E MTB
*C*ommunications

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

EDITORIAL

Dear Society members, dear friends of mathematical and theoretical biology.

This is the *11th edition* of the "Communications in Mathematical and Theoretical Biology" appearing quite late in the current year due to an unexpected delay in the procedure to select the winner of the ***Reinhart-Heinrich Doctoral Thesis Award 2008*** out of 14 received applications (see *page 22*). We are very thankful for the again broad and qualitatively high response demonstrating the promising scientific movement within the community of young researchers in Mathematical and Theoretical Biology.

The same impressions and feelings had, as I think, everybody who participated in the *7th European Conference on Mathematical and Theoretical Biology ECMTB'08* that was gently and "scottishly" organized by Mark Chaplain, Sandy Anderson and Fordyce Davidson at Edinburgh in the beginning of July last year (for a report see *page 4*). The forthcoming *8th European Conference ECMTB'11* will take place in ***Krakow, Poland,*** *28 June – 2 July 2011*, with Ryszard Rudnicki as the main organizer and, again, in junction with the Annual Meeting of *SMB*, whose forthcoming president *Michael Mackey* has already offered his generous support.

After an extensive discussion on the ***General Assembly of ESMTB*** in Edinburgh (see minutes on *page 14*) the ESMTB statutes have been changed, so that Board members can serve as candidates for a second 6-years period. Along this line, in September 2008 five new Board Members have been elected for the next period, with the ESMBT treasurer *Andreas Deutsch* staying "on Board" and continuing to run our Society web page (see below) together with his group at Dresden University. In particular, from there you can download the regularly edited ***ESMTB Infoletter*** providing information about forthcoming conferences, workshops, schools and open positions. Clearly, this infoletter lives from your inputs! Please, collect and send any relevant announcement or material to info@esmtb.org.

After the 'Bologna process' has induced major changes in the teaching curricula at most European Universities, it would be good to have an interactive data base collecting all ***European Curricula in Mathematical Biology, Biomathematics, Theoretical Biology*** or related topics (see also *page 11*). Please, send any information or questions to the responsible board member: jean-christophe.poggiale@univmed.fr.

Finally, we wish the new Board and the new ESMTB President *Carlos Braumann* (see his letter on *page 3*), whom I would like to congratulate as former president in the name of our Society, a constructive and successful working period – which might depend to a large amount on the collaborative action of the Society members.

Wolfgang Alt
Managing Editor

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The **closing date** for submissions to the next issue of the Communications *(ECMTB # 12)* is set to be **January 31th, 2010.** Please send, preferably by e-mail, any information, reports or other material to the managing editor

Wolfgang Alt*, Theoretische Biologie, IZMB, Universität Bonn, Kirschallee 1-3, D-53115 Bonn, Germany*
wolf.alt@uni-bonn.de

Those who are interested in the Society or want to have more information, please visit our Society website at
www.esmtb.org
The page can be used by members to pay their fee, or, by not-yet-members to register. Thanks!

CALL FOR MEMBERSHIP FEES 2009

ESMTB membership includes automatic and free subscription to the **print edition** of the
Journal of Mathematical Biology
-- The official journal of the Society --

Please register at www.esmtb.org and send your payment of the required annual fee for 2009 by bank draft transfer or electronically (PayPal).

Membership Fees per year**:**

a.   The **Individual Annual Membership Fee** is:
- 50 Euro (full member)
- 40 Euro (ISTMB, JSMB, NVTB, SFBT, SMB full member)
- 25 Euro (student, developing country or Eastern European member)
- 20 Euro (student SMB member)

b.   The **Institutional Annual Membership Fee** is:
- 200 Euro

Details for bank draft transfer:
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   Account Name: ESMTB
   Account Number: 04 076 801 01
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   Bank Address:
   Dresdner Bank, Dr. Kuelz-Ring 10
   D-01067 Dresden, Germany

Further information:
Prof. Dr. Andreas Deutsch, ESMTB treasurer
Center for Information Services and High
Performance Computing
Dresden University of Technology

Andreas.Deutsch@tu-dresden.de

SOCIETY NEWS

Letter of the New ESMTB President
Carlos Braumann (Evora, Portugal)

Dear Colleagues:

Due to the elections for the ESMTB Board, part of the Board was renewed. As nature renews itself every springtime, it is only natural that the first meeting of the renewed Board was held on March 21, 2009, in the nice city of Marseille. In that meeting, the departing President and the Treasurer reported on 2008 activities and we have defined the main goals for the coming future (and who will supervise the different tasks).

We also had with us *Ryszard Rudnicki*, who is in charge of the 8th European Conference on Mathematical and Theoretical Biology to be held in Krakow (Poland) in 2011, jointly with the Annual 2011 Meeting of the Society for Mathematical Biology. We were put up to date with the preparations and discussed some of the very important organizational issues of our Conference. It is going to be a great event, joining Europeans and Americans in the organization, but having colleagues from all over the world participating, a celebration of Mathematical and Theoretical Biology and its most recent developments in one of our most beautiful East European cities. We are counting on your active participation.

The Board also elected the new President, Vice-President, Secretary, and Treasurer and, of course, took care of several miscellaneous current affairs. As a result of these elections, the Board composition is now as follows:

Andrea Pugliese (vice-president)
Andreas Deutsch (treasurer)
Carlos A. Braumann (president)
Christine Jacob
Daphne Manoussaki
Eva Kisdi (secretary)
Hans Westerhoff
Jean-Christophe Poggiale
Miguel Herrero
Peter Jagers

The Board warmly thanked the departing Board members *Helen Byrne, Luigi Preziosi, Rafael Bravo de la Parra* and *Wolfgang Alt* for their invaluable services to ESMTB and continues to count on their help on several of the tasks.

I am delighted to report that the departing President, *Wolfgang Alt*, who did so much for the consolidation and expansion of ESMTB, will continue as an Advisor to the Board (and as Editor of the Communications and President of the Committee for the Reinhart Heinrich Doctoral Thesis Prize), which means that we will all continue benefiting from his great qualities and experience. I am equally delighted to report that *Ryszard Rudnicki*, the ECMTB 2011 Organizer, will also be an Advisor to the Board.

ESMTB is a collective enterprise and needs all its members to participate actively and to help fulfilling the Society's duties and responsibilities in the development of the blooming field of Mathematical and Theoretical Biology. If not yet a member, think about joining, not only for the benefits, which are substantial, but to become involved in this joint effort.

While thanking you for your continuous support of ESMTB, the whole Board is looking forward to working with you in the next three years.

Best regards,
Carlos

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Report on the 7th European Conference on Mathematical and Theoretical Biology

ECMTB08: The View from Behind the Curtain

Organising any major international conference always comes with its fair share of joys and hopes, griefs and anxieties. Organising a major international conference located in a city at a distance of 100km from your own base (Dundee-Edinburgh) perhaps adds an additional layer or two of complexity. However, being involved in

organising a European Conference on Mathematical and Theoretical Biology, one is immediately aware of the historical and cultural threads running through this event (Alpe d'Huez, Lyon, Heidelberg, Amsterdam, Milan, Dresden…) and on reflection, we hope that the historic Scottish capital of Edinburgh ("The Athens of the North") was felt to be a fitting addition to this august list. 555 participants attended the meeting during the 5 days of the conference and were treated to a scientific feast of 13 plenary talks, 40 minisymposia (around 150 presentations), 46 Contributed Talk Sessions (around 270 presentations) and 47 Posters. The overall standard of all forms of presentation was incredibly high and it is impossible to select particular "highlights". In addition to the scientific success of the meeting, it was also a great social success. Offering complimentary

drinks on the first two evenings of a meeting such as this is a certain way to get people talking and interacting with one another and setting the tone for the whole meeting itself, continued throughout the week in formal (Springer Reception, Playfair Library) and informal (Edinburgh's many excellent pubs) surroundings.
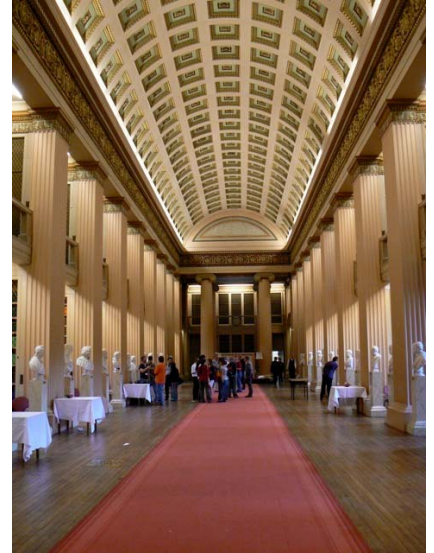
Perhaps the real highlight of the week was the "Ceilidh" that took place in Dynamic Earth after the Conference Dinner. After a slightly slow start, it did not take long before everyone on the dance floor was fulfilling the description of a good conference as described in the conference booklet as:

"*a stochastic interacting many-particle system with periodic self-aggregating tendencies*"

although with the help of instructions from the band and a few "locals" who knew the dance steps *a priori* it was perhaps less stochastic (more deterministic) than perhaps you might have imagined. In any event it was a lot of fun!

With the "ECMTB flame" now passed on, we wish our Polish colleagues solidarity and success for Krakow 2011 and hope to see you all there.

<div align="right">

ECMTB08 Organising Committee
Mark Chaplain, Dundee

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General Assembly of the ESMTB and its new Board

During the 7th European Conference on Mathematical and Theoretical Biology at Edinburgh (ECMTB'08) the triennial General Assembly of our Society (ESMTB) took place on Thursday, June 1, 2008 (see the minutes on *page 14*). The President *Wolfgang Alt*, gave an activity report for the years 2006 – 2008 and expressed his thanks to the very cooperative work within the ESMTB Board.

Those members remaining "on Board" are listed here together with the e-mail code, under which they can be reached:

Carlos A. Braumann braumann@uevora.pt
Eva Kisdi kisdi@mappi.helsinki.fi
Christine Jacob cjacob@jouy.inra.fr
Jean-Christophe Poggiale
jean-christophe.poggiale@univmed.fr
Hans Westerhoff
Hans.Westerhoff@manchester.ac.uk

Due to a clearly positive outcome of the ballot on the change of the Statutes (yes: 139 – no: 9) as proposed during the General Assembly (see *page 16*), the treasurer of our Society, *Andreas Deutsch*, was allowed to continue as a candidate for the new Board elections. Thus, the final list of candidates including their "profiles" was sent to all members by e-mail for voting.

Evaluation of the on-line votes, **146 out of 303 ESMTB members** yielded the following

Result of the Board election ballot, September 2008:

1.	**Andreas Deutsch** (Germany)	96
2.	**Andrea Pugliese** (Italy)	90
3.	**Peter Jagers** (Sweden)	53
4.	**Daphne Manoussaki** (Greece)	52
5.	**Miguel Herrero** (Spane)	51
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6.	Vincent Jansen (Denmark)	50
7.	Ryszard Rudnicki (Poland)	47
8.	Geza Meszena (Hungary)	36

The first five candidates constitute the additional new members of the Board for the years 2009 – 2015.

Then, during the first Board session that took place in Marseille beginning of March 2009, the *ESMTB treasurer* was confirmed:

Andreas Deutsch deutsch@tu-dresden.de

In addition, **Wolfgang Alt** and **Ryszard Rudnicki** have been elected as Board Advisors.

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Below, the written profiles of all the new board members are published together with their e-mail codes:

Miguel A. Herrero
herrero@mat.ucm.es

Miguel A. Herrero, with his Ph.D. in Mathematics, is currently Professor of Applied Mathematics at Universidad Complutense of Madrid (UCM), Spain. His research interests include the theory of differential equations (with particular emphasis in reaction-diffusion systems) and continuum mechanics. His recent work deals with subjects such as mathematical models of chemotaxis, blood coagulation processes and optimization methods in radiotherapy.

Dr. Herrero has served in a number of Committees and Editorial Boards. He currently is member of the Scientific Committee of the Spanish Royal Mathematical Society (RSME), and has been Associate Editor for SIAM Journal of Mathematical Analysis (1999-2005). Currently he is the Associate Editor for European Journal of Applied Mathematics (EJAM), as well as for the Birkhäuser series of monographs in Modelling and Simulation in Science, Engineering and Technology. He has performed evaluation activities for a number of agencies in Spain, the European Union and the U.S. He was elected Head of the Department of Applied Mathematics of UCM for the period 2004-2008, and he is currently a member of the Scientific Committee of the IMI (Institute of Interdisciplinary Mathematics) at UCM.

He believes that ESMTB could enhance its already significant role in a number of ways. These include (but are not restricted to) fostering international cooperation within (and outside) the European area, establishing extended partnerships with biomedical institutions and companies, and paying particular attention to career development for young scientists, who will provide the scientific leaders of the future.

Peter Jagers
jagers@chalmers.se

My interest in theoretical biology has its roots in branching processes and population dynamics. My main contribution there, I believe, is the formulation of general branching processes, more realistic than classical ones in allowing reproduction repeatedly during life and a diversity of types of individuals. For such populations, not dying out, I established an asymptotic stabilisation of the population composition, and the whole pedigree. Basically I am thus an applied probabilist, working with basic, and I hope, biology relevant patterns.

But I have also worked with concrete matters from biology, ranging from modeling and analysis of cell kinetics to PCR. My most recent published work concerns the time and path to extinction of (rather) big subcritical populations (PNAS 2007). Just recently I proved (together with *Andreas N. Lageras*) a more theoretical result on branching processes that extends this extinction work: supercritical general branching processes, conditioned to die out, are subcritical branching processes. (This is folklore for simple branching processes. The problem is that the overall conditioning on extinction might induce dependencies between individuals and also affect individual life histories in an inhomogeneous manner.) Presently, I am working (with a number of colleagues) on a simple but strict branching model for adaptive dynamics, allowing sympatric speciation. Not easy! I am also continuing my work on extinction.

