E MTB
Communications

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

In January 2011, our European Society for Mathematical and Theoretical Biology (ESMTB) has completed its 20th year of life – time to inspect its evolution during these two decennia of birth and growth, and simultaneously to elucidate the perspectives of its future development, now being an "adult" Society well embedded into a world-wide interdisciplinary network within the scientific community. One of its founders and later Presidents, *Vincenco Capasso*, presents his **Memories on the 20th anniversary of the foundation of ESMTB 1991** *(see page 28).* In the same spirit of simultaneous review and outlook is a letter by the current President, *Carlos Braumann (see **page 3**).*

There will be a good opportunity to jointly celebrate our "Society birthday" during the shortly beginning **8th European Conference on Mathematical and Theoretical Biology ECMTB'11** which soon takes place in **Krakow**, Poland, 28 June – 2 July 2011, and which hopefully can be attended by the majority of Society members and many other researchers, teachers and students in our field (see **page 13** and the Conference Website: http://www.impan.pl/~ecmtb11).

Moreover, the *General Assembly of ESMTB* will be held on Wednesday, 29 June 2011, 20 – 22 h in the announced location at the Conference site in Krakow. Candidates for the New Board elections will be nominated there.

During the Conference *(Friday, 1 July, 17-19 h)* also the *Reinhart-Heinrich Doctoral Thesis Prize 2010* will be awarded to Tina Toni, who is going to present a plenary lecture on here outstanding research work (see, from **page 14** on, the laudatio on her, followed by publication of the extended summaries of all 3 best theses).

Let us also mention one further important anniversary marking the historical revenue of our field: This year the seminal *Journal of Theoretical Biology* celebrates its 50th year of existence. You might want to have a look into the editorial of the January issue of JTB, volume 268.

The current issue does not contain any section on *New Books* or *Journals* though this was intended, also not the usual section: *Presentation of Working Groups.* Please think about how you as a Society member can contribute to the next issues, for example, by presenting your *Research Group*, or by writing reports on *Past Activities* (as conferences, workshops, summer schools) or by just sending your opinion, critique or suggestions.

Thanks to all for their continuing support.

The Editorial Board
June 2011

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Please send by e-mail any information, reports or other material for the next issue of Communications *(ECMTB # 14)* as soon as available, best before **March 31th, 2012,** to *Wolfgang Alt, Theoretical Biology (IZMB), University Bonn:* 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
This page can be used by members to pay their fee, or, by not-yet-members to register. Thanks!

ESMTB membership includes free electronic subscription of the official journal of the Society
Journal of Mathematical Biology
and reduced low subscription rates to the **print edition** (25 Euro) as well as for several other journals.

Please register at www.esmtb.org and send your payment of the required annual dues for 2011 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:
Bank: Commerzbank
Account Name: ESMTB
Account Number: 04 076 801 01
Bank Code No.: 850 800 00
SWIFT-BIC: DRES DD FF
IBAN: DE 18 85080000 0407680101
Bank Address:
Commerzbank, Dr.Külz-Ring 10
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Letter by the President
Carlos Braumann

Dear Colleagues and Members.

Two decades have passed since the foundation in 1991 of our Society at the Alpe d' Huez Conference. Since then the field of Mathematical and Theoretical Biology has undergone a huge growth, and the same happened to the Society's membership. While celebrating this 20th anniversary, it is a good occasion to look at current events and at future prospects.

At the moment I am writing, we are a few days away from our triennial Conference, the European Conference on Mathematical and Theoretical Biology (ECMTB 2011), now a major event in the scientific community, to be held in the beautiful city of Krakow in Poland. It promises to be a great scientific meeting, with participants from all over the world, and we are grateful to Ryszard Rudnicki and the Organizing and Scientific Committees for their efforts. I am particularly happy that the Annual Meeting of our sister Society, the Society for Mathematical Biology, is being held together with ECMTB 2011. We are already preparing ECMTB 2014.

Cooperation with our sister societies, with reduction in fees for double membership and cooperation in events, is very important to foster the progress of Mathematical Biology. Great progresses were made but we shall continue our efforts to further extend and deepen such cooperation.

