkiss, E.D. Bell, S.P. Ellner, M.B. Forrest.* **8.** Overview; *J.N. Perry.* **9.** A glossary of terms used in non-linear dynamics; *D.R. Morse, J.N. Perry, R.H. Smith.*"

The FitzHugh-Nagumo Model: Bifurcation and Dynamics

C. Rocsoreanu, A. Georgescu,, N. Giurgiteanu
Kluwer Academic Publishers, 2000, 248pp., ISBN 0792364279, $105.00 (hbk)

"This application-oriented monograph presents a theoretical and numerical investigation of all types of oscillators and bifurcations (such as Hopf, Bogdanov–Takens, Bautin, and homoclinic) generated by the FitzHugh–Nagumo model. The wide diversity of the oscillators as used in electrophysiology, biology, and engineering is emphasised. Various asymptotic behaviours are revealed. The dramatic changes in oscillations connected with the emergence or disappearance of concave limit cycles are investigated. Codimension of bifurcations is minutely analysed. New types of codimension one and two bifurcations of planar systems were found. A detailed global bifurcation diagram concludes the work."

Analysis and Control of Age-Dependent Population Dynamics

Sebastian Anita, University Al.I. Cuza' Iasi, and Institute of Mathematics, Romanian Academy
Kluwer Academic Publisher, 2000, 212pp., ISBN 0-7923-6639-5, $83.00 (hbk)

"This volume is devoted to some of the most biologically significant control problems governed by continuous age-dependent population dynamics. It investigates the existence, uniqueness, positivity, and asymptotic behaviour of the solutions of the continuous age-structured models. Some comparison results are also established. In the optimal control problems the emphasis is on first order necessary conditions of optimality. These conditions allow the determination of the optimal control or the approximation of the optimal control problem. The exact controllability for some models with diffusion and internal control is also studied. These subjects are treated using new concepts and techniques of modern optimal control theory, such as Clarke's generalized gradient, Ekeland's variational principle, Hamilton–Jacobi equations, and Carleman estimates. A background in advanced calculus and partial differential equations is required."

A Course in Mathematical and Statistical Ecology

Anil Gore, Sharayu Paranjpe, University of Pune
Kluwer Academic Publishers, 2000, 304pp., ISBN 0-7923-6715-4, $138.00 (hbk)

"This book touches upon major areas in the field of ecology and covers a wide range of topics. Beginning with classical mathematical models for population dynamics and their use in population management and harvesting, it covers the traditional as well as the most recent non-standard methods of abundance estimation. The recent interest in the study of biodiversity is discussed at length. The last chapter on models for animal and plant behaviour is perhaps the first attempt to put the two together. Many exercises, theoretical as well as data analytical, which reflect authors' interaction with practicing field ecologists, are provided."

Design Principles for the Immune System and Other Distributed Autonomous Systems

Irun Cohen, Lee A.Segel, Weizmann Institute
Oxford University Press, 2001, 320pp., ISBN 0195137000, GBP 32.50 (pbk)

"Distributed autonomous systems are collections of interacting agents that function without a "leader." Biological examples of such systems would include metabolism, the immune system, and ant colonies. Other examples are found in robotics and artificial intelligence. This book takes a theoretical approach to the analysis of the immune system. It includes chapters by several of the world's leading immunologists, and comparative chapters on other models of distributed autonomous systems (such as Bert Holldobler on ant signalling, and Doug Hofstadter and Melanie Mitchell on software codelets). The book presents a different perspective on immunology, with a prominent enough author line-up to attract the attention of the immunological community, and should also appeal to a wide range of workers in various fields concerned with "bootstrapping" or complex systems that function without central or "top-down" control."

Fluctuations and Scaling in Biology

Tamas Vicsek, Eotvos University (ed.)
Oxford University Press, 2001, 256pp., ISBN 0198507909, GBP 24.95 (pbk)

"Techniques first employed in statistical physics have been used increasingly by life scientists over the last decade to study biological phenomena. This book presents observations and models of collective phenomena in systems ranging from bacteria to humans. Vicsek summarises recent approaches and new results in a unified and coherent approach. Many interesting phenomena are discussed, including fractal pattern formation, group motion amongst diverse organisms and the mechanisms by which fluctuations are rectified in the tiny molecular machines in the cell."

Virus Dynamics: Mathematical Principles of Immunology and Virology

Martin Nowak, Institute for Advanced Study, *Robert M. May*, University of Oxford
Oxford University Press, 2000, 250pp., ISBN 0198504187, GBP 45 (hkb), ISBN 0198504179, GBP 22.50 (pbk)

"This book describes the emerging field of theoretical immunology, in particular the use of mathematical models to describe the spread of infectious diseases within patients. It reveals insights into the dynamics of viral and other infections, and the interactions between infectious agents and immune responses. Structured around the examples of HIV/AIDS and hepatitis B, the authors show how mathematical models can help researchers to understand the detailed dynamics of infection and the effects of antiviral therapy. Models are developed to describe the dynamics of drug resistance, immune responses, viral evolution and mutation, and to optimise the design of therapy and vaccines."

Branching in Nature: Dynamics and Morphogenesis of Branching Structures, from Cell to River Networks

Fleury, V., Gouyet, J.-F., Leonetti, M. (eds.)
Springer-Verlag, 2001, 476pp., ISBN 3540418881, DM 139.00 (pbk)

"There is increasing evidence that branching processes in nature proceed by similar mechanisms in many seemingly different systems. This book encompasses all fields of science, investigating branching morphogenesis and pattern formation in cells, plants, organs and river networks to name but a few. International experts have contributed to this volume and taken care that the lectures remain accessible to graduate students and non-specialist researchers. Les Houches School, October 11-15, 1999."

Computational Modeling in Biological Fluid Dynamics

Fauci, L.J., Tulane University*, Gueron, S.,* Technion-Israel Institute of Technology (eds.)
Springer-Verlag, 2001, 238pp., ISBN 0387952330, DM 169.00 (hbk)

"This volume contains invited and refereed papers based upon presentations given in the IMA workshop on *Computational Modeling in Biological Fluid Dynamics* during January of 1999, which was part of the year-long program "Mathematics in Biology." This workshop brought together biologists, zoologists, engineers, and mathematicians working on a variety of issues in biological fluid dynamics. A unifying theme in biological fluid dynamics is the interaction of elastic boundaries with a surrounding fluid. These moving boundary problems, coupled with the equations of incompressible, viscous fluid dynamics, pose formidable challenges to the computational scientist. In this volume, a variety of computational methods are presented, both in general terms and within the context of applications including ciliary beating, blood flow, and insect flight."