I am a professor of Mathematical Statistics at Chalmers University of Technology in Gothenburg. I am also the First Vice-President of the Royal Swedish Academy of Science and was the President of Bernoulli Society 2005-2007. I am a coordinating editor of the Advances in Applied Probability and Journal of

Applied Probability, one of three editors for the Springer book series "Probability and Its Applications", and an associate editor of the Mathematical Population Studies.

There is more on my homepage
www.math.chalmers.se/~jagers

funding opportunities to the members of the society, seek grants that will enable young researchers attend scientific meetings, help in the organization of meetings, workshops and summer schools and help co-organize joint meetings with different European societies that represent fields of biology.

Daphne Manoussaki
daphne@science.tuc.gr

I am an assistant professor at the Technical University of Crete, Greece, as well as a researcher of the Institute for Applied and Computational Mathematics at FORTH (Foundation for Research and Technology, Hellas).
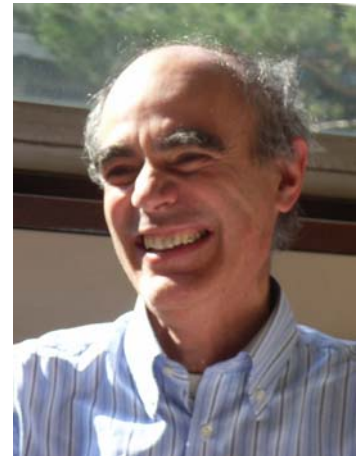
My undergraduate education was in (mostly pure) mathematics, and I received my Ph.D. in applied mathematics from the University of Washington. I'm interested in cell physiology as well as tissue morphogenesis and function. In particular, I am interested in the relationship between cell organization, tissue geometry and tissue function. In trying to understand such systems, whenever possible, I try to use a combination of image processing techniques (so as to extract information from biological image data), continuum mathematical models that describe the different interactions between the key players in a system, and perturbation techniques and / or numerical methods for the subsequent analysis of the model equations.

I enjoy teaching and am interested in creating or promoting learning opportunities (via e.g. summer schools) for young students as well as for researchers of theoretical backgrounds or experimental backgrounds that want to enter the field of theoretical biology. Having worked in different European countries as well as the US, and having seen the disparate funding situation in different countries, I, like many of us, feel that funding for basic research should be increased. I am interested in communicating the different

Andrea Pugliese
pugliese@science.unitn.it

I am Professor at the Department of Mathematics of the University of Trento, Italy, where I have been working since 1984. My undergraduate education was in Mathematics at the University "La Sapienza" of Rome, then I studied Ecology and Evolution at the State University of New York at Stony Brook, where I obtained a Ph.D. in 1986 with a thesis on life history theory. Afterwards, my main research interests have focussed on different aspects of epidemic models, from theoretical studies of coexistence or evolutionary issues, to applications to specific systems, tied with data analysis, concerning tick-borne infections or influenza epidemics.

I have been in the Scientific or Organizing Committee of several conferences of ESMTB (1999, 2002, 2008) and of other conferences in the field, as the CMPD conference of 2004 in Trento. I have been a member of ESMTB since its foundation, and I have seen it developing strongly, thanks to the efforts of its Board members, and becoming able to give visibility to the field in Europe and to provide support to young scientists in the field. I will try to continue this work, aiming at a further increase of memberships, at an extension of the support for conferences and smaller workshops (by giving them visibility and, if feasible, also financial support), at an improvement of the use of the

Society web page for exchanging information (courses, student exchanges, thesis discussed, grant information...). I would also like to improve the collaboration with related societies both in mathematical biology (SMB, Japanese society...) and in related fields (e.g. evolutionary biology, applied mathematics...).

Ryszard Rudnicki
rudnicki@us.edu.pl

I am professor at the Institute of Mathematics of the Polish Academy of Sciences, the head of the Department of Biomathematics, and Vice Director of the Mathematical Center of Science and Technology in IMPAS.

I graduated in Mathematics at University of Silesia (Katowice, Poland) 1980, received my Ph.D. in 1987, habilitation in 1993 and the scientific title of professor in 2001. I was supervisor for four PhD theses.

My main research topics concern population dynamics, physiology and genetics, but I also try to develop some mathematical tools useful in biological applications. This research includes some problems from the theory of stochastic semigroups as well as chaotic and probabilistic methods in dynamical systems.

I have taken part in five European Union projects as a coordinator of packages like "Modelling and analysis of cellular populations" and "Mathematical biology, neural networks". Within these projects I organized tree conferences concerning mathematical modeling in biology and medicine.

I am a member of the organizing and scientific committee of two annual conferences in applied mathematics in Poland. Moreover, my institute runs the "Mathematical Research and Conference Center" in Bedlewo and the "Stefan Banach International Mathematical Center", where conferences, schools and workshops can be organized. Both places have a very good condition for such meetings, they are relatively cheap and Banach Center has funds for organizing conferences. Taking part in European Union projects, I have gained experience which can be helpful in finding support for biomathematical conferences, summers schools and meetings of working groups.

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Minutes of the ESMTB Board Meeting
Evora, 8 March 2008

Meeting starts at 10:05 am.

Present: Wolfgang Alt (WA, chair), Carlos Braumann (CB), Andreas Deutsch (AD), Christine Jacob (CJ), Eva Kisdi (EK; minutes), Jean-Christophe Poggiale (JP).
Absent with apology: Rafael Bravo de la Parra (RB), Helen Byrne (HB), Luigi Preziosi (LP), Hans Westerhoff (HW).

Welcome and Adoption of agenda
WA welcomes the Board and all thank CB for his kind hospitality. The Agenda is accepted.

1. Report by the President: Contact with other societies

V. Capasso contacted ESMTB on behalf of the International Society for Stereology (ISS). Capasso, also as the representative of ESMTB, attended the board meeting of ICIAM and will be invited to report at the ESMTB board meeting in Edinburgh. ESMTB proposed scientific board members for the next ICIAM Congress (decision forthcoming in April).

The EMS Committee for Raising Public Awareness of Mathematics (RPA) enquired if ESMTB has plans or existing activities in this direction and whether RPA could be of assistance. JP will contact Riitta Ulmanen of EMS. Mats Gyllenberg continues to be our

delegate to EMS, and will be invited to report during the Edinburgh board meeting.

Presently there is no plan for a joint conference with SMB but the Board intends to approach SMB for a joint conference in 2011. SMB's President or delegate will be invited to the Edinburgh board meeting.

JP briefly summarises the activities of the French speaking society SFBT, and is invited to write an article on SFBT for the Communications.

2. Report by the Treasurer

The two-volume Proceedings of ECMTB 2005 (Dresden), Mathematical Modeling of Biological Systems, have been published by Birkhäuser (see Communications #10, pp. 32-33).

The Computational cell biology minisymposium at ICIAM was well received, and the computational cell biology special issue of JMB will appear this year.

The ESMTB flyers and postcards have been printed. Communications #10 have appeared online.

ESMTB has launched a travel grant to support society members (especially student members) with a maximum of 500 Euros per grant (see Minutes of the Board Meeting in Torino, Communications #10, p. 6). In the first year (2007), 12 applicants out of 17 were granted.

Financial data
The 2005 and 2006 accounts have been audited. On 4 March 2008, the balance of the Society's bank account is 5,874 Euros; this sum does not yet contain the assets of the Dresden 2005 Conference (see Minutes of the 2007 Torino Board Meeting, Communications #10, p. 5).

Revenues in 2007 were from membership fees (9,855 Euros) and a refund from the ECMTB05 Proceedings (2,200 Euros), which total 12,055 Euros. Regular expenditures include the JMB subscription for members, printing and posting the Communications, flyers and postcards, the

EMS membership fee, domain registration for www.esmtb.org and moderate bank account fees (total of 4476 Euros paid in 2007; note that payment to Springer did not follow calendar years and was low within this year). In addition, the Society paid 8 travel grants (4,065 Euros, with 4 more grants already awarded but not yet transferred in 2007), and supported three schools (Sarajevo Biomathematics School 2,000 Euros, FEBSYSBIO 1,000 Euros, Biomathematics Summer School in Graz 1,500 euros). Total expenditures in 2007 were 13,041 euros.

Estimated revenues in 2008 are 10,000-12,000 Euros from membership fees. Next to the regular expenditures as above, the Reinhardt Heinrich Prize will be awarded to two winners (see Communications #10, pp. 10-16), and the Society will continue to support schools and award an increased number of travel grants to support young researchers in particular to attend ECMTB08 in Edinburgh.

Membership development
The Society membership has consolidated. In 2007, the Society had 225 paying members, 12% more than in the preceding year. Membership fees remain the same as in previous years and can be paid by bank draft transfer (preferred) or via PayPal.

Travel grants and the electronic InfoLetter are new membership benefits introduced in 2007, in addition to the continuing benefits of receiving the Journal of Mathematical Biology, reduced journal subscription rates, reduced conference fees, and receiving the Communications. The Reinhart Heinrich Doctoral Thesis Award, first awarded in 2007, and continuing financial support of schools add to further the goals of the Society.

3. Preparations for the General Assembly of ESMTB and for the elections of new Board members

The General Assembly will take place during the Edinburgh conference ECMTB08, on 1 July (Tuesday) 18:15 - 19:45. Preliminary topics include (cf. Communications #10, p. 5): Report by the president; Presenting the winners of the

first Reinhart Heinrich Doctoral Thesis Award 2007; Report by the treasurer; Discussion of prominent issues; Presentation of candidates for the election of 5 new Board members for the period 2009-2014. AD will send invitations to the General Assembly to all Society members.

The Board discussed a preliminary list of possible candidates for the elections of new board members. Candidates will be asked to write a brief profile of themselves, where they also describe how they intend to work for the Society. All members of the Society can propose a candidate by sending the name and the country of the suggested ESMTB member (plus the support by at least one other member) to the President, Wolfgang Alt (wolf.alt@uni-bonn.de) by 25th June 2008 (cf. Communications #10, p. 5). Nominations can also be made during the General Assembly in Edinburgh. Elections will be conducted by electronic ballot as in 2005.

4. Further preparations for the Edinburgh Conference ECMTB08

The Society will have a stand at the conference with information materials and online membership application available.

The Society intends to organise a public event promoting the Journal of Mathematical Biology during the Edinburgh conference. The new thematic special issue on Computational Biology will be presented along with the Society's new Perspectives in Mathematical and Theoretical Biology series. Catriona Byrne is to be invited to represent Springer Verlag. WA organizes this event with the help of CB.

Conference Proceedings
The six board members (WA, AD, CJ, EK, HW, HB) on the Scientific Committee of ECMTB08 will also act as co-editors of the Proceedings. Mark Chaplain as Editor-in-Chief negotiates with Birkhäuser to publish conference proceedings. Plenary speakers (with only one exception) have agreed to contribute a chapter, and all symposium organisers will be invited to contribute a review of the symposium topic. The Board reviews the list of accepted symposia and

decides to ask for the symposium descriptions in order to start structuring the Proceedings. EK contacts Mark Chaplain about details of the Proceedings and of the review process of contributed talks at ECMTB08.

5. Journal of Mathematical Biology and the Communications series

The Board reviews the new series "Perspectives in Mathematical and Theoretical Biology", printed in JMB as part of the Society's 2-page material (see Communications #10, p. 4). New titles and possible contributors are considered. EK will prepare draft guidelines for future contributors; series editor HB will be asked to finalize them. Short comments on previous Perspectives with author replies will be published in a Discussion Box. The Board intends to confer with the outgoing and incoming Managing Editors of JMB, other editorial board members present, and Catriona Byrne of Springer during the Edinburgh conference.

The 10th issue of the Communications (ECMTB, the Official Communication Bulletin of the Society) is in print and has appeared on the Society website www.esmtb.org. This celebratory issue is longer and contains e.g. the presentation of the first winners of the Reinhart Heinrich Doctoral Thesis Award. WA and AD are ready to continue to edit the Communications also after their term on the Board, and JP offers to join the Editorial board of the Communications.

CJ raises the question whether members could choose if they wish to receive the Communications in print or only in electronic form for convenience and to save costs. This would however cause extra administrative work, and a smaller number of printed issues would not proportionally decrease the printing costs; in addition, this would make the Communications less attractive for paid advertisements.

The Communications will now be published yearly (the Infoletter provides quick means of information exchange electronically). The

submission deadline for the 2009 issue of the Communications is 31 December 2008.

6. The Reinhart Heinrich Doctoral Thesis Award

In 2007, the Society awarded for the first time the Reinhart Heinrich Doctoral Thesis Award to the author of the best PhD thesis of the year. There were 11 applications for the first award, and the general quality was high. The two winners are Barbara Boldin and Antonio Politi (see Communications #10, pp. 10-16). The deadline for nominations for the 2008 award is 30 October 2008, proposals are to be sent to WA (wolf.alt@uni-bonn.de).

7. Schools

The Society supported the Graz Summer School and Workshop: Biomedical Modeling and Cardiovascular-Respiratory Control: Theory and Practice", held between July 22 and August 4, 2007. This was the first of a series of four schools and associated workshops organised within the Marie Curie Conferences and Training Courses Program (see Communications #10, pp. 27-28).

RB sent by email a preliminary list of organisers of future summer schools. EK adds the Helsinki Summer School on Mathematical Ecology and Evolution, a new bi-annual series of schools, of which the first will take place 25-31 August 2008.