Our official journal, the Journal of Mathematical Biology, published by Springer, has reached the highest standards and is certainly a reference in Mathematical Biology. Following our recent agreement with Springer, its distribution to our members is now mainly electronic. Although this has several advantages and is free of charge to our members, the printed version is also available for a nominal fee. The short section "Perspectives" is run directly by ESMTB under the co-ordination of Helen Byrne and plays a relevant role by showing the views of main researchers on profiling the current status of their areas and reflecting on the challenges that lie ahead. It also welcomes comments from the readers.

Recently, we have achieved an agreement with the European Mathematical Society concerning join annual EMS-ESMTB Summer Schools. The first one was the EMSTB-EMS Helsinki Summer School on Mathematical Ecology and Evolution, held in Turku, Finland, in August 2010. The second is the EMS-EMSTB-CIM Summer School on Dynamical Models in Life Sciences, to be held in July in Évora, Portugal and the 2012 Summer School will be announced soon. We welcome credible candidacies for the organization of future EMSTB-EMS Summer Schools.

But we also give support to other relevant Summer schools and to scientific meetings. There are also travel grants for young researchers, as well as reduced registration fees for our members at such events.

Our web page was recently remodelled and, judging from the comments we have received from the users, considerably improved. Our members receive regularly electronic *Infoletters* by e-mail.

The *European Communications in Mathematical and Theoretical Biology*, matches a long tradition with a constant endeavour to explore new avenues. As a recent survey has shown, it has become a must to our members.

The *Reinhart Heinrich Doctoral Thesis Award* distinguishes every year the best doctoral theses on Mathematical and Theoretical Biology. It is quite rewarding to see the growing number of candidate theses of very high quality from all

over the world, making the task of the jury increasingly difficult. This is a clear sign of the maturity achieved by our field.

Also ESMTB has achieved maturity, with steady progresses during its 20 year lifetime. It is a time to rejoice but also a time to look ahead at new challenges.

ESMTB Board members have six year mandates. Every three years, half the Board is replaced according to the result of the elections. Soon after the General Assembly to be held at Krakow during ECMTB 2011, we will have such elections by electronic vote and the elected new Board members will serve from 2012 to 2017. Please do not forget to cast your vote when the elections are called.

Having served the Board for six years, the last three of which as President, I will be stepping down soon and a new President will be elected by the Board. This is another good reason to look at the new challenges that the renewed Board and the whole Society may face in the near future.

Though ESMTB and its members have taken a prominent role in the development of Mathematical and Theoretical Biology as a mature scientific discipline, thus contributing to the progress of Science and of mankind, the role of ESMTB on teaching, apart from some articles in our Newsletter, has been quite indirect. But the progress of a discipline and its future prospects are highly dependent on our success in passing the message, the know-how and the enthusiasm to future generations and to the authorities responsible for the educational policies. Promoting the use of mathematical and theoretical modelling in the teaching of Biology and of biological applications in the teaching of Mathematics is one worthy task at all levels of the educational systems from basic to secondary and higher education. Promoting real interdisciplinary projects in teaching, in close connection with research environments, is an even more demanding task. We should have a forum for the discussion of those issues. We, individually and through ESMTB, should become more involved. We should help promoting student and teacher exchanges in the

area of Mathematical Biology. For that, it would be helpful to construct a data base of University programs on which Mathematical Biology plays a major role, a task the Board has planned but which has only taken the first preparatory steps. We have good cooperation with Mathematical Biology societies in different parts of the world, as well as with mathematical societies like EMS and ICIAM, although strengthening these ties with joint endeavours would be most desirable. However, we lack real ties with biological societies.

Mathematical and Theoretical Biology have a remarkable impact in the progress of society, in health, in natural resources management, in agriculture or in food industry, just to give a few examples. Policy makers and research funding agencies, particularly in the European Union, should be made more aware of that. So the industry and other current or potential users and their concerns should be listened and conveyed to our membership to help the progress of our discipline and its usefulness to Society.

These are just some ideas for the future of ESMTB. We should have no illusions. They are not easy to implement and will take a long time to achieve progresses comparable to the solid ground we have achieved on other issues. But now that we have reached such solid ground on our initial program, it is the right time to put our minds to work on the best ways to achieve these new goals and to get started, progressing step by step. Of course, this is a broad agenda for which the Board needs more than ever to call upon the cooperation of ESMTB members.