Theoretical Aspects of Evolutionary Computing

Kallel, L., Naudts, B., Rogers, A. (eds.)
Springer-Verlag, 2001, 497pp., ISBN 3540673962, DM 119.00 (hbk)

"This book provides tutorials to the theory of Evolutionary Computing, covering the main approaches to understanding the dynamics of Evolutionary Algorithms. It combines this with recent, previously unpublished research papers based on the material of the tutorials. The outcome is a book which is self-contained to a large degree, for both graduate students and researchers from other fields who want to get acquainted with the theory of Evolutionary Computing, and to active researchers in the field."

Computational Biology

Gascuel, O., Laboratoire d'Informatique, de Robotique et de Microelectronique de Montpellier*, Sagot, M.-F.,* Institut Pasteur (eds.)
Springer-Verlag, 2001, 165pp., ISBN 3540422420, DM 70.00 (pbk)

"This book presents a selection of revised full papers accepted for presentation at the *First International Conference on Biology, Informatics, and Mathematics*, JOBIM 2000, held in Montpellier, France, in May 2000. The 13 papers included in the book were selected after two rounds of reviewing and revision from a total of 67 submissions. Among the topics addressed are algorithms, comparative genomics, evolution, phylogeny, databases, knowledge processing, genome annotation, graph theory, combinatorial mathematics, macromolecular structures, RNA and proteins, metabolic pathways and regulatory networks, and statistics and classification."

Mathematical Models in Population Biology and Epidemiology

Brauer, F., University of British Columbia, *Castillo-Chavez, C.*, Cornell University
Springer-Verlag, 2001, 416pp., ISBN 0387989021, DM 129.00 (hbk)

"The goal of this book is to search for a balance between simple and analysable models and unsolvable models which are capable of addressing important questions on population biology. Part I focuses on single species simple models including those which have been used to predict the growth of human and animal population in the past. Single population models are, in some sense, the building blocks of more realistic models -- the subject of Part II. Their role is fundamental to the study of ecological and demographic processes including the role of population structure and spatial heterogeneity -- the subject of Part III. The book includes both examples and exercises."

Matrix Population Models: Construction, Analysis, and Interpretation, *Second Edition*

Hal Caswell, Woods Hole Oceanographic Institution

Sinauer Associates, 2000, ISBN 0-87893-096-5 (hbk), $64.95

" *Matrix Population Models*, Second Edition, is a comprehensive treatment of matrix population models and their applications in ecology and demography. It begins with simple cases, presented in detail so that beginning students can learn how to use these powerful models. It goes on to cover advanced topics in stochastic and non-linear models. Analytical methods and theoretical issues are illustrated with empirical examples throughout.
The decade since the publication of the First Edition of this book has seen enormous progress in the theory and application of matrix population models. The new edition includes greatly expanded treatment of stochastic and density-dependent models, sensitivity analysis, and statistical inference, and new chapters on parameter estimation, structured population models, demographic stochasticity, and applications of matrix models in conservation biology."

New journal of Biostatistics

Oxford University Press has launched a new journal, Biostatistics, edited by Scott Zeger (Johns Hopkins) and Peter Diggle (Lancaster University). To promote the journal, Oxford has created an e-mail table of contents alerting service allowing anyone interested to receive an e-mail listing the table of contents of new issues as they mail. This service is particularly useful for statisticians whose libraries receive the journal, as well as those considering subscribing themselves. The alerting service is free, and we keep e-mail addresses strictly confidential. Anyone can sign up by visiting Biostatistics online at
http://www.biostatistics.oupjournals.org.

Patricia Bowers Hudson
Oxford University Press
2001 Evans Road
Cary, NC 27513
pbh@oup-usa.org

The Ecology of Wildlife Diseases

P. J. Hudson, A. Rizzoli, B.T. Grenfell, J.A.P. Heesterbeek, A.P. Dobson (eds.)
Oxford University Press, 2001, 200pp., ISBN 0198506201 (hbk), ISBN 0198506198 (pbk)

"This book consists of nine chapters in which a collective of 50 ecologists, veterinarians, evolutionary biologists, epidemiologists, population biologists and mathematicians describe the current status and future research questions in understanding the dynamics of infections in natural animal populations. It follows a similar set-up as *The Ecology of infectious diseases in natural populations* (Grenfell and Dobson, eds., Cambridge University Press, 1995), but where that volume approached the topic from the modelling side,

the present book starts from the empirical side and works towards interaction with modelling. There are chapters on heterogeneity in macroparasitic infections, parasites and host population dynamics, parasite community ecology and biodiversity, microparasite transmission and persistence, spatial aspects of disease dynamics, tick-borne infections, pathogens in biological conservation. Many case studies are discussed in detail and modelling approaches are given in boxes. There are about 1000 references."

Forthcoming events

The 2nd International Conference on Computational Science

(Amsterdam, 21-24 April 2002)

http://www.science.uva.nl/events/ICCS2002

SIMAI 2002
VI Congresso della Societa' Italiana di Matematica Applicata e Industriale

(Chia, CA, 27-31 maggio 2002)
E-mail: simai@iac.rm.cnr.it
http://www.iac.rm.cnr.it/simai

Sixth International Conference on Cognitive and Neural Systems

Boston University, May 29 - June 1, 2002

Sponsored by the Center for Adaptive Systems and the Department of Cognitive and Neural Systems at Boston University with financial support from the Office of Naval Research. Invited and contributed talks and posters. Abstract deadline: January 31, 2002.
Contact: Cynthia Bradford, Boston University CNS Department, 677 Beacon Street, Boston MA 02215
fax: 617-353-7755
cindy@cns.bu.edu
Or see:
http://www.cns.bu.edu/meetings

Biocomp2002: Topics in Biomathematics and Related Computational Problems at the Beginning of the Third Millennium

3-9 giugno 2002, Vietri sul Mare
Web site:
http//cds.unina.it/~biocomp/

Conference on Mathematical Modelling of Population Dynamics

Bêdlewo, Poland, June 24-28, 2002.