The president of EMS informed us about their support of two series of summer schools organised by CIME and IMPAN, respectively, and enquired if ESMTB would be interested in a similar arrangement. In his email of 18 January 2008, RB called for a broad search for topics and organisers of summer schools instead of one (or few) long series (see the call for summer schools in the Society News in Communications #10). EK argues strongly for free competition for financial support of schools instead of long-lasting support of current picks. JP will contact EMS in this matter and report at the Edinburgh board meeting.

8. Bologna Process and Curricula for Mathematical Biology

A database of Mathematical Biology curricula is under construction. JP (with the help of CJ and AD) will make a webpage for this database such that users can insert entries into the database. The aim is to make the system with a core database available at the Edinburgh conference for members to see and add more entries.

JP's research group has worked out a program for cross-education between students of biology and mathematics: this will be described in detail in the Communications. WA calls for other examples of cross-education and possibility of exchange of materials. A forum to discuss mathematical biology textbooks would be helpful.

9. Diverse

There is some more discussion of the Public Awareness initiative of EMS and the growing awareness of the need for mathematics in the bioscience community. AD describes a couple of innovative outreach activities. JP will investigate existing outreach initiatives e.g. in connection with the Science Night programs.

The last meeting of the current board will take place in Edinburgh during the ECMTB08 conference. The following guests will be invited to report and discuss joint issues:

> *Mark Chaplain* (Conference organization and Proceedings)
> *Vincenzo Capasso* (relations to ICIAM)
> *Mats Gyllenberg* (relations to EMS)
> *Avner Friedman* (president of SMB)
> Managing editors of JMB
> *Catriona* Byrne (JMB)

The meeting ends at 17:00.

> *Eva Kisdi*
> *ESMTB Secretary*

Minutes of the ESMTB Board Meeting
Edinburgh, 1 July 2008

Meeting starts at 13:20.

Present: Wolfgang Alt (WA, chair), Carlos Braumann (CB), Rafael Bravo de la Parra (RB), Helen Byrne (HB), Andreas Deutsch (AD), Christine Jacob (CJ), Eva Kisdi (EK; minutes), Jean-Christophe Poggiale (JP), and Luigi Preziosi (LP).

Invited guests present during the first part of the meeting (items 1-3 of the Agenda): Catriona Byrne (Springer Verlag), Vincenzo Capasso (ICIAM), Mark Chaplain (organiser of ECMTB'08), Odo Diekmann (JMB), Avner Friedman (SMB), Mats Gyllenberg (JMB and ECM), Mark Lewis (JMB), and Nanako Shigesada (JSMB).

Absent with apology: Hans Westerhoff.

Welcome and Adoption of agenda

WA welcomes the Board and the invited guests; all introduce themselves briefly. The Agenda is accepted.

1. Joint issues with sister societies

ECMTB'11
WA informs the Board that Ryszard Rudnicki (Poland) could guide the organisation of the Society's next conference, ECMTB'11. CB contacts Rudnicki to finalize plans. (Note: Rudnicki is contacted immediately, and agreement is reached such that during the Assembly, ECMTB'11 is announced to take place in Krakow, Poland.) Since the ICIAM conference of the same year will be between 18 and 22 July 2011, ECMTB'11 is planned for the end of June / beginning of July to avoid collision of events. Sister societies SMB and JSMB are invited to arrange ECMTB'11 as a joint conference. Avner Friedman (SMB) is positive about the initiative and informs the Board that the board of SMB will meet and consider this invitation on 29 July 2008.

Summer schools
ESMTB currently supports a series of four summer schools organised by Mostafa Bachar, Jerry Batzel and Franz Kappel within the Marie Curie Conferences and Training Courses Program, held in Graz, Copenhagen, Rome, and Dundee (see Communications #10, pp. 27-28).

Mats Gyllenberg briefly describes the Helsinki Summer School in Mathematical Ecology and Evolution, organised this year for the first time and intended to become a biannual series of summer schools. This year's school is fully funded by the Academy of Finland, but for future schools, support from ESMTB and EMS is sought.

The funding scheme of EMS is discussed briefly. EMS has indicated its willingness to provide joint support with ESMTB; yet it appears from the EMS website that EMS has committed itself to prolonged support of two series of schools already chosen. Mats Gyllenberg will keep contact with EMS (Mario Primicero) concerning this issue. WA encourages applications for joint support of ESMTB and EMS for schools.

2. Journal of Mathematical Biology (JMB)

Scope and editorial board
WA briefly reviews possible expansions of topics covered by JMB and whether adding new members to the editorial board is warranted. Odo Diekmann and Mark Lewis agree that there is no pressing need for new editors (with the possible exception of an expert in physiology) and enlarging the editorial board is not desirable.

Perspectives in Mathematical and Theoretical Biology
HB reports that more input and a more proactive management is needed for the *Perspectives*; a time schedule will be set up for the authors who already offered to contribute in order to ensure uninterrupted publication of the series. Mark Lewis proposes to publish also commentaries on regular papers as part of the *Perspectives* series; the Board agrees for those which fit the scope and style of Perspectives (which is not the case for technical comments).

EK has prepared a draft Author Guidelines of the *Perspectives* and a short call for articles. Previously, a Discussion Box was planned for publishing reactions to earlier *Perspectives* (see minutes from the Evora board meeting on 8 March 2008). After a lively discussion, it is decided that such reactions will be published in the JMB series only if they live up to the standards of *Perspectives*; shorter comments and associated discussions will be possible online on the Society's website, where all Perspectives articles are also available. EK will reformulate the Author Guidelines accordingly.

State of JMB
WA briefly reviews the new special issues of JMB on computational biology. Catriona Byrne informs the Board of journal statistics: The impact factor of JMB is 1.489 and, more importantly, the articles are cited for a long time (half life >10 years). It is a very positive sign that the number of downloads has increased considerably (from 31,000 in 2005 to 57,000 in 2007), full text indexing in Google was one important factor in this increase. Mark Lewis asks the Society to further promote submissions to JMB as to its own journal, and he will write a corresponding call to be sent to all Society members.

3. Proceedings of ECMTB'08

Mark Chaplain reports that Birkhäuser is willing to publish the Proceedings of the Edinburgh conference ECMTB'08 in its book series Mathematics and Biosciences in Interaction. Plenary talks will fill Volume 1; all plenary speakers except Tyson have agreed to contribute. The call will be sent shortly to minisymposium organisers to write review articles based on their symposia for Volume II. The responsible Board members (WA, AD, CJ, EK, HW, HB) will help with the reviewing and editing process.

The Board thanks its invited guests for all their efforts and ideas. All invited guests leave at this point.

4. Report by the Treasurer and planned change of the Statutes

The Board reviews the Treasurer's Report handout prepared by AD, which every participant of the Assembly will receive (*see details of the report in the minutes of the Assembly*). Cash auditors A. Anderson and D. Morale have approved the Society's bank account data.

The Board feels that it is essential for the future of the Society that AD, together with his group at the Technical University of Dresden, will continue to support the Society in the many ways AD has done including the maintenance of the webpage and all other electronic services, and handling the Society records and finances. Unfortunately, a possible election candidate from the Technical University of Dresden has stepped back. In order to make it possible to elect AD for a new term on the Board now, and to make it possible to re-elect a board member who provides essential services possibly in the future, the Board will propose a change in the Statutes in the Assembly and will hold an electronic ballot over the new Statutes.

WA reads the proposed change of the Statutes. This text is not repeated here since the Assembly has considerably changed this proposal (see the minutes of the Assembly for the final text submitted to the ballot). The Board accepts the change of statutes by open voting (8 yes, 0 no, 1 abstention) and nominates AD as an election candidate (8 yes, 0 no, 1 abstention).

The Society will have two electronic ballots, first over the change of the Statutes (closing date 15 September) and then the elections of new Board members (closing date 15 October). If the new Statutes are accepted, JP will record the change (the Society is registered in France and is subject to French law).

There is a brief discussion about how the Society will finance those services in the future which it receives currently free of charge from the Technical University of Dresden.

5. Candidates for the new Board and preparation for the elections

Election candidates proposed by the Board are those listed in the minutes of the Assembly. During Assembly, members can nominate further candidates provided that the candidate is present at the Assembly and is a member of the Society. Nominations were also possible by email to the President before the Assembly.

6. Preparations for the ESMTB General Assembly (in the evening of the same day)

The Board agrees with the Agenda of the Assembly (see in the minutes of the Assembly). A report by JP is also planned for the Assembly (eventually did not take place) on the Mathematical Biology Curricula information system. JP is working on setting up an interactively updated database that contains Bachelor, Master and PhD programmes in Mathematical and Theoretical Biology in Europe.

7. Diverse

The Awarding Committee of the Reinhart Heinrich prize will have to be changed: WA will be replaced with the new President of the Society and Oleg Demin has to be replaced, perhaps with a colleague from the East European countries.

The present Board will not meet any more. The first meeting of the new Board is scheduled for February 2009. CB will convene the Board and JP will organise the meeting in Marseille.

HB will continue as editor of the Perspectives series in JMB and WA will continue to edit the Communications.

The Board expresses heartfelt thanks to the President and to all leaving Board members.

The meeting concludes at 15:50.

Eva Kisdi
ESMTB Secretary

Minutes of the
GENERAL ASSEMBLY of ESMTB
Edinburgh, 1 July 2008

Assembly starts at 18:30. Present are President Wolfgang Alt, all Board members except Hans Westerhoff, Mark Chaplain, host and organiser of the ECMTB'08 Conference, and about 50 members and interested visitors.

1. Mark Chaplain welcomes the Assembly, Wolfgang Alt thanks Mark Chaplain for hosting the Assembly and organising the conference.

2. Report by the President

Wolfgang Alt (President) briefly introduces Board members and their duties. In 2006-2007, the Board had also two East European counselors; unfortunately, the counselors have stopped working as Attila Csikasz-Nagy moved to Italy and Oleg Demin went unreachable. Summary of Board activities (meetings, activity via email). Brief highlights of membership data, travel grant, celebrations, 15th anniversary of the Society in 2006 (see Communications #8).

Review of the Society's tools for dissemination of information:
- Webpage at http://www.esmtb.org/ maintained by Treasurer Andreas Deutsch and his group at the Technical University of Dresden
- Infoletter sent monthly by email to all members by Andreas Deutsch
- Communications edited by Wolfgang Alt and published annually

The Society awarded the Reinhart Heinrich Doctoral Thesis Award for the first time on the previous day, 30 June 2008, in a special ceremony during ECMTB'08 in Edinburgh, where also the wife and son of Reinhart Heinrich were cordially welcome. The *ex aequo* prize winners of 2007 are *Barbara Boldin* and *Antonio Politi*. The award consists of either an invitation to deliver a special lecture during the ECMTB Conference or a travel grant to visit an event in Mathematical and Theoretical Biology according to the prize winner's choice. The deadline for

nominations for this year's Award is 30 October 2008.

The Journal of Mathematical Biology (JMB) is the official journal of ESMTB. Editors-in-Chief Mark Lewis and Odo Diekmann, together with Mats Gyllenberg (who will be Editor-in-Chief from 1 January 2009 replacing Odo Diekmann), will put out a special call for papers to all Society members. JMB will introduce supplementary online material where videos etc. can be placed. JMB is open for publishing more papers on various applications of Mathematical Biology. The Society introduces the series Perspectives in Mathematical and Theoretical Biology in JMB, edited by Helen Byrne with the help of Society Board members.

Concerning Summer Schools, the Society supported the successful application of Mostafa Bachar, Jerry Batzel and Franz Kappel (Univ. Graz) for four summer schools and associated workshops in the Marie Curie Conferences and Training Courses Program on "Mathematical Modeling of Human Physiological Systems with Biomedical Applications"; the four schools are held in Graz, Copenhagen, Rome, and Dundee over four years starting 2007. The Helsinki Summer School on Mathematical Ecology and Evolution is held for the first time in 2008 and expected to become a biannual series with future support from the Society. It is foreseen that ESMTB and EMS will jointly support summer (or winter) schools: Wolfgang Alt calls all members to organise schools in relevant areas.

The next Conference of the Society, ECMTB'11, will be held in Krakow, Poland, organised by Ryszard Rudnicki. The location was chosen to encourage participation from East European countries.

Questions and comments by members:
- V. Capasso proposes to include the Society membership fee into the Conference registration fee
- Ellen Brooks Pollock proposes to set up a mentoring system for ESMTB'11 as it was done in ESMTB'05 in Dresden, and volunteers to organise it.

3. Report by the Treasurer

As Andreas Deutsch (Treasurer) reported, finances of the Society have permitted a substantial increase in the Society's returns to its members, even though membership fees have not increased. Next to benefits established earlier, the Society supports summer schools, the mobility of young scientists in the form of travel grants, founded the Reinhart Heinrich Doctoral Thesis Award, and improved dissemination of information via the webpage and the monthly Infoletter.

Each participant of the Assembly receives a printed handout with detailed data on membership development, financial support to summer schools, travel support, the account balance and plans for fiscal year 2008, and means of spreading information about the Society, including a preview of the website at www.esmtb.org and the Infoletter.

Membership development: The number of paid members increased almost 2.5-fold between 2003 and 2007, and is expected to reach 275 in the current year. Most members are full or (reciprocal-full) members; institutional membership should be promoted. Bank transfer is preferred for paying membership fee within Europe, as this payment method is free of charge.

Support of summer schools: The Society supported five summer schools in 2005-2008 with individual sums between 1000 and 2000 euros and with an increasing total support per year. The supported events were the following: Biomathematics Summer School in Graz (twice, in 2005 and in 2007); Sarajevo Biomathematics School in 2006; FEBSYSBIO 2007; Biomathematics Summer School in Copenhagen (2008). The Society calls for applications for support for summer or winter schools in Mathematical and Theoretical Biology.