As a founding member, it was particularly rewarding to having had the opportunity to serve ESMTB by working at its Board for six years and actively participating in the collective effort that contributed to the progresses made. For that opportunity, I am grateful to the ESMTB members. I am grateful to my Board colleagues for the cooperative discussions on policies and for being such nice persons, always available to help a colleague on his/her tasks. We shall all be grateful to the Advisors to the Board in the last three years: Wolfgang Alt (former President, Editor of the Communications

and President of the RH Doctoral Award jury) and Ryszard Rudnicki (ECMTB 2011 organizer). Likewise, we shall all be grateful to the ESMTB members (some of which former Presidents or Board members) that have taken several tasks on behalf of ESMTB. The best thing, however, were the friendships that resulted and those shall not be thanked, but rather nurtured and enjoyed.

Hope to meet you soon, probably at ECMTB 2011.

Best regards
Carlos A. Braumann
ESMTB President

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Minutes of the ESMTB Board Meeting

Dresden, 7 November 2009

Meeting starts at 13:00.

Present: Carlos Braumann (CB, chair), Andreas Deutsch (AD), Miguel Herrero (MH), Christine Jacob (CJ), Peter Jagers (PJ), Eva Kisdi (EK; minutes), Daphne Manoussaki (DM), Andrea Pugliese (AP), Wolfgang Alt (WA, advisor), Ryszard Rudnicki (RR, advisor).

Guest participants: Catriona Byrne (Springer Verlag), Olga Chiarcos (Springer Verlag), Mats Gyllenberg (editor-in-chief of JMB), Christian Hoffmann (Technical University Dresden, ESMTB website editor).

Absent with apology: Jean-Christophe Poggiale, Hans Westerhoff

Round of welcome
CB welcomes the Board and the Guests participants invited to this meeting, and thanks AD for organising the Board meeting in Dresden. The Agenda is accepted with a minor change in the order of points, allowing Guest participants to leave early.

1. Journal of Mathematical Biology

Mats Gyllenberg briefly reports on the excellent status of the journal: JMB is highly regarded as the top journal of its field. Olga Chiarcos distributes a new draft of the Journal Publication Agreement between ESMTB and Springer Verlag.

Aims and scope; Mission statement
The description of the journal (*Aims and scope*) is discussed in detail. Compared to the version used earlier, the text is streamlined and the list of research areas is updated. It is agreed that the *Mission statement* of JMB, formulated by the Board, is included in the Journal Publication Agreement as an Attachment.

Perspectives
The 2-page/issue space of ESMTB is raised to 30 pages per year to accommodate the series *Perspectives in Mathematical Biology* edited by Helen Byrne and the Board. It is agreed that Mats Gyllenberg will be involved with veto right over submissions. EK has prepared the author guidelines to be placed on the Society website.

Special issues
Existing and possible future special issues of the journal are reviewed. It is agreed that special issues may originate from symposia but conference proceedings are not published by JMB.

Member benefits
The negotiations settle at the following agreement on mutual benefits between ESMTB and Springer Verlag:

Springer provides ESMTB members with
- free online access to JMB
- subscription to the print version of JMB at a special rate of 25 euros a year (to be ordered together with renewed membership)
- a discount of 20% on all mathematical biology books published by Springer during a two-month period each year (currently April-May)

ESMTB supports Springer via

- scientific guidance for JMB as specified in the Journal Publication Agreement
- promotion of Springer at ESMTB conferences (booth, advertising space)
- promotional space for Springer on its website
- publishing short Springer announcements in the InfoLetter and in the ESMTB Communications
- promoting JMB to Society members

Springer has initiated a Society Zone area on its website to facilitate social networks of scientists with similar interests; this may be of benefit to ESMTB members as well.

[Note added later: The Journal Publication Agreement, containing the above benefits in its main text and the revised text of the *Aims and Scope* as well as the *Mission statement* as Attachments, was signed by all parties in February-March 2010. A separate Agreement is signed allowing ESMTB members to subscribe to the journal *Theory in Biosciences* at a reduced rate, 79 euros a year.]