The conference is organized by the Institute of Mathematics, Polish Academy of Sciences and the Institute of Mathematics, University of Silesia within the EU Programme Centre of Excellence coordinated by the Stefan Banach International Mathematical Centre through the Package "Mathematical Modelling and Analysis of Cellular Populations".
SCOPE
The conference will focus on mathematical modelling and model analysis of populations at various levels, including cells, genes, biomolecules and of population dynamics in Evolution; Ecology; Epidemiology and infectious diseases; Physiology; Immunology and cancer growth. Mathematical aspects of these topics include the following non-exhaustive list
- Different scales and techniques of modelling
- Deterministic and stochastic models.
- Behaviour of populations such as stabilization, oscillation, growth, extinction.
- The onset of chaos, bifurcation.
SPONSORS
- European Commission
- Polish State Committee for Scientific Research
- Institute of Mathematics, Polish Academy of Sciences University of Silesia.

Conference e-mail: cmmpd@ux1.math.us.edu.pl
Conference web page: www.math.us.edu.pl/cmmpd/
Mailing address: Institute of Mathematics Polish Academy of Sciences "Population Dynamics"
Bankowa 14/343; 40-007 Katowice, Poland

Opening Conference of DIMACS
Special Focus on Computational and Mathematical Epidemiology'' (2002-2007)

Rutgers University, USA, June 28-July 2, 2002

This is to be a 5 year program, starting in June 2002, aimed at creating interdisciplinary partnerships, introducing mathematical scientists to the problems of epidemiology and to researchers working in the field, introducing epidemiologists and biologists to new mathematical and computational methods that might be relevant, and educating students and postdocs interested in the area. There will be a large opening conference on computational and mathematical epidemiology, inviting a large number of the players in the special focus to attend. In addition to major invited talks, we will include considerable time for discussion about how to get the most out of the special focus, including how to coordinate among workshops and working groups, potentials for visits, ways to recruit new people to work in the field, etc. Keynote lectures will be given by Rita Colwell (Director of NSF) and Nancy Cox (Head of the Influenza Branch of CDC). Co-chairs for the conference are: Simon Levin (Princeton, Ecology and Evolutionary Biology), Fred Roberts (Rutgers, Mathematics).

ECMTB2002.
Mathematical Modelling & Computing in Biology and Medicine.

Milano, Italy, 2-6 July 2002.

Mathematical and Theoretical Biology is a diverse field in which interdisciplinary collaboration is essential for progress. The field ranges from experimental research linked to mathematical modelling to the development of more abstract mathematical frameworks and theories in which observations about the real world can be interpreted and from which new hypotheses for testing can be generated. Recently, great attention has been devoted to the development of efficient algorithms for complex computations and visualisation, notably in molecular biology and genetics.

Mathematical and Theoretical Biology has profound connections with many current problems of great relevance to society. Insights and predictions from mathematical modelling are increasingly used in decision support to medicine (e.g., immunology and spread of infectious diseases, cancer research, cardio-vascular research, neurological research, optimisation of medical treatments, imaging), in climate studies, agronomy and the management of environment and natural resources. Recent developments in areas such as biotechnology (e.g., genome projects, genetic modification) add new focal points of activity to the field.

The main goal of ECMTB 2002 is to foster interdisciplinary collaboration between mathematicians and bioscientists and to act as the main forum for the exchange of recent research results and new research directions inside the wide community of scientists working in theoretical biology and medicine, in Europe and beyond.

Location

The conference will be held in the campus of Città Studi (three subway stops from the Central Railway Station) close to the centre of Milan.

Programme
The major areas of present day activity in mathematical and theoretical biology and medicine will receive attention in plenary lectures, invited lectures, parallel sessions of contributed papers, poster sessions and special sessions of poster presentations (see below). Attention will be duly paid to topics that will increasingly become important in the near future, such as those identified in the thematic programme "Unlocking the resources of the living world and the ecosystem" of the Fifth Framework Programme of the EC. The topics of specific focus will be: Biotechnology and Bioengineering, Cardiovascular Systems, Cell Signalling, Cellular Organisation, Bioinformatics and Computational Biology, Ecology, Environmental Sciences, Evolution, Immunology, Infectious Diseases, Individual Based Models, Regulatory Gene Networks, Biomedical Imaging.
For further information:
http://ecmtb.mat.unimi.it/

International Scientific Committee.
De Roos, P. Cinquin, P. Deuflhard, A. Goldbeter, W. Jaeger, P. Jaegers, P. Lansky, P. Maini, H. Metz, R. Nisbet, C. Peskin, S. Rinaldi, L. Segel.
Local Organising Committee.
V. Capasso (Coordinator), E. Beretta, S. Cerutti, P. Cerrai, P. Colli Franzone, A. De Gaetano, A. Fasano, P. Fergola, A.Gandolfi, E. Galli, M. Gatto, F. Grandori, A. Mari, C. Matessi, A. Morabito, D. Morale, G. Naldi, S. Paveri-Fontana, L. Preziosi, A. Pugliese, L. Sacerdote.
Board of ESMTB
V. Capasso (President), Z. Agur, O. Arino, M. Chaplain, M.Gyllenberg, J.A.P. Heesterbeek, M. Kaufman, V. Krivan, A. Stevens, P. Tracqui
Sponsors
CIMAB, Centro Interuniversitario per la Matematica Applicata all'Ambiente
SIMAI, Societa' Italiana per la Matematica Applicata ed Industriale
EMS, European Mathematical Society
ICIAM, International Committee for Industrial and Applied Mathematics.
Funding Institutions
European Union, MIRIAM, Università di Milano, Politecnico di Milano, Consiglio Nazionale delle Ricerche (CNR), AGENZIA 2000, PROGETTO STRATEGICO Metodi e Modelli Matematici nello Studio dei Fenomeni Biologici, IASI, Domus Galilaeiana, STMicroelectronics.
Liaisons
A. Hastings (SMB)
M. Mimura (JSMB)

The International Congress of Mathematical Biology (ICMB)

Guilin, Guangxi Province, P. R. China.
August 15-18, 2002.