Travel support: Each successful applicant received 500 euros to help attending scientific events in Mathematical and Theoretical Biology, including ECMTB'08. The travel support was first awarded in 2007 to 12 young scientists; in

2008, there were 15 travel grants awarded. Young scientists are welcome to apply for future support.

Balance sheet: The Society expects ca 12000 euros as revenues from membership payments for 2008. Regular expenditures consist of payment to Springer for the members' copies of JMB, support of schools, travel grants, the Reinhart Heinrich prize; publishing the Communications and flyers; EMS membership fee; domain and bank account fees. The bank account balance on 31 May 2008 was 6 133 euros.

Information dissemination: The Society's website has improved along members' suggestions and serves as the main source of information. Articles in the series Perspectives in Mathematical and Theoretical Biology, published in JMB, are available for download, as are all issues of the monthly Infoletter.

Cash auditors A. Anderson and D. Morale have approved the Society's bank account data. The Assembly accepts the report unanimously.

Questions and comments by members:
- Ellen Brooks Pollock asks if membership without receiving a hardcopy of JMB should be introduced. Andreas Deutsch answers that this could be considered next year, when the Society's contract with Springer has to be renewed. Electronic downloads of JMB articles from Springers' website have doubled in the past 2 years, which hints that the contract could shift focus from hardcopy to electronic access.

4. Change of the Statutes

Wolfgang Alt (President) proposes changing the Statutes in order to allow, in a carefully restricted way, to re-elect a member of the Board for another term of six years without a break. The current Statutes explicitly exclude serving on the Board for more than six consecutive years. The immediate reason for the proposed change is the exceptional role that Andreas

Deutsch and his group at the Technical University of Dresden plays in supporting the Society via the webpage and all other electronic services, and in maintaining the Society records and finances. The Society receives generous and indispensable technical help from Dresden, but finding another Board member candidate who could continue after Andreas Deutsch's term is over has failed.

The proposed new text of the Statutes was opposed by Members primarily because it was judged to be too complicated and restrictive. After a lively debate, the Assembly agreed upon setting a maximum of 2 consecutive terms of 6 years each, with only one additional restriction, namely that no one can be President for more than 6 years. The proposed new text of the Statutes thus reads (changes in bold):

"A4.1. Only full members can be members of the Board. The Board consists of ten persons, elected by secret mail ballot, voted by the majority of the full and honorary members (one member = one vote). **Each Board member is elected for a term of six years.** The terms should overlap such that every three years five new Board members are elected. Board members cannot be elected for more than **two consecutive terms and the post of President cannot be filled by the same person for more than six years.** The term begins on January 1st the year after the election."

There will be an electronic ballot over the proposed new text of the Statutes; if accepted, the new Statutes will be effective from 1 January 2009. The closing date of the ballot will be 15 September 2008.

5. Elections of the new Board members

The election of 5 new Board members, also by secret electronic ballot, will be held after the ballot over the Statutes, closing on 15 October 2008.

The Board proposes the following election candidates (all have agreed to their nomination):

Andreas Deutsch (Germany)
-- ESMTB Treasurer
Miguel Herrero (Spain)
Peter Jagers (Sweden)
Vincent Jansen (England)
Daphne Manoussaki (Greece)
Geza Meszena (Hungary)
Andrea Pugliese (Italy)
Ryszard Rudnicki (Poland)

President Wolfgang Alt asks for more nominations from the Assembly but none arrives. (Nominations were also possible by email to the President before the Assembly.)

The profiles of the 8 candidates will be sent to all Society members together with the electronic ballot information by the end of September.

The following members will complete their term on the ESMTB Board at the end of 2008:

Wolfgang Alt (Germany)
Helen Byrne (England)
Rafael Bravo de la Parra (Spain)
Andreas Deutsch (Germany)
Luigi Preziosi (Italy)

Vincenzo Capasso thanks all Board members stepping down at the end of the year - all applaud. The Assembly ends at 19:50.

Eva Kisdi
ESMTB Secretary

Brief Announcements

Another Award has been presented to one of the former ESMTB Presidents:

Lappeenranta University of Technology awards
Prof. Vincenzo Capasso
Department of Mathematics, University of Milano, Italy
in recognition of your achievements in promoting European collaboration between academia, technology and society in the field of industrial mathematics, in areas including applied research, education development and network building
the Honorary Doctorate
of Science in Technology
Lappeenranta ,16 May 2008

Mathematical Models in Ecology and Evolution 2009
10-11 September 2009, University of Bristol

Following the great success of the inaugural meeting in 2007 at Sussex, the 2009 meeting will have a Darwinian flavour, in honour of the bicentenary of Darwin's birth, and 150 years since the publication of The Origin of Species. While not a mathematician himself, Darwin's ideas find natural expression in the form of mathematical models, allowing further development and refinement of the theory. MMEE 2009 will showcase the latest developments of formal models in evolution and ecology, and will include keynote addresses on the mathematical modelling of Darwin's key theories and insights from:

• Professor Rob Boyd, Department of Anthropology, University of California Los Angeles
• Professor Alan Grafen, Department of Zoology, University of Oxford
• Professor Hanna Kokko, Department of Biological and Environmental Science, University of Helsinki
• Professor Franjo Weissing, Department of Biology, University of Groningen

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Abstracts of no longer than 250 words should be sent to James.Marshall@bristol.ac.uk by June 12th 2009. The organisers welcome abstracts for talks and posters (please indicate your preference if you have one). For more details see
www.cs.bris.ac.uk/mmee2009
We look forward to receiving your abstract, and to seeing you in Bristol in 2009.

Best wishes, the conference organizers
James Marshall
John McNamara
Alasdair Houston

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Otto Wartburg International Summer School and Workshop on
"Regulatory (Epi-)Genomics"
29 August – 6 September 2009, Berlin

The aim of this program is to bring together researchers and students from different backgrounds (like molecular biology, bioinformatics, biological physics, mathematics) to discuss the mechanisms underlying transcriptional regulation.
The topic of this summer school is the connection between transcription factor binding events and epigenetic phenomena, like DNA methylation and histone modifications. We plan an integrated program, which comprises advanced level lectures during the first days and leads to topical research seminars in the second part. The schedule will leave sufficient time for discussion and interaction among students and lecturers.

Invited speakers:
Boris Lenhard - Bergen
Nick Luscombe - Hinxton
Erik van Nimwegen /
Mihaela Zavolan - Basel
Nikolaus Rajewsky - Berlin
Dirk Schübeler - Basel
Peter Stadler - Leipzig
Amos Tanay - Rehovot
Jerry Workman - Kansas City

Peter Arndt - Ho-Ryun Chung - Martin Vingron
Max Planck Institute for Molecular Genetics,
Berlin   http://ows.molgen.mpg.de

ECCS'09
European Conference on Complex Systems
21 – 25 September 2009, University of Warwick

For more information visit the web page at http://eccs09.info/

The conference will cover the full range of complex systems interdisciplinary research with the following tracks:

- **Policy, Planning & Infrastructure**
  Policymaking; Urban Planning; Internet; Transport & Power networks; Medical & Health Systems

- **Collective Human Behaviour and Society**
  Economics & Finance; Sociology; Psychology; Game Theory

- **Interacting Populations and Environment**
  Climate Change; Pollution; Demography; Ecology; Epidemiology

- **Complexity and Computer Science**
  Robotics; Grids, Clouds & Novel computing; Ubiquitous computing.

- **Fom Molecules to Living Systems**
  Self-assembly & self-organisation; Neuroscience; Systems Biology; Medicine & Physiology.

- **Mathematics and Simulation**
  Mathematics; Modelling; Simulation; Theoretical Physics

Also, several satellite conferences will take place. Expression of interest in participation can still be sent to markus_a_k@mac.com

For the organizers

Markus Kirkilionis (Organising Chair)
Francois Kepes (Programme Chair)

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There is a *Special Session on Biomathematics* and related topics at ICNAAM 2009
21 – 25 September 2009, Crete
see http://www.icnaam.org/

If interested, please contact
ezio.venturino@unito.it

Parameter Estimation in Physiological Models
Euro Summer School Lipari (Sicily-Italy) 13-26 September 2009

The 2009 Summer School is part of a series of 4 events from 2007 to 2010: each event consists of a summer school and associated workshop on modeling of human physiological systems with medical applications. The events are sponsored by the European Union under the program Marie Curie Conferences and Training Course.

AIM AND FOCUS
The Lipari 2009 summer school will be dedicated to the study of modeling from the side of parameter estimation (when the investigator presumes a functional form for the family of models representing the system, and is trying to identify the relevant parameter values) and from the side of qualitative study of the models, both deterministics and stochastic (with the goal of assessing congruency of behavior of the model with the known features of the experimental system under investigation). This school will address mathematical modeling and statistical estimation in a single framework; will tightly integrate methods and applications; and will provide understanding of the methodological problems in this field and a frame of reference for more individually focused study after-school.

COURSES
The school will be organized along the following main courses:
- Qualitative behavior of solutions (Yongwimon Lenbury, Franz Kappel, Pasquale Palumbo)
- Introduction to Inverse Problems (Thomas Banks, 4 units)
- A-priori model identifiability and robust identification (Eric Walter)
- Numerical Integration (Oscar Angulo-Torga, Luis Abia)
- ML Population Estimation (Marc Lavielle)

- Bayesian Estimation (Aristides Dokoumetzidis, Mathieu Kessler)
- Kalman filtering and Nonlinear Observer techniques (Alfredo Germani, Hien Tran)
- Parameter Estimation for Stochastic Differential Equations (Susanne Ditlevsen, Valentine Gentot-Catalot)
- Stochastic Geometry (Vincenzo Capasso, Alessandra Micheletti)

SCIENTIFIC WORKSHOP
The scientific workshop on "Mathematical modeling of the Glucose/Insulin system" will take place during the last two days of the school. It will cover the following topics:

Thursday Sept. 24th : "Modeling and control of glucose homeostasis"
- Morning, "Modeling": Giovanni Pacini, Andrea Mari, Jiaxu Li, Roman Hovorka
- Afternoon, "Control": Claudio Cobelli, Pierdomenico Pepe, Pasquale Palumbo, Jorge Bondia

Friday Sept. 25th : "Modeling insulin secretion"
- Morning, "Cellular level models": Jean-Claude Henquin, Alessandro Bertuzzi, Morten Gram Pedersen
- Afternoon, "Models for insulinemia oscillations": Niels Pørksen, Iva Tolic, Andrea De Gaetano
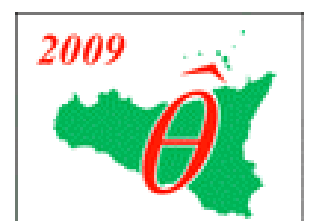
RESEARCH GROUP

Chair of Biomathematics   *Institute of Mathematics and Computer Science*
Ernst-Moritz-Arndt University   *Robert-Blum-Str. 2*
Greifswald, Germany   *D-17487 Greifswald*

http://www.math-inf.uni-greifswald.de/biomathematik

The research group, headed by *Volkmar Liebscher*, is part of the department (institute) of mathematics and computer science of Greifswald University. It is the core part of a curriculum in biomathematics, which is unique in this form among German universities. The main research field is the analysis of statistical and probabilistic methods with a view on applications in biology and medical sciences. In more detail, the group is concerned with statistical modeling for the analysis of molecular biology data, stochastic modeling, e.g. of regulatory networks and population dynamics, statistical image analysis and nonparametric statistics, combinatorial optimization, with applications to phylogenetics, and computability in general algebraic structures. Below, we want to illustrate the second and third topic only.
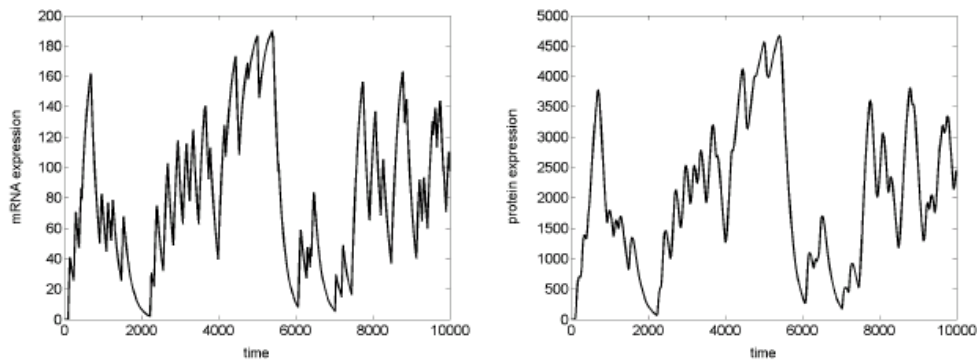

Figure 1: Simulation of an auto regulatory process by a piecewise deterministic process, left: time course of mRNA, right: time course of protein.
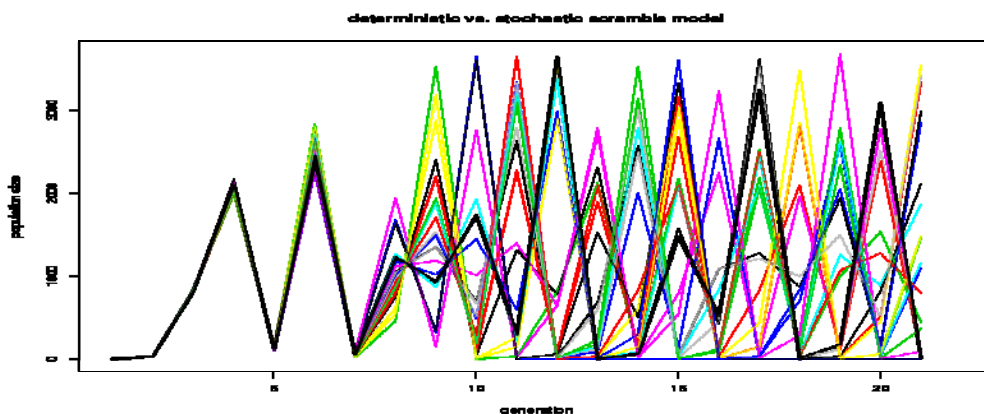

Figure 2: Simulation of stochastic Ricker model in the chaotic phase. One observes that stochasticity dominates the chaotic behaviour.