2. ESMTB website

Christian Hoffmann (Technical University Dresden) has designed and built a completely new website for the Society, which he shows to the Board. The Board congratulates him on an excellent job. Only minor modifications are proposed.

3. Report by the President

A brief report by President CB on the following:
- RR represented ESMTB in the last meeting of EMS. (In the future, Mats Gyllenberg will continue to be the Society's representative.)
- Vincenzo Capasso continues to be the Society's representative at ICIAM
- PJ and EK work with the organizers of the ESMTB-endorsed conference " The Mathematics of Darwin's Legacy" (Lisbon, November 23-24, 2009).

4. Report by the Treasurer

Membership development: The membership of ESMTB increased by 25% in the 2-year period from 2006 to 2008. In 2008, the number of members was 258. (Because membership payment is collected throughout the year, with a significant number of members paying only at the end of the year, the current year's figure is not yet available.)

ESMTB support of schools: Since 2005, ESMTB supported six summer schools with a total of 7000 euros. In the current year, the Lipari International Summer School on BioInformatics and Computational Biology received a grant from ESMTB.

ESMTB travel support: In 2009, five young scientists received travel grants (500 euros each).

Balance: In the period 1 January – 31 October 2009, ESMTB's revenues were a total of 5460 euros. Members' fees are the only revenues in 2009; unfortunately the 2008 ECMTB conference did not result in financial assets due to the high rental costs paid for the premises. Expenditures include the ESMTB Communications (printing and mailing), travel grants, support of schools, EMS membership fee, promotion (fliers, posters). On 31 October 2009 (before paying fees to Springer), the Society's balance is + 28132.67 euros. Note that a large amount is due to the financial success of ECMTB 2005, and the revenues are moderate in comparison.

Communication, information, promotion: The ESMTB website is fully renewed. The ESMTB InfoLetter is published monthly and distributed electronically. Fliers and posters are printed for promotional purposes.

5. ESMTB Member survey

AD reports that 100 members (out of ca 250) responded to the membership survey carried out earlier this year. The survey shows that the services provided by the Society, especially the website and the InfoLetter, are well received. Reciprocal membership with other societies (except SMB) is low, which is somewhat

surprising since ESMTB does have reciprocal membership with many of the national societies; this possibility may need to be better advertised. A blog may be started on the Society website to provide an online forum for discussions, CJ will investigate the possibility.

6. Report by members of the Board

MH reports on the funding situation: unfortunately the ERC has no grants the Society could apply for. The possibilities for raising money from foundations and private sponsors are discussed, especially in connection with the upcoming ECMTB 2011 conference.

EK reports the scientific program of the ESMTB-endorsed conference " The Mathematics of Darwin's Legacy" (Lisbon, November 23-24, 2009) and circulates the detailed plans for the first EMS-ESMTB summer school, "The Helsinki Summer School in Mathematical Ecology and Evolution" (Finland, August 22-29 2010). The Conference Proceedings from ECMTB 2008 (Edinburgh) will not appear as an independent volume, therefore it is proposed to publish the submissions as a special journal issue. EK will negotiate with the journal editor; WA, AD and Helen Byrne will act as editors for the special issue.

WA reports on the status of the Communications. Reports from working groups and accounts on mathematical biology education would be very welcome. The Communications will continue to be published also in print.

7. Preparations for the ECMTB 2011 conference in Kraków

RR outlines his plans of the structure of the conference and its budget. The details are thoroughly discussed.

8. Policy on supporting summer schools and conferences

CB proposes to set up a standard application procedure for financial support provided by the Society to summer schools and conferences. AD argues that the current demand can still be handled more informally; yet a call could be publicized e.g. with a November deadline for the next year's events, and with a list of information the Society requires to be able to make a decision.

In response to the invitation from EMS to organise joint summer schools in the series *Applied Mathematics Summer Schools*, ESMTB will organise an annual series of EMS-ESMTB schools. Mats Gyllenberg will be the representative of EMS for this series [this information was confirmed by EMS after the Board meeting]. In even years, the Helsinki Summer School on Mathematical Ecology and Evolution will be the EMS-ESMTB school (the 2010 edition of this series becomes the first EMS-ESMTB school, see above). In odd years, ESMTB invites separate organisers; DM will be responsible for this.