This congress is also a satellite meeting of ICM-2002 (see WWW.ICM2002.org.cn) on Mathematical Biology. Now, the conference has already begun to accept the abstract for its conference paper. Updated information of the conference can be found on the following homepage:
http://math.la.asu.edu/~kuang/guilin.html
or
http://www.gxnu.edu.cn/ICM2002/English.htm

The 12th International Conference on Mechanics in Medicine and Biology (ICMMB 12)

Lemnos Island, Greece, September 9 - 13, 2002

International Conferences on Mechanics in Medicine and Biology consist of a series of biennial events presenting an interdisciplinary forum of engineering, medicine and biology.

Papers, which deal with any aspect of biomechanics ranging from fundamentals to clinical applications, are invited, and papers dealing with the evolution of knowledge and technologies into commercial products are especially welcomed. The following topics will receive special attention as subjects of Mini Symposia:

Artificial Organs, Biological Fluid dynamics, Biomechanics: Muscle & Modeling, Biomechanics of the Knee & Spine, Bone Structure Remodeling, Cardiovascular Devices and Mechanics, Cardiovascular Flow Mechanics, Cardiac Mechanics, Coronary Flow Mechanics, Cell Mechanics: Mechanics of Active Cells, Dental Mechanics, Hemodynamics, Implant Desing / Materials, Imaging, Modeling and Computer Methods, Injury or Trauma Biomechanics, Morphogenesis and Pattern Formation, Medical Vision and Optometry, Melanoma: Modeling, Morality and Laws in Genetics, Orthopedics, Hearing Mechanics, Oculomotor Mechanics, Organs Transplantation, Rehabilitation Sport Mechanics and Ergonomics, Scaling Laws and Similarity in Biology, Tissue Mechanics.

Deadlines:
February 1, 2002: Early registration.

Information: T. K. Karalis, Democritos University of Thrace,
P.O.Box 306, 67100 Xanthi, Greece.
Tel: 0030-541-73215 and 0030-541-79644
Fax: 0030-541-24110
E-mail: tkaral@civil.duth.gr

CM3SE Multi-Conference on Computational and Mathematical Methods in Science and Engineering

(Alicante, 20-25 September 2002)
http://www.ua.esp/cmmse2002/

Schools

Short course on epidemic modelling

University of Trento, April 15-19, 2002.

The Ph.D. program in Mathematics and the Department of Mathematics of the University of Trento organize a short course titled Deterministic and stochastic modelling of epidemics. The course will take place at the Department of Mathematics, starting April 15 at 9:00, ending April 19 at 13:00.
Lecturers will be:
Herbert W. Hethcote (University of Iowa) (8 hours) "Three Basic Epidemiology Models", "Periodicity in Epidemiology Models (effects of seasonality and delays)", "Models for Heterogeneous Populations", "Vaccination Strategies for Pertussis, Varicella and Rubella".
Gianpaolo Scalia Tomba (University of Roma Tor Vergata) (6 hours) "Stochastic models for epidemics: SIR and SIS in closed or open homogeneous populations; in populations with households", "Recent statistical techniques for parameter estimation in epidemic models"
Mimmo Iannelli (University of Trento) (4 hours) "Age Structured Epidemiology Models", "Models for tubercolosis"
Andrea Pugliese (University ofTrento) (4 hours) "Models for the competition
among parasite strains and the evolution of virulence"
Some exercise sessions will be organized. There will also be room for some presentations by the participants.
The precise program and schedule will be communicated later, and will be available on the Web page http://www-math.science.unitn.it/dottorato/scuolabio.html
The course is directed to Ph.D. students, or researchers, in Mathematics with an interest in biological models; or to students or researchers in the biomedical sciences, interested in understanding the basic methods and results of the mathematical models used in epidemiology.
No previous knowledge on mathematical models for epidemics is assumed, but
it is expected that participants know the basic concepts in the theory of ordinary differential equations, and of Markov chains.
For information on the course, please contact Andrea Pugliese at: pugliese@science.unitn.it
The participation is free, but interested people are asked to inform the secretary of the Ph.D. program either via

mail: Signora Miriam Stettermaier, Dipartimento di Matematica, via Sommarive 14, 38050 Povo (TN),
or via e-mail :
miriam@science.unitn.it
or fax : +39-0461-881624.
An application form is available on the Web at http://www-
math.science.unitn.it/dottorato/scuolabio.html
The secretary may also provide help for accomodation.

First Announcement
School on Population Dynamics

Bêdlewo, Poland, June 17-21, 2002.

The school is organized by the Institute of Mathematics, Polish Academy of Sciences and the Institute of Mathematics, University of Silesia within the EU Programme Centre of Excellence coordinated by the Stefan Banach International Mathematical Centre through the Package "Mathematical Modelling and Analysis of Cellular Populations".

Scope
The meeting will focus on mathematical theory and methods applied to study populations of entities, including cells, genes, and biomolecules. There are five main topics:
Adaptive Dynamics; Ecology; Epidemiology; Physiology; Structured Populations Dynamics.
Each topic will be covered in four to five 45 min lectures. The mathematics behind these topics is mainly devoted to qualitative and quantitative behaviour in ordinary differential equations, partial differential equations, delay-differential equations, integro-differential and integral equations, dynamical systems, control theory, as well as stochastic processes.

Sponsor
European Commission
Polish State Committee for Scientific Research
Institute of Mathematics, Polish Academy of Sciences
University of Silesia

Courses
Ovide Arino, Ecology, 4 units; Odo Diekmann, Adaptive Dynamics, 4 units; Mimmo Iannelli, Epidemiology, 4 units; Michael C. Mackey, Physiology, 4 units; Glenn F. Webb, Structured Populations Dynamics, 4 units.
In addition to the courses, there will be a series of one-hour lectures given by members of the scientific committee and communications by participants (15 min). The target audience is mainly composed of advanced graduate students and PhD students.
Applications are also encouraged from researchers who may wish to explore a different field or take part in interdisciplinary studies.