Stochastic Modeling

Our favorite stochastic models are Markov jump processes. In the figures we show a simulation from Markov chains derived from a stochastic version of the Ricker model and a piecewise deterministic process, a mixture of a continuous time Markov chain and ordinary differential equations in a model of auto regulatory gene expression (see Figs. 1 and 2). Other recent scenarios included hybridization on a DNA-microarray and dynamics of ions in axons.

Parsimony in Nonparametric Statistics

In statistics, a histogram is a graphical display of the frequency distribution of some measured data in form of a bar chart. Because of its easy interpretability it is a favored method of analysis.

But the construction of a histogram for a given real-valued data set is a difficult problem since it is not clear how to choose the number and width of the bins. We developed a fully automatic procedure that

$$\hat{F} \in argmin\{\Phi(F): F \in T\}$$

specifies the number and width of the bins in a satisfactory manner. Therefore we consider a tube   of piecewise constant boundaries around the empirical cumulative distribution function. As an estimate of the true but unknown distribution function one usual determines a minimal point, where   is a functional on the set of all distribution functions measuring smoothness or other complexity criteria. In our case we forced the estimator   to be piecewise linear and to have minimal number of knots, the derivative of   is used as an approximate density of the data. (See a typical example in Fig. 3.)
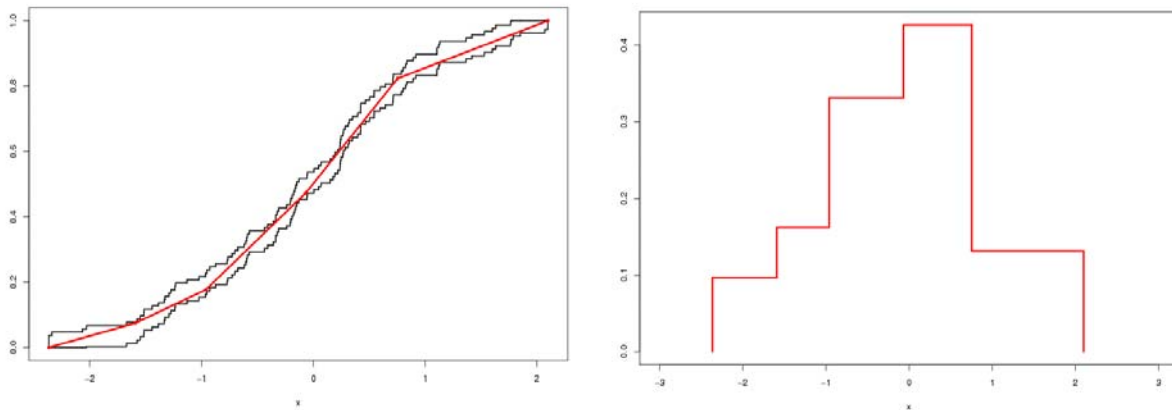

Figure 3: Tube and piecewise linear function with minimal number of knots (left). Resulting histogram (right).

Volkmar Liebscher
volkmar.liebscher@uni-greifswald.de

Reinhart-Heinrich Doctoral Thesis Award 2008

During the last year, until the required date October 31, 2008, the awarding committee obtained the applications from **14 young scientists**, who had recently finished their PhD thesis. The committee is impressed by the quantity and quality of the received applications. Again, the theses represent a broad and interesting range of actual research topics in our growing field of Mathematical and Theoretical Biology.

The committee pre-selected six candidates, whose complete theses then served as the basis for nominating an ordered list of up to 3 best candidates by each member of the committee. The ranking produced a unique ordering of the best three theses, so that the **awarding committee has the honor to declare**

- ***Thomas MAIWALD** (Germany)*

as winner of the Reinhart-Heinrich Doctoral Thesis Award 2008

The following next best theses were sent by
- ***Michel DURINX** (Belgium)*
- ***Antti TANSKANEN** (Finland)*

Please, read below the brief "laudationes" for each of these three young scientists and, further down, their thesis summaries. The other three pre-selected candidates were

- ***Fernando PERUANI**
  (Argentina/Germany/France)*
  see the abstract in *ECMTB#10, p. 22*
- ***Philip GERLEE** (Sweden)*
- ***Sheta BANSAL** (U.S.A.)*

Thanks to all for their gentle cooperativity!

Thomas MAIWALD
Thomas_Maiwald@hms.harvard.edu

Dynamical Modeling of Biological Systems

Advisors: Jens Timmer, A. Blumen (Freiburg)

This is a very impressive thesis with a large amount of detailed work and a very broad scope within modern Systems Biology. A lot of good old ideas are put together into a functioning framework of model supported data analysis. In particular, as the most impressive piece of work, Thomas Maiwald manages to develop (and describe) a comprehensive computer tool (Potters wheel) together with the underlying mathematical concepts and convincing applications. Moreover, he specifies this into a mathematical model for a typical biological process, namely the dynamics of the *TGFbeta* pathway. The strong advantage compared to the other theses is that he really uses experimental data to support his model and to estimate

parameters. This allows him to discuss subtleties of the model in detail and to extract conclusions, which would not be possible otherwise. We see here a very convincing example for the frequently demanded mutual interaction between experiment and modeling.

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Michel DURINX
michel.durinx@gmail.com

Life amidst Singularities

Advisors:
J.A.J. Metz, T.J.M von Dooren (Leiden)

Michal Durinx presents a thesis with really excellent results on adaptive dynamics along the lines of the theory that has been developed by the Metz school. He describes the dynamics of interacting and physiologically structured populations. Although heavily dealing with mathematics, he manages to explain concepts and mathematical derivations in a clear way and, moreover, to present results also in an artistic and sometimes humoristic way. One would have liked to see more comparison to experimental ("real world") data, but this might be hard to obtain within the usual framework of evolutionary ecology.

Antti Juho TANSKANEN
Antti.Tanskanen@iki.fi

Mathematical Models on the Impact of Noise and Dyadic Molecular Structures on the Properties of a Cardiac Myocyte

Advisors:
Mats Gyllenberg, Elja Arjas (Helsiniki)

Antti Juho Tanskanen offers significant contributions to help elucidate the impact of noise in calcium-induced calcium release and other noise sources on cardiac functioning and its medical consequences (for example, on polymorphic tachycardia) using a fruitful interplay between mathematical theory, simulations and experimental results. The thesis presents and induces a real understanding of the area. Moreover, originating from it, an impressive set of papers has appeared.

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## "Dynamical Modeling of Biological Systems"

Doctoral Thesis by Thomas Maiwald
(Extended summary)

This thesis is divided into five chapters concerning
(1) strategies to reduce systematic errors in quantitative Western blotting,
(2) the concept of in silico labeling to track the flux of unobserved species computationally,
(3) the development of PottersWheel, a Matlab toolbox for modeling and multi-experiment fitting,

(4) feasibility analysis and experimental design given realistic laboratory conditions, and
(5) modeling and investigation of the TGFbeta/SMAD signaling pathway.

The findings are based on close collaborations with the group of *PD Ursula Klingmüller* from the German Cancer Research Center in Heidelberg, especially *Marcel Schilling*, *Peter Nickel*, and *Sebastian Bohl*, with *Stefan Legewie* from the Humboldt University, Berlin, and *Clemens Kreutz* and *Stefan Hengl* in the group of *Prof. Jens Timmer*, University of Freiburg.
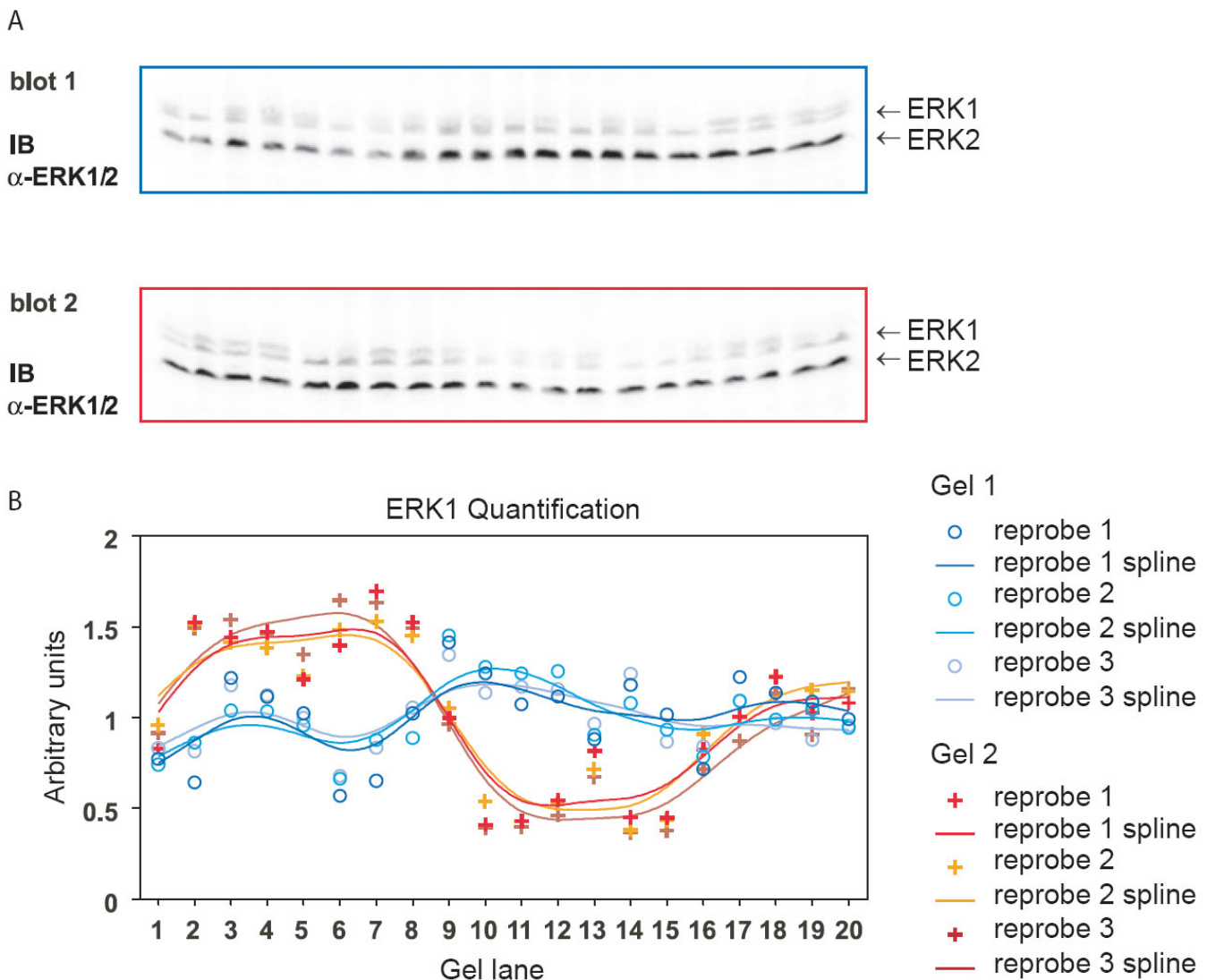

Figure 1: A constant amount of Erk1 is quantified by Western blotting using two gels. Instead of the expected constant line, strong lane-dependent correlations occur, heavily differing between the gels. In a time-course experiment with chronological gel loading, i.e. lane i corresponding to time-point i, the measurements could be mistaken for oscillatory behavior leading to wrong

(1) Western blotting is a widespread approach to determine the proteins in a given solution. Combined with chemiluminescent detection methods, quantitative results about the proteins' concentration can be obtained. However systematic errors during the blotting process significantly decrease the achieved data quality potentially leading to wrong conclusions about the measured biochemical system (Fig. 1) [1]. In the case of time-course experiments, the correlation structure of the error may lead to spurious dynamics of the investigated system. Therefore, randomized gel loading is suggested where consecutive time-points are loaded into distant gel lanes. This approach dramatically reduces the impact of the systematic error. Within a detailed simulation analysis it is demonstrated that randomization reduces the standard deviation of the measured data points to the true values by approximately 50%. Simultaneously, estimation of the blotting error using external or endogenous proteins with constant concentration and of a similar molecular weight as the protein of interest can be used for normalization. Since the blotting error is a local phenomenon, normalization may worsen the data quality if the normalizer protein does not migrate during electrophoresis in close vicinity to the protein of interest. Therefore, normalization is rejected, if the mean square distance of the data to a first estimation of the true trajectory is larger than for the original data. The normalization approach exploits that the blotting error is a continuous function of the gel lane and can be estimated by a smoothing spline in gel-domain. The protein of interest is often a continuous function of time or dosage. Then, the true trajectory can again be estimated by a smoothing spline e.g. in time-domain. In order to render possible a higher number of samples per experiment than lanes available within a single gel, a method to merge the data from several gels has been developed. All concepts have been implemented into the software GelInspector allowing other researchers to employ the normalization and merging procedures. The approaches were applied to experiments in stimulated cell lines or primary hepatocytes.

(2) Mathematical models of dynamic systems facilitate the computation of characteristic properties which are not accessible experimentally. We developed a novel approach called In Silico Labeling to calculate the half-life and sojourn time of species in arbitrarily complex non-linear reaction networks. To investigate a substance of interest, it is computationally labeled in order to track it on its way, e.g. through the cell. Application to a non-linear model of the STAT signaling pathway enabled the calculation of the time-dependent half-life. By this method, the total cellular sojourn time of the STAT protein in Epo stimulated BaF3 cells was determined to be 13 minutes, which is in agreement to a previously published nuclear sojourn time of 6.5 minutes.