Scientific Committee
Ovide Arino, Odo Diekmann, Marek Kimmel, Andrzej Lasota (President of the Committee), Michael C. Mackey, Philip K. Maini, Feliks Przytycki (Main Coordinator of the Project of Centre of Excellence), Ryszard Rudnicki (Coordinator of the Package), Ziad Taib.

Organizing Committee
Tomasz Kulpa, Katarzyna Pichór, Ryszard Rudnicki (Chair), Marta
Tyran-Kamiñska.

School Fee
The number of participants is limited to 50. Given the funding obtained from the European Commission and other sources, the standard cost to participants is 250 EURO. The school fee includes accommodation, full board (three meals), registration fee, refreshments during sessions and social programme. Further reduction of fees is possible for a limited number of participants.

Contact addresses.
School e-mail: cmmpd@ux1.math.us.edu.pl
School web page: www.math.us.edu.pl/cmmpd/school/
Mailing address:
Institute of Mathematics
Polish Academy of Sciences
"Population Dynamics"
Bankowa 14/343
40-007 Katowice, Poland

Application
Early applications are encouraged, especially concerning talks or financial support.
Compile and return the Application Form directly from the school's web page
www.math.us.edu.pl/cmmpd/school/
The application form may also be sent by e-mail or standard mail to the conference addresses.

ESMTB Biomathematics Euro Summer School.

Urbino (Italy) July 8-19, 2002.

The beautiful art city of Urbino in central Italy will host the annual ESMTB Summer School, devoted this year to dynamical systems in biomedicine. Dynamical systems constitute a fundamental mathematical and computational framework within which many processes in biomedicine can be described. From tumor growth to hormonal regulation, from the spread of disease to neuronal transmission, the crucial feature of many biological and natural phenomena is their evolution in time. The purpose of the school is to present some fields of application of mathematical modelling of dynamical systems to physiology and medicine, and concurrently to give a presentation of some of the mathematical techniques used in such modelling.
The school will offer five courses centered on the biological background and on the mathematical modelling of relevant biomedical phenomena: the spread of cardiac electrical excitation, with the possible study of arrhytmias; the physiology of blood flow in the pulmonary circulation; the system controlling glucose blood levels by means of the hormone insulin; the activity and synchronisation of neurones; the mechanism of production of blood cells with attendant regulations and possible derangements.
Differential equations, with or without delay, are the natural mathematical tool for the study of dynamical systems. Computationally intensive techniques have also

enjoyed increasing recognition, in the wake of the more widespread availability of cheap computing power. The school will therefore also offer two methodological courses, respectively on Delay Differential Equations and on Numerical Methods

The School is addressed to doctoral students in mathematics or allied disciplines (engineering, physics, statistics) looking for exposure to medical problems and to young biologists and physicians intending to employ mathematical tools in their research.

The school will be organised along the seven main courses, together with a workshop, invited lectures and participant lectures. Teaching units (lectures by instructors and invited speakers) will be 40' each including 5' questions and discussions, separated by substantial intervals. Lectures by participants (20') will be arranged in couples and follow the same schema. Main courses and workshop will be plenary, while invited talks and student presentations will be split into two parallel sessions. Participants will be given ample opportunity to interact with instructors during and after hours, as well as completing didactic projects in groups of mixed extraction. Financial support will be available for participants: the school has been granted financial aid by the European Commission, which makes it possible to offer the complete two-week package (tuition, full accommodation, meals and coffe-breaks, social programme, one year ESMTB membership) at a standard cost of 335 Euro (cost to European or assimilitated nationals, 35 years of age or less; see web page for details).

Courses (coordinators) (Number of units)
Periodic haematological diseases and leukemia (Jacques Belair) (10 units)
Modelling and cellular automata in the study of cardiac arrhythmias and ventricular fibrillation (Alain Bardou) (8 units)
Modelling Pulmonary Vascular Pressures (George Cremona) (8 units)
Models for the Glucose-Insulin system (Andrea De Gaetano, Andrea Mari) (12 units)
Neuronal modeling (Khashayar Pakdaman) (10 units)
Delay Differential Equations (Edoardo Beretta) (14 units)
Numerical methods (Rodolfo Bermejo) (10 units)
Scientific Committee
Luis Abia, Ovide Arino, Alain Bardou, Jacques Belair, Edoardo Beretta, Rodolfo Bermejo, George Cremona, Andrea De Gaetano, Oliver Jensen, Yang Kuang, André Longtin, Philip Maini, Andrea Mari, Khashayar Pakdaman, Fortunata Solimano, Yasuhiro Takeuchi.
Organizing Committee
Ovide Arino, Edoardo Beretta, Andrea De Gaetano (Managing Director), Simona Panunzi and Fortunata Solimano.
Location and Infrastructure
The school will be held entirely within the hilltop campus "Collegio del Colle" ("College-on-the-Hill") of the University of Urbino, in Central Italy.
For additional information see:
http://www.biomatematica.it/urbino2002/

Positions available

Assistant professor position bioengineering, biomaterial, and/or related field department of applied science, college of William and Mary

The Applied Science Department of the College of William & Mary invites applicants for a tenure-track position at the assistant professor level in biomedical engineering, biomaterials and/or a related field, emphasizing either computational or experimental tools. The new faculty member will be asked to contribute significantly to leadership in the effort of the Department and the College to strengthen life sciences activities. Further, he or she will be strongly encouraged to form collaborations with faculty in other W&M units and with external institutions as appropriate.

Excellence and high commitment in the teaching of undergraduate and graduate students is expected of all faculty at the College. The Applied Science Department occupies facilities on William & Mary's main campus in Williamsburg and at the Applied Research Center at Jefferson Laboratory in nearby Newport News.

Candidates should submit a complete CV, copies of no more than five refereed publications in the above areas and have at least three letters of recommendation submitted on their behalf to: New Faculty Search, Department of Applied Science, The College of William & Mary, PO Box 8795, Williamsburg, VA 23187-8795. Review of materials is expected to continue until the position is filled. The College is an EEO/AA employer.

Statistics Lectureship,
University of Newcastle, UK
E-mail: e.b.martin@ncl.ac.uk
http://www.ncl.ac.uk/engmaths/

Scientist for Modelling of Bioprocesses
at Bayer AG, Leverkusen
E-mail: andreas.schuppert.as@bayer-ag.de

Mathematical Biology Positions, UBC

Junior level position (UBC Dept of Mathematics)
Mathematical Biology (and other areas)

The Mathematics Department at the University of British Columbia is seeking candidates for at least one tenure-track Assistant Professorship, subject to funding, with a starting date of 1 July 2002. Exceptional candidates at the Associate Professor or Professor level may be considered. Applicants must have a superb research record in one of the following areas: Financial Mathematics, Mathematical Biology, Partial Differential Equations, Scientific Computing or Industrial/Applied Mathematics. The successful applicant is expected to interact with related groups in the Mathematics Department and have demonstrated interest and ability in teaching. The salary will be commensurate with experience and research record. Applicants should send a current cv including a list of publications, statement of research and eaching interests and a list of four referees to

Professor George Bluman, Head
Department of Mathematics
University of British Columbia
#121 - 1984 Mathematics Road
Vancouver, B.C. Canada V6T 1Z2

Tenure Track Position, Comput. & Appl. Math., Rice University

Rice University
Department of Computational & Applied Mathematics
www.caam.rice.edu

The Department of Computational and Applied Mathematics invites applications for a senior or junior tenure track position, preferably in Mathematical Biology, to begin August 2002.

A senior appointment would be at the associate or full professor level, with or without initial tenure, depending on experience and qualifications. A senior candidate must have established an exceptional record of research, including leadership and funding. In addition to a strong commitment to research, there should be a demonstrated commitment to teaching at the undergraduate and the graduate levels and experience in directing Ph.D. students. A junior appointment would be at the assistant professor level.
Candidates must have a Ph.D., a demonstrated potential for excellence in research and a strong commitment to teaching.
Rice University is a private research university with a long tradition of excellence in undergraduate science and engineering education. The Computational & Applied Mathematics Department hosts research programs in Optimization, Numerical Linear Algebra and Partial Differential Equations. A number of our faculty is active in the Keck Center for Computational Biology,

www.bioc.rice.edu, and the Rice/Baylor Neuroscience Program, www.ruf.rice.edu/~neurosci.

Applicants should send a letter of application; a brief statement of research accomplishments, interests and goals; a curriculum vitae and selected reprints; and have three letters of recommendations sent to:

Chair, Staffing Committee
Computational & Applied Mathematics Department
MS 134
Rice University
P. O. Box 1892
Houston, Texas 77251-1892

Review of applications will begin on January 31, 2002 and continue until the position is filled.
Rice University is an affirmative action/equal opportunity employer.

Open positions in applied mathematics

Two tenure-track assistant professor positions beginning August 2002.
Demonstrated excellence in scholarship and teaching, plus a Ph.D., are required. One position is in computational mathematics or statistics; the other is in biomathematics, including mathematical and computational biology, bioinformatics, and biostatistics. Both positions reside in the Department of Mathematics: the first is part of a university initiative in computational science; the second is part of an interdisciplinary initiative between the Departments of Mathematics and Biology.
 Submit application letter (specifying for which position(s) you wish to be considered), AMS paper coversheet (available at http://www.ams.org/), CV, research description, and three or more recommendation letters (at least one concerning teaching) to either the Computational Search Committee or the Biomath Search Committee, Department of Mathematics, College of William & Mary, P.O. Box 8795, Williamsburg, VA 23187-8795. Review begins November 15 and continues until appointments are made. The College is an EEO/AA employer. Please send email inquiries about the computational mathematics position to comath@math.wm.edu and about the biomathematics position to bimath@math.wm.edu. The department can also be contacted by telephone
 (757-221-1873) or by fax (757-221-7400).

Director and Tenure-Track Positions, Biomathematics Program, NCSU

Biomathematics program at NC State University seeks applications for Director and for tenure-track positions at all levels. Require Ph.D. in a mathematical or biological science, research program in modeling biological systems & grad training in probability or statistics. Duties include research and teaching.
Inquiries to:

gerig@stat.ncsu.edu.
For details and contact information see
http://www.stat.ncsu.edu/admin/positions.htm#BMA

Positions in Applied Mathematics, Mathematical/Computational Biology

Instituto Mexicano del Petróleo, Applied Mathematics and Computing Program, Mexico.
Positions in Applied Mathematics including Mathematical and Computational Biology.
Funded in 1965 the IMP (Mexican Petroleum Institute) has as its main objectives to conduct basic and applied research, to develop technologies applicable to the National Petroleum Industry, and to train highly qualified personnel at all levels in the areas of production, exploitation and refinement of oil products.
Applications are invited for qualified PhD candidates for several available Postdoctoral Research positions, Visiting Professor positions, and Tenure-Track positions in Applied Mathematics. All positions are for a one or two year period subject to a positive review at the end of the first year if applicable. The tenure track positions are reviewed also at the end of the second year. Spanish is not a necessary requirement but it is expected that all successful candidates will achieve some proficiency in the Spanish language by the end of the first year. Salaries are determined upon academic and professional experience qualifications. Salaries in each category are competitive on international standards.
The successful candidate will be incorporated into the IMP Research Program on Applied Mathematics whose aim is to develop mathematical and computational methodologies to be used in research areas related to petroleum exploration, exploitation, refinement, transportation and production. Applications are encouraged in the following areas:
mathematical/computational biology, control theory, mathematical statistics, optimization, and numerical analysis.
Candidates are expected to participate as part of interdisciplinary research teams already constituted or being constituted in the areas of priority for the IMP.
Interested applicants should submit a curriculum vitae and two letters of recommendation to: Dr. Jorge X. Velasco-Hernandez, Instituto Mexicano del Petroleo, Programa de Matematicas Aplicadas y Computacion, Eje Central Lazaro Cardenas 152, CP. 07730 Mexico DF. Further particulars can be obtained at the email address pimayc@imp.mx. Applications will be received until the positions are filled.

Tenure/Tenure-track/Scott/Visiting Positions, Math., U of Utah

The Department of Mathematics at the University of Utah invites applications for the following positions. Availability of positions is contingent upon funding. The hiring committee will select candidates based on excellence in research and teaching.