(3) The program PottersWheel has been developed to provide an intuitive and yet powerful framework for data-based modeling of dynamical systems which can be expressed as sets of ordinary differential equations [2]. Its key functionality is multi-experiment fitting, where several experimental data sets from different laboratory conditions are fitted simultaneously in order to improve the estimation of unknown model parameters, to check the validity of a given model, and to discriminate competing model hypotheses (Figs. 2 and 3). Stochastic, deterministic, and hybrid optimization techniques can be applied in single fits or to generate fit-sequences which allow for parameter identifiability analysis [3]. Chi-square and Likelihood ratio tests rule out insufficient models and exemplify what can be concluded from experimental data given a certain noise level. Interactive design of external driving input functions helps to optimize the expected information of further experiments. Models are either created using text files comprising a chemical reaction network or differential equations or by drag and drop via a graphical model designer. Dynamically generated C MEX files of the differential equations and the use of FORTRAN integrators provide fast simulation and fitting procedures.
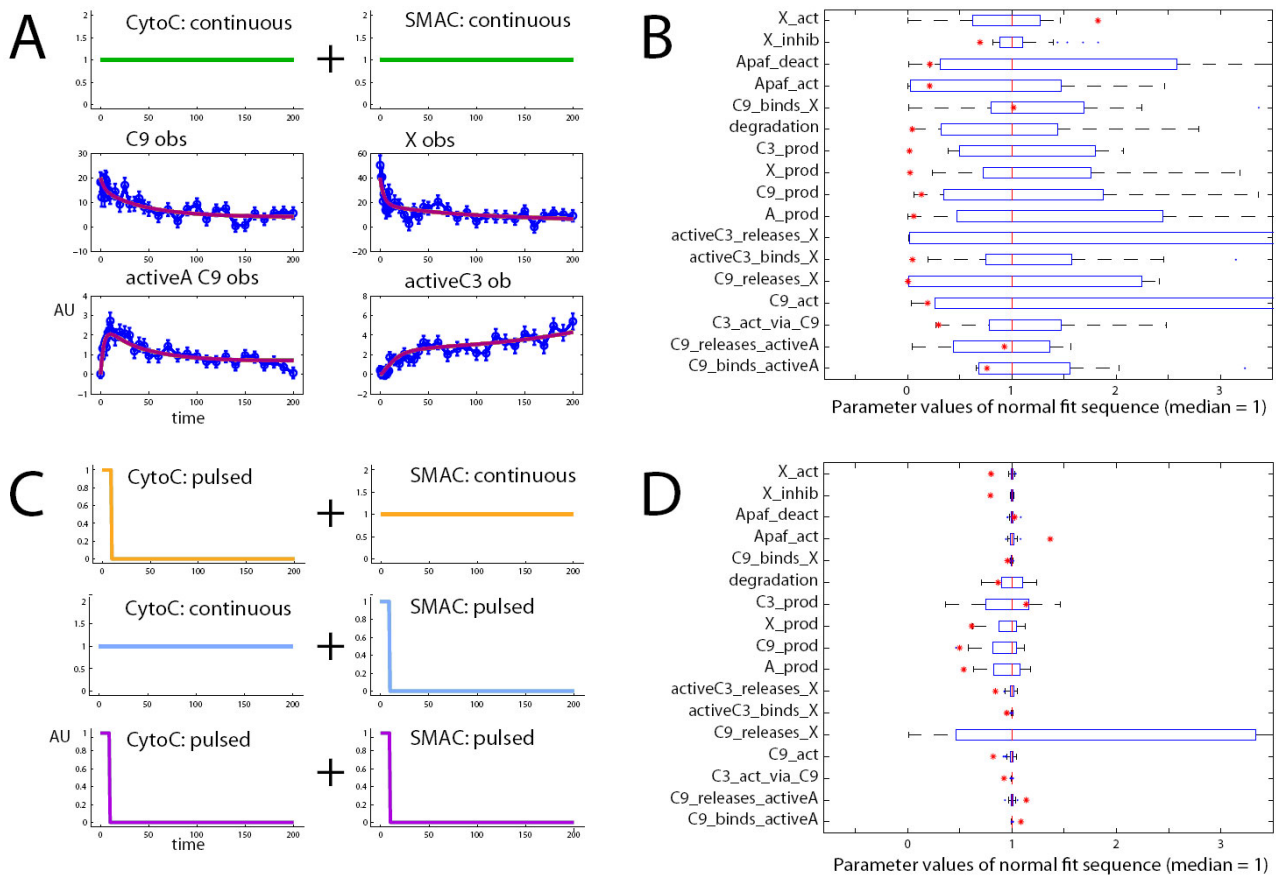
Figure 2: Application of multi-experiment fitting onto simulated data from an Apoptosis benchmark model. If only one experiment with continuous stimulations for each driving input player Cyto-c and SMAC (A, 4 observables, 10% rel. + 10% absolute error) is fitted 200 times with varying initial guess for the parameters, the distributions of the calibrated parameter values are rather broad: The parameters are not identifiable (B). C: Combination with additional three experiments with different input characteristics leads to significantly narrowed parameter distributions (D). Note that the distributions represented by the horizontal bars should not be mistaken for confidence intervals. Therefore, true values (red stars) may lie outside of the parameter distributions.
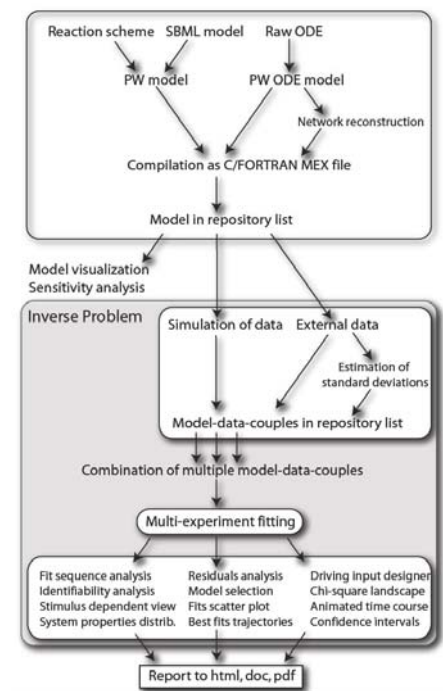
Figure 3: PottersWheel workflow. Either a biochemical reaction scheme is implemented as a PW model definition file, or an SBML model is imported. Alternatively, a raw set of ordinary differential equations (ODE) can be used to create a PW ODE model for which the reaction network can be reconstructed. Loading of the model into the repository list results in the compilation of a C/FORTRAN file. Then, the model can be used for model visualization or methods of the direct problem, e.g. sensitivity analysis. In order to approach the inverse problem, one or more data sets have to be attached to the model either by simulation or from an external data source. Optionally, the standard deviation of the data points can be estimated. Several model-data-couples can be combined for multi-experiment fitting. Afterwards, a variety of fit-based analyzes are available investigating for example the identifiability and confidence intervals of the calibrated parameters. Finally, each analysis can be appended into an automatically generated report saved as a html, doc, or pdf file.

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PottersWheel is designed as a Matlab toolbox, comprises 200.000 lines of Matlab and C code, includes numerous graphical user interfaces, and is available at www.potterswheel.de.

(4) An experimental design approach is suggested in order to discriminate competing biological hypotheses taking into account given laboratory constraints like measurement noise or technically feasible stimulations [4]. A minimal but sufficient set of most informative experiments is compiled to significantly distinguish the models under consideration (Fig 4). The key strategy is the use of multi-experiment fitting, where different stimulations, e.g. pulsed and continuous, are fitted simultaneously.
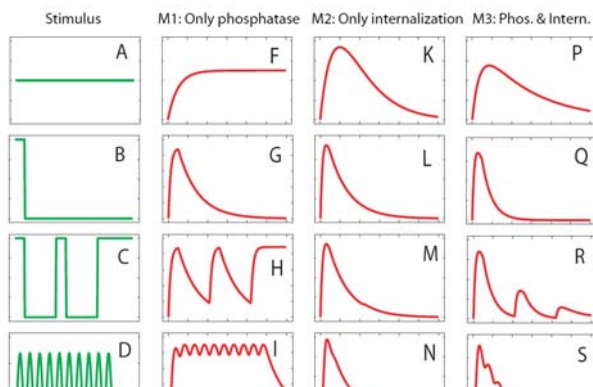
Figure 4: Impact of different stimulations (green) onto the time-course of the phosphorylated receptor (red) of three receptor models M1, M2, and M3. If experimentally feasible, stimulation C would be sufficient to distinguish the models from each other.

(5) The TGFbeta/SMAD signaling pathway is an important functional unit in the context of mitosis and cellular differentiation. Based on mRNA and protein data of primary hepatocytes, a mathematical model consisting of 57 reactions, 36 kinetic and 10 scaling parameters has been established. A total number of 46 data sets belonging to seven different experimental conditions was available, from which 32 were used simultaneously for model calibration and 14 data sets were only used for model prediction. Standard deviation of measurements was either determined based on independent measurements,

on estimated error models, or via spline-based moving variance calculation. Initial protein concentrations were not fitted as they are determined as basal levels. For this, numerical integration was started before time of stimulation, so that steady state levels were reached at t=0. In order to circumvent local minima, a two-step strategy was applied within PottersWheel. First, 2800 uniformly distributed positions in the space of physiologically reasonable parameter values were used as starting conditions. Fitting was applied with a deterministic trust region optimizer with a Chi-Square tolerance and a fit parameter tolerance of 1e-4, and a maximum of 600 iterations. Based on the best fit, a fit sequence with 1600 fits was applied, with perturbation of the calibrated parameter values before each fit. The final best fit had a Chi-Square value of 355. Applying a Chi-Square test and given $N = 506$ data points, the model hypothesis cannot be rejected ($p = 0.9998$), i.e. the model is compliant with the measurements.

[1] M. Schilling*, T. Maiwald*, S. Bohl, M. Kollmann, C. Kreutz, J. Timmer, U. Klingmüller *Computational processing and error reduction strategies for standardized quantitative data in biological networks* FEBS Journal 272 , 2005, 6400-6411, *equal contribution

[2] T. Maiwald and J. Timmer, *Dynamical modeling and multi-experiment fitting with PottersWheel,* Bioinformatics 2008, 24:2037-2043

[3] S. Hengl, C. Kreutz, J. Timmer, T. Maiwald *Data-based identifiability analysis of nonlinear dynamical models,* Bioinformatics 2007, 23, 2612-2618

[4] T. Maiwald, C. Kreutz, A. Pfeifer, S. Bohl, U. Klingmüller, J. Timmer *Dynamic pathway modeling: Feasibility analysis and optimal experimental design* Annals New York Acad. Sci. 115, 2007, 212-220

"Life amidst singularities"

Doctoral thesis by Michel Durinx
(Summary)

If traits change over evolutionary time through small steps only, are there patterns we can predict? Can we make general statements or does everything depend on the specific properties of each system? Michel Durinx's PhD thesis shows that a surprising amount is independent of the type of model used.

Adaptive Dynamics studies evolution driven by rare mutations with small impact. Whether or not a mutant trait successfully spreads is related to its invasion fitness, which is essentially the expected number of descendents; if it's less than one per mutant carrier then the mutation can never spread. The usual pattern is for the successful invader to replace its ancestor, but for a special type of traits both can coexist and continue to evolve. Thus the ecosystem's complexity increases, for example from having a single generalist herbivore to several specialists.

In this field, a wide range of model types is used, with caricatural or detailed life histories, with continuous or discrete time, with sexual or clonal reproduction, and so forth. Each type brings its own complications, especially in communities with multiple traits present. Durinx introduces a normal form from which it's seen that for sufficiently similar residents, the most important terms of the multitrait invasion fitness function can be determined from the single trait invasion fitness function, independent of the complexity of the population dynamics. At the end of the first part of the thesis, a recipe is given for simulating and analyzing arbitrarily complex evolutionary dynamics by studying a Lotka-Volterra system instead. In the second part, Durinx shows that there is a model type dependency in the third order terms of the multitrait invasion fitness, so that codim-1 bifurcations may or may not have different unfoldings. In the third part of the thesis, it is shown that allowing sexually dimorphic traits generically disrupts sympatric speciation scenarios, as evolutionary branching points become saddle points --- both sexes come to
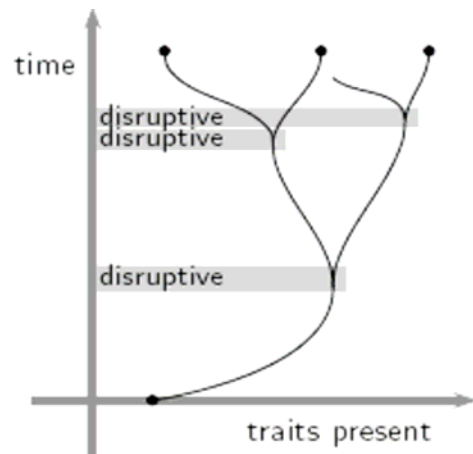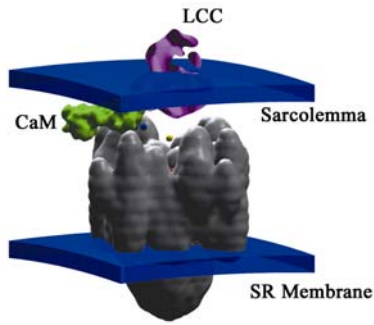

occupy a resource niche, preempting specialized subpopulations. The last part is another assessment of sympatric speciation models, as the probability of the evolution of assortative mate choice is compared to that of dominance evolution.