1. Up to three full-time tenure-track or tenure appointments at the level of assistant, associate, or full professor. The department is primarily interested in applicants who work in the research areas represented in the department and who received their Ph.D. degrees prior to 2001.
2. One or more Visiting Faculty positions of one year or less in any of the rofessorial ranks, depending upon availability.
Completed applications for faculty positions will be considered starting October 1, 2001, and positions may be offered from that date on. However, applications will be accepted up to May 1, 2002, or until positions are filled.
To apply for any of these positions, you are strongly encouraged to fill out an application at
www.math.utah.edu/pos, or at www.mathjobs.org.
Alternatively, you may send the AMS cover sheet. To complete your application, send a curriculum vitae, bibliography, and three letters of recommendation. Visiting professor applicants should indicate the part of the year they wish to visit. Incomplete files will not be considered.
Please send this information to Committee on Staffing, Department of Mathematics, University of Utah, 155 S. 1400 E., JWB 233, Salt Lake City, UT 84112.
The University of Utah is an Equal Opportunity, Affirmative Action Employer and encourages applications from women and minorities, and provides reasonable accommodation to the known disabilities of applicants and employees.

Faculty Positions at Colorado State University

Faculty and Other Positions
Regular Tenure Track Positions
The Department of Mathematics at Colorado State University invites applications for two regular tenure-track faculty positions and a postdoctoral position beginning Fall of 2002. The individuals appointed must hold a doctorate at the time of appointment and be capable of fulfilling the highest expectations in research and in teaching. The appointment level for the regular faculty positions are open. For one of the faculty positions we are specifically seeking an individual to take over the Directorship of the Individualized Mathematics Program, through which the Department teaches its precalculus offerings. This position offers an outstanding opportunity to combine research in mathematics education with a strong curricular development focus. The areas of emphasis for the other faculty position and the postdoctoral position are not determined, but we intend to appoint individuals with whom our existing faculty can effectively interact.
The Department currently has areas of strength in algebra, algebraic geometry and topology, analysis and applied analysis, combinatorics, dynamical systems, mathematics education, numerical analysis, optimization, partial differential equations, pattern analysis, scientific computing, and symbolic computation. We have 178 undergraduate majors and 45 graduate students, with 30 FTE tenure-track faculty.

Colorado State University has an enrollment of 23,000 students and is located in Fort Collins, Colorado, an attractive community of over 115,000 located 30 miles from Rocky Mountain National Park. More information may be obtained via the Department's Web page at http://www.math.colostate.edu.

Position in Multiscale Modeling and Simulation
Division of Engineering and Applied Science California Institute of Technology.

A tenure-track assistant professor position in the area of applied mathematics, focused on multiscale modeling and simulation, in the Division of Engineering and Applied Science at the California Institute of Technology is open to candidates with exceptional research and instructional ability. The length of the initial appointment is four years and it is contingent on the completion of the PhD degree. esearch topics of interest include: dynamics and dynamical systems, model reduction of large systems, modeling and simulation across multiple length scales, stochastic systems, and uncertainty management. Candidates should have a strong foundation in mathematical and computational analysis relevant to their research program. Applicants should apply on-line by visiting http://www.acm.caltech.edu/search/
and following the instructions outlined there. You will be asked to submit a letter of application; a brief statement of research accomplishments, interests, and goals; curriculum vitae; selected reprints; and have four letters of recommendation (at least one commenting on teaching) sent to the address indicated on the website.
Review of applications will begin January 15, 2002 and will continue until the position is filled.
Caltech is an Equal Opportunity/Affirmative Action Employer. Women, minorities, veterans, and disabled persons are encouraged to apply.

_____

POST-DOC
_____

Predoctoral and Postdoctoral Positions
Center for BioDynamics Boston University

The Center for BioDynamics (CBD) at Boston University has predoctoral and postdoctoral positions available. The CBD is a multi-disciplinary center devoted to research and training at the interfaces of dynamical systems, biology and engineering. Current research themes include computational neurobiology, gene regulatory networks, fluid and solid mechanics, and applied biodynamics. We seek candidates interested in working across disciplinary boundaries, with multiple members of the CBD.
The CBD is connected to many departments and other research centers at Boston University, providing a stimulating research environment. Associated senior faculty members are T. Kaper, N. Kopell, G. Wayne (Math), J. Collins, J. White (Biomedical Engineering). M. Hasselmo (Psychology), P. Barbone and J. Baillieul (Aerospace and Mechanical Engineering), S. Redner (Physics). For further information about the CBD, please see our web page at
http://cbd.bu.edu.
To apply for a Postdoctoral Fellowship, please send
1) A statement that includes your background, career goals, how this position satisfies those goals, and your suitability for this position
2) Your C.V.
3) Three letters of recommendation to:
  Ms. Geri Duffy
  Center for BioDynamics
  Department of Mathematics
  111 Cummington Street
  Boston University
  Boston, MA 02215
Interested Ph.D candidates should apply to one of the associated departments and mention interest in the CBD. Please refer to the BU Graduate School Admissions Office (http://www.bu.edu/apply/#graduate) for all application materials.
Related predoctoral and postdoctoral positions are available in PMCN (see ad).
Predoctoral and Postdoctoral Fellowship Burroughs Wellcome Training Program in Mathematical and Computational Neuroscience (PMCN) Boston University
The goal of PMCN is to facilitate the transition of a small and outstanding set of predoctoral and postdoctoral fellows from the mathematical and physical sciences to a range of areas in neuroscience. Financial support for both PhD candidates and postdoctoral fellows is available. The program features special seminars, mentoring by faculty and advanced trainees, and a dynamic and well-networked intellectual life provided by multiple supporting institutional modules. These include a new degree-granting Program in Neuroscience (PIN; http://www.bu.edu/pin) the graduate program of the Biomedical Engineering department (BME; http://bme.bu.edu) and the Center for BioDynamics (CBD; http://cbd.bu.edu).
Predoctoral fellows will enroll in one of two PhD programs (PIN or BME) that focus on the combination of experimental and computational neuroscience.
Burroughs Wellcome Postdoctoral Fellows will design individualized programs that include neuroscience courses and one or more research projects that emphasize combined computational and experimental approaches to neuroscience. In addition, fellows may participate in the CBD, which helps physical scientists and engineers to address research problems at the interfaces among mathematics, physics, biology and engineering.
H. Eichenbaum and N.Kopell direct PMCN. The senior faculty members are P.Cook, K.Harris (biology), M. Hasselmo, H. Eichenbaum, D. Somers, C. Stern (psychology), S. Colburn, J. Collins, J. White (biomedical engineering), T.Kaper, N. Kopell, G. Wayne (math). For further information and instructions about applications, see our website at http://pmcn.bu.edu or

email pmcn@bu.edu. Our mailing address is PMCN, C/0 G. Duffy, Department of Mathematics, Boston University, 111 Cummington St., Boston MA 02215.
Related predoctoral and postdoctoral positions are available at the CBD (see ad).