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"Mathematical Models on the Impact of Noise and Dyadic Molecular Structures on the Properties of a Cardiac Myocyte"

Doctoral Thesis by Antti Tanskanen
(Summary)

In cardiac myocytes (heart muscle cells), coupling of electric signal known as the action potential to contraction of the heart depends crucially on calcium-induced calcium release (CICR) in a microdomain known as the dyad. During CICR, the peak number of free calcium ions (Ca^{2+}) present in the dyad is small, typically estimated to be within range 1-100. Since the free Ca^{2+} ions mediate CICR, noise in Ca^{2+} signaling due to the small number of free calcium ions influences Excitation-Contraction (EC) coupling gain. Noise in Ca^{2+} signaling is only one noise type influencing cardiac myocytes, e.g., ion channels playing a central role in action potential propagation are stochastic machines, each of which gates more or less randomly, which produces gating noise present in membrane currents. How various noise

the impact of noise on CICR, computationally-efficient yet spatially-detailed models of CICR are developed. The results of this thesis show that (1) gating noise due to the high-activity mode of L-type calcium channels playing a major role in CICR may induce early after-depolarizations associated with polymorphic tachycardia, which is a frequent precursor to sudden cardiac death in heart failure patients; (2) an increased level of voltage noise typically increases action potential duration and it skews distribution of action potential durations toward long durations in cardiac myocytes; and that (3) while a small number of Ca^{2+} ions mediate CICR, Excitation-Contraction coupling is robust against this noise source, partly due to the shape of ryanodine receptor protein structures present in the cardiac dyad.

sources influence macroscopic properties of a myocyte, how noise is attenuated and taken advantage of are largely open questions. In this thesis, the impact of noise on CICR, EC coupling and, more generally, macroscopic properties of a cardiac myocyte is investigated at multiple levels of detail using mathematical models. Complementarily to the investigation of

FURTHER RECENT THESES

"Infection dynamics and parameter inference in models for seasonal and pandemic influenza"
Ph.D. Thesis by Antonella Lunelli, University of Trento, Italy, December 13, 2008

Advisor: Andrea Pugliese

The thesis is about the mathematical modelling of seasonal and pandemic influenza. A significant part is dedicated to the model developed to simulate the spread of a pandemic strain of influenza in Italy and to evaluate the effect of possible control strategies. The model has an SEIR (Susceptible – Exposed – Infectious – Removed) structure and a stochastic component. The population has been divided in classes according to the age and spatial distribution of the Italian population and a contact matrix has been estimated from census and transportation data. The evaluation of the effectiveness of possible control measures has been performed systematically, simulating a variety of scenarios, including different hypothesis on intervention efficacy and pandemic severity.

In the second part of the thesis particular attention is given to a specific aspect of pandemic modelling, i.e. the evaluation of the effectiveness of antiviral treatment. Implementing the same antiviral strategy in different models, it is shown that the evaluation of antiviral effectiveness can be very sensitive to model assumptions, including hidden assumptions implicit in the model structure. This finding stresses the need for carefully defining the structure of the models to obtain results useful for policy makers in pandemic planning.

In the last part a first analysis of seasonal influenza data, collected in Italy during the last epidemic seasons, is presented and integrated with the analysis of simulated data that helps to interpret the results obtained with real data. The study of seasonal influenza is useful both for obtaining estimates of key epidemiological parameters and for a better understanding of the transmission mechanism. This may help in controlling annual epidemics and in designing more realistic models for pandemic simulation. Possible future directions of this work are illustrated, which are worth exploring to better understand the dynamics of influenza.

HISTORY OF THEORETICAL AND MATHEMATICAL BIOLOGY

150 years – 'Origin of Species'
100 years – Concepts 'Gene' and 'Umwelt'

On the Role of Theory and Mathematics, 'Dynamics' and 'Functions'

Wolfgang Alt, Theoretical Biology, Bonn

In the current year we are celebrating Charles DARWIN (1809-1882) and his revolutionary theory of species descent by 'natural selection' published 1859 in his seminal book *"The Origin of Species"* that describes the phylogenic process of 'speciation' by preferred survival of individuals having more advantageous 'traits'. This quite simple idea, which in a refined version including random 'genetic variation' has generally been accepted as *synthetic theory of evolution* since more than 50 years, is based on the equally simple idea, that in principle such 'traits' are inherited to the progeny. While the nowadays orthodox view restricts this to 'innate' traits, even DARWIN subsumed the possible inheritance of traits that have been 'acquired' by an individual during its life time. This so-called 'Lamarckian principle' was the general view of the 18th and 19th century, thus it had also been formulated exactly 200 years ago by Jean Baptiste LAMARCK (1744-1829) in his seminal book *"Philosophie zoologique"* (Paris 1809). More important is that there he had offered an own materialistic (i.e. purely physico-chemical) theory of life ontogeny and phylogeny: The common basis for the individual epigenetic development and the formation of species is 'stepwise differentiation', whereby a mechanical interplay of physical factors (substances and 'fluida') depends on the current organic structure and, vice versa, induces new forms of organization and organic function, mainly in response to environmental conditions.[1]

It does not seem to be a curiosity of history, rather a more fundamental element in the development of theoretical biology that the 'materialistic' variant of the 'Darwinian' evolution theory, heavily supported and proclaimed during the 19th century by prominent bioscientists as Ernst HAECKEL (1834-1919), August WEISMANN (1834-1914) and Max VERWORN (1863-1921), was not accepted by the major biological community in the beginning of the 20th century, even after MENDEL's laws had been re-discovered and chromosomes been detected as the 'molecular' carrier of heredity. Indeed, the word *'gene'* was first introduced 1909, exactly 100 years ago, by the Danish botanist Wilhelm JOHANNSEN (1857-1927) in his book *"Elemente der exakten Erblichkeitslehre"* for defining a general theoretical concept of *'genotype'* of inherited traits as decoupled form the corresponding *'phenotype'*. Only this simplifying construction could enable the subsequent development of ***Mathematical Population Genetics*** by FISHER, WRIGHT and HALDANE around 1930, based on earlier mutation equilibrium formulas by PEARSON, HARDY and CHETVERIKOV, later augmented in KIMURA's neutral selection theory, and nowadays extended into general evolution theories of ***Adaptive Dynamics***. However, most of the theoretical biologist between 1900 and 1930 asked for more 'mechanic' or 'organic' explanations of the adaptation process itself: so the youngest student of HAECKEL, namely Julius SCHAXEL (1887-1943), who in 1919 launched the first monograph series *"Abhandlungen zur Theoretischen Biologie"* and who required a deeper research into the *'particular conditions'* of morphogenesis and epigenetic development, in addition to the *"acknowledged effect of selection"*[2]. Thereby he referred to the notion of 'conditional reproduction probability' for measuring 'selective advantage', as it had been emphasized by the mathematician Eduard STUDY

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[1] see the article by W. Lefèvre in: I. JAHN & M. SCHMITT (Hrsg.) "Darwin & Co. Eine Geschichte der Biologie in Portraits" Bd.I. München: Beck 2001. p. 194ff.

[2] J. SCHAXEL "Grundzüge der Theoriebildung in der Biologie". Jena ²1922. p.169

(1862-1930).[3] Until today the 'Evo-Devo' question remains, whether genotypic and phenotypic variation can be just explained by independent probabilities for genetic mutation and recombination, or whether they depend on epigenetic control processes in the developing organism, e.g. gene repair or expression control via (transiently inheritable) DNA methylation.

In his critical review of contemporary theoretical biology SCHAXEL did not only address the still ongoing *EvoDevo debate*, but also the initiation of *Ecology* as a desirable *"relational research (Beziehungsforschung) of potential and realized adaptations within the individual life time and life space"*. More pronouncing he claimed that the individual *"life space (Lebensraum) constitutes itself by the adaptations (Angepass-theiten)"*, so that internal life processes obtain their 'goals and fulfillness' through a dynamic interaction ('Wirkungszusammenhang') with something exterior of the individual.[4]

This concept of a constitutive dynamic relation between an living 'interior' and an 'exterior' had been introduced, again exactly 100 years ago, by the Baltic-German zoologist Jakob von UEXKÜLL (1864-1944) in his seminal publication *"Umwelt und Innenwelt der Tiere"* (Berlin 1909) and further elaborated in his book *"Theoretische Biologie"* (Berlin 1920). The key notion in UEXKÜLL's theory of environment ('Umwelt') is that each individual organism with its 'organic/dynamic structure (Gefüge)' lives, adapts and survives by applying various *'functional cycles of action and perception'*, thus constructing its own 'Umwelt' as *'world of acting (Wirkwelt)'* and *'world of sensing (Merkwelt)'*. Any object only appears as a 'counter-structure (Gegengefüge)' between the internally represented 'Wirkwelt' and 'Merkwelt'.[5] In his typical Kantian style he says: *"By sensing and acting, the subject re-*

crystallizes, as to say, all objects in its own interest and thereby shapes a secure 'Umwelt', whose center it is itself."[6] As we would formulate today: adaptation to environmental conditions is an active process with inner and outer 'feedback cycles' that are internally regulated by *'functional rules'* of self-sustainability. Moreover, according to UEXKÜLL morphogenetic development is regulated by *'construction rules'* realizing themselves via 'interactive play with gene impulses' – an early vision of today's *functional gene expression*.

This general (holistic <u>and</u> mechanistic) theory of organisms as *functionally self-regulating and self-sustaining dynamical systems*, formulated by UEXKÜLL ca. 70 years ago, earlier expressed by the botanist Johannes REINKE (1849-1931)[7], later by the zoologist Erwin BAUER (1890-1938) and the theoretical biologist Ludwig von BERTALANFFY (1901-1972)[8], resembles the concepts of 'autopoesis' by MATURANA and VERELA, but stays in contrast to the extremely 'one-way' oriented molecular concept of 'selfish gene' by DAWKINS. In my opinion, it should be much more recognized as proper base for further development and refinement of mathematical models in trying to capture the essential mechanisms of life. As a genuinely biological notion, *'functions'* must not be seen as mathematical 'one-way functionals' to be optimized (like 'energy' in physics or 'fitness' in evolutionary algorithms) rather as multiple feedback mechanisms (like in *renewal equations*, for example). Finally, when using non-linear *'dynamical systems'* for general biological network modeling (as it had been started by LOTKA in the 1920es), the physical concepts of 'forces' and 'movement' have to be replaced by the original notion of the Greek verb *'dynamai'* and the related old-high German verb *'zawen'* with its true organic meaning of *'to put to work, to fit, to be able, to succeed, to be valid durably'* – thus, future modeling in biocsiences might find some essential support from at least one century of theoretical biology.

[3] in a reply "Eine Lamarckistische Kritik des Darwinismus" *Zeitschr. Ind. Abstammungs- und Vererbungslehre* **24**: 33-70 (1920) to the Darwin critique pulished by O. HERTWIG "Das Werden des Organismus". Jena ²1918

[4] J. SCHAXEL "Grundzüge der Theorienbildung in der Biologie". Jena ²1922. p.331ff.

[5] See the article by T. RÜTING in *ECMTB#6*, p.11

[6] J.v. UEXKÜLL "Theoretische Biologie". Berlin ²1928. p. 185ff., p. 212ff.

[7] See my article in *ECMTB#3*, p.16

[8] See the article by R. SCHIMMING in *ECMTB#5*, p.11

PAST ACTIVITIES

SBMC 2008
Conference on Systems Biology of
Mammalian Cells
22 –24 Mai, 2008, Dresden

The annual conference on Systems Biology of Mammalian Cells (SBMC) is organized since 2006 by HepatoSys, a Federal German Research Initiative for Systems Biology of Hepatocytes. This year it took place at the Kulturpalast in Dresden a unique Baroque-style city with a fascination which has evolved throughout a turbulent history.

Systems Biology is one of the most prominent newly emerging interdisciplinary science areas: "Systems Biology brings order and sense to the flood of data coming from experimental research on molecules and cells with mathematical precision," summarizes Prof. Dr. Siegfried Neumann, Senior Consultant R&D at Merck, Darmstadt, and Vice Chairman of the HepatoSys Steering Committee.

The main aims of SBMC are to connect the academic scientific community and industry, to provide attendees with an almost unique opportunity to meet outstanding researchers and to promote the achievement of discoveries that benefit society.
This year more than 400 participants took this excellent opportunity to exchange ideas on technology trends and best practices and to discuss recent advances in Systems Biology with outstanding scientists.

The 2008 conference program was designed to cover different aspects of contemporary and prospective biological systems. The latest development in theoretical approaches, cutting edge technologies, basic cell and developmental biology as well as medical approaches have been presented and discussed during five different sessions.

In the following I would like to mention some among the interesting talks.

- **Session: New theoretical approaches and cutting edge technologies**
  Bela Novak (Oxford, UK) proposes that irreversible transitions in the cell cycle cannot be attributed to a single molecule or reaction, but derive from feedback signals in the molecular regulatory mechanisms and are consequences of underlying 'toggle-switches' which have the properties of bistability and hysteresis.

- **Session: Signaling networks**
  Jose M. G. Vilar's (New York, USA) recent research focuses on the TGF-beta pathway, which plays a central role in tissue homeostasis and morphogenesis. He applied computational modeling methods to show that coupling of signaling with receptor trafficking results in a highly versatile signal-processing unit. Such computational approach allows to suggest specific changes in receptor trafficking patterns that can lead to phenotypes that favor tumor progression.

  Mariko Hatakeiama (Yokohama, Japan) investigates the time course events of the intracellular signaling (phosphoproteome) and transcription (microarray) that are activated by the two ligands in MCF-7 cells, by performing experimental data-based modeling of ErbB signaling network and molecular dynamics (MD) simulation. His recent results indicate that ligand-induced intracellular signaling and early transcription are quantitatively regulated in a ligand dose-dependent manner.

- **Session: Self-organization and collective phenomena**
  Jennifer Lippincott-Schwartz (Bethesda, USA) describes how mitochondrial state and cell cycle progression at G1-S are linked. Exploiting live cell imaging strategies, her results suggest that the functional link between mitochondrial form and cell cycle progression at G1-S is dependent on the membrane dynamism and energy-producing properties of mitochondria.

- **Session: Developmental Pattern Formation**
  Frank Juelicher (Dresden, Germany) studies how shapes and dynamics of graded morphogen profiles regulate the expression of genes in target cells in a distance to the source depending manner. Nonlinearities provide the system with interesting properties. In particular, the robustness of the gradient profile as a function of the source strength is a natural consequence of nonlinearities.

- **Session: Biomedicine**
  Hans V. Westerhoff (Manchester, UK & Amsterdam, Netherlands) proposes an innovative approach based on systems biology and network-based methods to devise network-based strategies, identify or design corresponding drugs for "multi-factorial diseases' such as type-2 diabetes, obesity, heart disease, cancer and arthritis.

MTZ-foundation Award for Medical Systems Biology honored this year three junior scientists with the prize sum of 5000 Euro for the best theses on Systems Biology: *Niels Bluethgen* (Manchester, UK), *Thomas Eißing* (Leverkusen, Germany), *Julio Saez-Rodriguez* (Boston, USA)

Aside from speakers belonging to the leading representatives of research in the field of Systems Biology, the SBMC brought together internationally renowned authorities, who in their work have already successfully bridged the gap between industry and research at the „Pre-Competitive Meeting for Industrials". The objective of this event is to bring together potential co-operation partners in order to strengthen the collaboration between research and industry in Systems Biology projects.

Among them: Professor Igor Goryanin and Dr. John Jeremy Rice. Gorianyn, chair for Computational Systems Biology at the University of Edinburgh and director both of the Edinburgh Centre for Bioinformatics and of the Centre for Systems Biology in Edinburgh, Goryanin developed one of the first software packages for modelling and simulating cellular networks,
http://www.bioinformatics.ed.ac.uk/epe/.
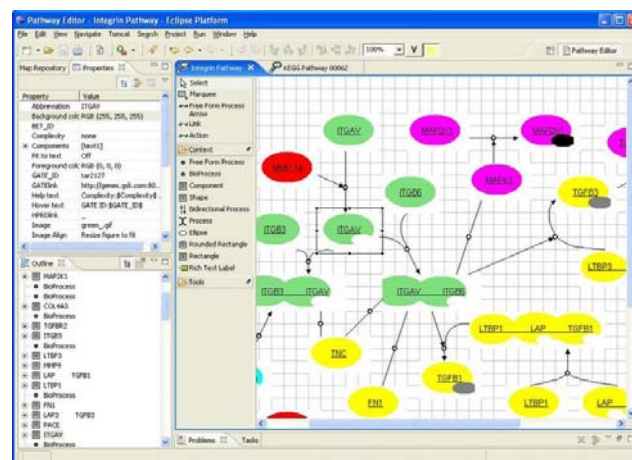
Rice works at IBM´s T. J. Watson Research Center in New York, USA. His objective is to link computer simulations with new methods of genome- and proteome-research. He is presently developing methods to deduce signal pathways of the cell from data collected in high flow -rate analyses.

SBMC 2008 has been a successful conference, marked by high quality participation, contacts that will lead to collaborations, and participants leaving with new ideas on technology trends and recent advances in Systems Biology.
Further information:
http://www.sbmc08.de/08/index.html

Perla Del Conte-Zerial
TU Dresden

4th Annual Vanderbilt Integrative Cancer Biology Center Workshop:
Current challenges in oncology, through the mathematical looking glass
2-6 August, 2008
Fields Institute, Toronto, Canada

The 4th VICBC workshop organized by Dr. *Lourdes Estrada*, Prof. *Vito Quaranta* and Dr. *Sandy Anderson* took place last summer at the Fields Institute in Toronto. This year it was part of an exciting Thematic Program on Mathematical and Quantitative Oncology coordinated by the Centre for Mathematical Medicine at the Fields Institute, the Vanderbilt Integrative Cancer Biology Center (VICBC) and the Ontario Institute for Cancer Research.
The main purpose of this annual workshop is to educate and train scientists to approach cancer biology problems. It facilitates communication across disciplines by developing a common language to bridge the gap between mathematics and oncology. Thus remarkable thematic lectures on cancer biology problems are given by clinical, experimental and modeling experts for each topic tackled.
A particular aspect of the workshop is the assignment of every participant to a working group, mixing experimentalists and theoreticians in biology, mathematics and computer science. Each group develops a model of a cancer-related phenomenon during the workshop and presents it on the last day.
This intense collaborative week takes place in a very friendly atmosphere, and results in many interactions between people with different disciplines and backgrounds. This is a wonderful experience! My recommendation: if you are interested in mathematical oncology then do not miss the next occurrence in summer 2009[*].

[*] See the future announcement on
http://www.vanderbilt.edu/VICBC/

Dr. Arnaud Chauvière
TU Dresden, Germany

9th International Conference on Systems Biology, ICSB 2008
22-28 August 2008, Gothenburg, Sweden

The ICSB series was initiated by Hiroaki Kitano in Tokyo in 2000 and has turned out to be equally attractive for experimental as well as theoretical scientists and students who share the interest in a quantitative and mechanistic understanding of biological systems. After the previous venues Pasadena, Stockholm, St. Louis, Heidelberg, Boston, Yokohama and Long Beach, ICSB this year drew more than 1000 participants to Gothenburg, August 22-28, and the local organisers around Stefan Hohmann were very well prepared (www.icsb-2008.org).
The plenary part of the excellent program focused on intracellular networks, cell regulation, multi-scale problems, disease mechanisms, biotechnology, genetic variability and evolution. After each plenary session, the invited speakers were kept busy answering questions at so-called speaker's corners, central places next to the poster area. Contributed talks were presented in 12 dedicated sessions, always three in parallel. During lunch breaks the panel discussions on industrial perspectives, funding programs and education aspects provided first hand contacts. Tutorials preceded the conference and it was followed by two days of satellite workshops. A novelty which was widely used were the "Arenas", similar to exhibition booths but for scientific initiatives like software projects, large scale projects, universities' master courses and so on. Especially the arenas of software projects like Cytoscape, Copasi and SBML developed into decent camps underlining the role of simulation and data integration for Systems Biology.

Lutz Brusch
Technische Universität Dresden

Continuing a success story, ICSB will reconvene.

For details, please see www.icsb-2009.org

The First Helsinki Summer School on Mathematical Ecology and Evolution

Linnasmäki Conference Centre, Turku, Finland 24-31 August, 2008

The first Helsinki Summer School on Mathematical Ecology and Evolution took place in the Linnasmäki congress centre in Turku, Finland. The school was organised by the biomathematics research group of the University of Helsinki under the auspices of the Finnish Centre of Excellence in Analysis and Dynamics Research generously funded by the Finnish Academy of Science. Around 40 participants, most of them PhD students from departments across the globe, attended the school and spent a week enjoying the pleasures of the Linnasmäki congress centre and the stimulating lectures by the distinguished speakers of the school. The topics of the school were: deterministic and stochastic population dynamics, evolutionary epidemiology, adaptive dynamics and species coexistence in variable environments. The school also awarded 8 ECTS credits for those participants who submitted the take home essays.

The aim of the school was to provide young researchers with and insight into several key topics in the ever growing field of mathematical biology. There was a good mixture of students with different backgrounds ranging from functional analysis to biophysics and the broad range of topics presented by different lecturers kept most of the students (interests) awake during the week of the school. The atmosphere of the school was very friendly and relaxed although the schedule of the school was quite tight which was potentially due to the high ambitions of the organisers. We had four lectures a day from Monday to Saturday, except on Thursday with a fifth one from 8pm(!), each lasting ninety minutes with frequent tea/coffee breaks for refreshment. I found many of the lectures interesting (especially to learn how to justify something by hand waving ☺) and the well prepared presentations of the lecturers helped to widen my horizon. I believe the school provided a good opportunity for junior researchers to grow professionally.

The self introduction session of the participants on the first day was highly enjoyable and turned out to be very useful in identifying common interests. In my opinion, one of the best features of the summer school was the free discussion session at the cafeteria. I believe that the personalised way of interaction with senior researchers during these discussion sessions and during meals turned out to be invaluable for many of us. Also the discussion sessions allowed for an exchange of ideas and different strains of viruses/bacteria across students. The concept and the potential of modelling conference-flu emerged but at the end this was left as an open problem.

Participants regularly gathered together either in the lobby or in the Finnish sauna frequently accompanied by a few bottles of cider what actually tasted better than expected, but maybe this was due to the highly enjoyable company of people. The above series of social events peaked last night at the organised boat trip to Loistokari island (and afterwards), where we had the opportunity to taste some excellent local food, as well as the Finnish Indian summer.

I was impressed by the organisation aspects and would like to thank Mats Gyllenberg (the director of the school) and his team making our fruitful stay in Turku very pleasant. Last but not least, I would like to wish good luck for the upcoming Helsinki summer (or winter) schools.

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Place of ECMTB'11
   Krakow, Poland

wANPE08: Workshop on Analysis and Numerics of Population dynamics and Epidemics models
15-17 December, 2008, Udine, Italy

The workshop wANPE08 on ``Analysis and Numerics of Population dynamics and Epidemics models'' took place at the International Centre for Mechanical Sciences (CISM) in Udine, Italy, on December 15-17, 2008.

The scientific committee, composed by Mimmo Iannelli (University of Trento), Andrea Pugliese (University of Trento), Rossana Vermiglio (University of Udine), was aiming to join together experts, researchers and PhD students for exchanging the most recent advances on the open problems in the contest of mathematical modeling for population dynamics and epidemics. The goal was to cover both theoretical and computational aspects in order to encourage and consolidate the collaboration between various mathematical disciplines, ranging from analysis to numerics through modeling.

The proposed targets have been fulfilled thanks to either invited and contributed talks of various nature (the final program and participant list can be seen at http://wanpe08.dimi.uniud.it).
Different modeling approaches (deterministic as well as stochastic differential equations, and also individual based simulations), have been presented. Their peculiarities have been stressed and the aspects where the numerical methods become a necessary aid have been pointed out. The most recent techniques, both direct and indirect, for the analysis of the asymptotic stability of equilibria have been discussed, too.
The participation has been large and over the initial expectation, confirming the deep interest of the international community on the proposed themes. During the three workshop days, several occasions of debate, exchange and confront (and also excellent gastronomic opportunities) have been created, hopefully bringing to new future scientific collaborations and further developments.

Andrea Pugliese
Trento, Italy

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Reinhart-Heinrich Doctoral Thesis Award

ESMTB announces the Reinhart Heinrich Doctoral Thesis Award to be presented annually to the best doctoral thesis from any area of Mathematical and Theoretical Biology.

Professor Reinhart Heinrich (1946 – 2006) began his research in theoretical physics, then moved into biochemistry and in 1990 became full professor and head of theoretical biophysics at the Humboldt University, Berlin. He is considered a forefather of the field that is now named Systems Biology, since he investigated various topics such as modeling metabolic networks and metabolic control theory, modeling of signal transduction networks, nonlinear dynamics as applied to biological systems, protein translocation, lipid translocation, vesicular transport, and even DNA repair.

Reinhart Heinrich was always searching for the principles behind observations, looking for different perspectives and connecting abstraction with biological evidence. In this way, he inspired numerous students, gave them insight and direction for future research in modern mathematical and theoretical biology, and organized a large number of memorable conferences.

Gratefully acknowledging his stimulating support of our interdisciplinary field and, in particular, his way of guiding students and young scientists, the Board of ESMTB has decided to annually award a Doctoral Thesis Award in honour of Reinhart Heinrich and his legacy in mathematical and theoretical biology.

After two years of broad response (with more than 10 applicants each) and successful selection of winners, see the documentation in the annual *European Communications (ECMTB No. 10 and 11),* ESMTB continues to **honour the annually best thesis** showing most impressing modelling ideas and useful innovative methods **with an award**. Responsible for the selection will be the

Awarding Committee consisting of:
> Wolfgang Alt
> Carlos Braumann (president of ESMTB)
> Andreas Deutsch
> Edda Klipp (former assistant to R. Heinrich)
> David Rand
> Andre de Roos

Award

The award comprises

- *an invitation to present a lecture at the next triennial ESMTB Conference or, alternatively, a travel grant by ESMTB for a scientific visit of the recipient's own choice.*
- *1 year of free ESMTB membership.*

The extended summary of the thesis receiving the award will be preferentially published in the next issue of ECMTB (*European Communications*) along with a brief laudatio.

Application

To be considered for this award, please send (by e-mail to wolf.alt@uni-bonn.de):

1. an *extended summary of your thesis* (about 3-10 pages)
2. a CV containing your current (or future) scientific affiliation.

Deadline for nominations is *30th October* of each year, by which time the nominated thesis should have received final acceptance by the doctoral granting institution. Candidates whose thesis is accepted after 30th October will be considered in the next calendar year. Names of potential applicants may also be suggested by any ESMTB member (by writing to wolf.alt@uni-bonn.de).

Shortlisted applicants will be asked to send their full thesis.

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The scheme on the front cover is Figure 3 (on *page 26*) in the extended summary of the thesis

"Dynamical Modeling of Biological Systems"
by Thomas Maiwald
Reinhart-Heinrich Prize Winner 2008