Postdoctoral Position In Mathematical biology.

University of Alberta, Edmonton, Canada.
Application is open until position is filled, or until Feb. 28. 2002.

A postdoctoral research position in Mathematical Biology is available in the Department of Mathematical Sciences at the University of Alberta, starting as soon as possible. The research will be related to the analysis of mathematical models for spatial spread.
Specific projects may include:
(i) Qualitative analysis of transport equations for chemotaxis,
(ii) Analysis of spatial patterns observed in chemotaxis models or
(iii) Mathematical modeling of fairy rings. Some teaching duties may also be included.

Candidates must possess a Ph.D. in Applied Mathematics or a related discipline, should be adept at computing, and should be willing to collaborate with both mathematicians and biologists on the research project.
The position includes $35 K salary, plus benefits, travel money, state-of-the-art computing and research facilities.
The position is for one year, with renewal for an additional year subject to successful performance, and is subject to the availability of funds.
Applications should include: CV, up to 2 or 3 publications/preprints and 3 letters of recommendation. These should be sent to: Thomas Hillen, Postdoc position, Department of Mathematical and Statistical Sciences, University of Alberta, Edmonton T6G 2G1, Canada.
Application via e-mail with reference to a Web page, which provides all necessary information, is also acceptable (thillen@ualberta.ca, subject: postdoc position).

Postdoctoral Researcher Positions

The Department of Biomedical Informatics (BMI) at the Ohio State University is currently inviting applications for postdoctoral positions in high-performance, data-intensive, and grid computing areas. Candidates should have a PhD degree in computer science or a related discipline and background in high-performance and distributed systems.

Position:
This is a research-oriented position; the postdoctoral candidate will be expected to actively participate in all aspects of research and help in supervising graduate

research assistants in their research projects. Most of our projects are multi-disciplinary and involve collaboration with both application developers and computer scientists from various institutions, including National Partnership for Advanced Computational Infrastructure (NPACI), San Diego Supercomputer Center (SDSC), University of Texas at Austin, Ohio Supercomputer Center (OSC), Computer and Information Science Department (CIS) at The Ohio State University, and University of Maryland.
The postdoctoral candidate should have ability to work in a team and collaborate with a multi-disciplinary group of researchers.
The initial appointment will be for one year, but the position is renewable per year basis. At the end of two years, postdoctoral researchers will have opportunity to be evaluated for tenure track position in the Biomedical Informatics Department.

Application:
Candidates should send a detailed CV, including a summary of thesis research, a research statement, a list of publications, copies of two selected papers, and three letters of recommendation to

> Ms. Max Bacher
> 3184 Graves Hall
> 333 West 10th Ave
> Columbus, Ohio, 43210
> USA
> Email: bacher-2@medctr.osu.edu

Postdoctoral Position: Theory of Resistance Evolution

A postdoctoral position is available for a theoretical ecologist/evolutionary biologist to study the evolution of resistance of insect pests to genetically modified crops with insecticidal properties. The postdoc will participate with a team including an insect ecologist (David Andow), a sociologist (Fred Buttel), an economist (Terry Hurley), and a theoretical ecologist (Tony Ives). A strong background in mathematics is essential.
The position is for 2 years starting at US$30,000/yr, with the possibility of continued funding for additional time. The starting date is preferably before 1 March 2002. All requirements for the PhD must be completed before the time of appointment. Please send CV, and the names and contact information for 3 references to:

> Tony Ives
> Department of Zoology
> UW-Madison
> Madison, WI 53706
>
> Phone (608) 262-1519
> fax (608) 265-6320
> arives@facstaff.wisc.edu

If you will be in Madison for the Ecological Society meetings, please contact me beforehand for a possible interview.

THE EUROPEAN SOCIETY FOR MATHEMATICAL AND THEORETICAL BIOLOGY (ESMTB)

APPLICATION FORM

(this form may also be found at www.esmtb.org)

If you would like to become a member of the ESMTB please fill in the following form. The membership dues are £ 25.00, € 40.00 per year (full member) and £ 15.00, € 25.00 (student member). Members from Eastern European countries should pay at the student rate.

Name:

Address:

Phone/Fax

E-Mail:

My choice of journal subscription at reduced rate is:

1. **No journal**

2. **Acta Biotheoretica (Kluwer). 45 £ per year.**

3. **Journal of Biological system (World Scientific). 45 £ per year.**

4. **Journal of Mathematical Biology (Springer Verlag). 70 £ per year.**

Membership Fee: £

Journal Fee: £

TOTAL: £

ECMTB: How would you like to receive the coming issue of the European Communications in Mathematical and Theoretical Biology (ECMTB)?

    __ by regular mail   __ download a web copy by yourself

Send this form, with payment of your annual membership fee, and indicating your method of payment, to:

Dr. M. Chaplain,
ESMTB Secretary and Treasurer,
Department of Mathematics,
University of Dundee, Dundee DD1 4HN, Scotland, UK
chaplain@maths.dundee.ac.uk

Methods of payment:
1) By CASH (pounds sterling or your own currency):
2) By CHEQUE: if paying cheque, please make the cheque payable to "ESMTB" (in POUNDS STERLING ONLY).
3) BANK DRAFT TRANSFER: payment may be directly to the ESMTB account, details of which are
         Bank: The Royal Bank of Scotland
         Balfour Street, Dundee,
         Dundee University Branch
         Account Name: ESMTB
         Sort Code: 83 18 38
         Account Number: 00 145 384

ECMTB February 2002 No. 3: CONTENTS