9. Diverse

The Board delegates CJ to the Ethics Committee of EMS.

The Board will continue its practice of frequent email discussions so that Board members will make and approve decisions quickly inbetween Board meetings.

The Board convenes next in Hania, Crete, in October 2010, the meeting will be organised by DM.

The meeting ends at 19:50

Eva Kisdi
ESMTB Secretary

Minutes of the ESMTB Board Meeting

Hania, Crete, 23 October 2010

Meeting starts at 9:45.

Present: Carlos Braumann (CB, chair), Andreas Deutsch (AD), Miguel Herrero (MH), Christine Jacob (CJ), Peter Jagers (PJ), Eva Kisdi (EK; minutes), Daphne Manoussaki (DM), Andrea Pugliese (AP), Ryszard Rudnicki (RR, advisor, organizer of ECMTB'11).
Guest participant: Mats Gyllenberg (editor-in-chief of JMB) during the discussion concerning the Journal of Mathematical Biology; teleconference with Olga Chiarcos (Springer Verlag).

Absent: Jean-Christophe Poggiale, Hans Westerhoff, Wolfgang Alt (WA, advisor, absent with apology but sent a detailed report and suggestions to the Board on the Communications, the JMB Perspectives, ECMTB'11, the Reinhard Heinrich award and the upcoming elections)

The Agenda is accepted.

1. Report by the President

CB briefly summarizes the main activities of the past year (via frequent email contacts, the Board members were continuously updated and took actively part in the decisions):

- The new contract with Springer Verlag is signed (see the minutes of the Board meeting in Dresden, 7 November 2009).
- The first ESMTB-EMS summer school has taken place in Finland, 22-29 August 2010 (separate report by EK)
- preparations for ECMTB'11 in Kraków are underway (see #5 below)
- Issue #12 of the Communications is published
- The ESMTB-endorsed conference "The Mathematics of Darwin's Legacy" has taken place (Lisbon, November 23-24, 2009)

- The decision on the next Reinhard Heinrich Award concluded
- Collaboration with EMS and ICIAM continues
- The new website is operational

2. Report by the Treasurer

Cash auditors Barbara Boldin and Rafael Bravo de la Parra have approved the Society's financial data of 2008 and 2009.

Membership development: In 2010, the Society has an estimated number of 250 paying members (because payments are received throughout the year, the definitive number can be given only at the end of the year). The new contract with Springer does not seem to harm membership development.

ESMTB support of schools: Since 2005, ESMTB supported nine summer schools, workshops and conferences with a total of 10000 euros. Of these, three events took place in 2010: CMPD3 in Bordeaux; Solstice & Automata 2010 (Nancy, France), an international conference on discrete models of complex systems and on cellular automata; and the First International workshop on Differential and Integral Equations with Applications in Biology and Medicine (Karlovassi, Greece). Supporting schools and conferences has an appreciable effect on attracting new members to the Society.

Travel grants: Relatively few (14) applications have been received in 2010, 12 applicants were given a grant of 500 euros each. This possibility is open to junior members of the Society.

Balance: From 2010 onwards, the Society does not have to pay a yearly fee to Springer. This ensures that financially the Society is in balance. Current revenues are exclusively from members' dues, expenditures include the Communications, support of schools and conferences, travel grants, ICIAM and EMS membership fees, the flier, website and account fees, and the last (2009) payment to Springer. On 15 October 2010, the balance was +27616 euros.

Other points: The InfoLetter receives 5-10 submissions per month and according to the member survey, it is well received. The flier has got a new, attractive design, and a new company produces it cheaper than before.

The member survey has received 120 responses, the data are summarized and briefly analyzed.

3. Report by Board members and Advisors

EK mediated between the Board and Acta Biotheoretica to publish the Proceedings articles from the ECMTB'08 Edinburgh conference as a special issue. The issue, edited by AD, Wolfgang Alt and Helen Byrne, is currently in print[1].

EK reports on the first ESMTB-EMS summer school held in Finland on mathematical ecology and evolution (22-29 August 2010; see separate report *on page ??*). The 2011 school "Dynamical models in life sciences" will be held in Portugal, organised in collaboration with Centro Internacional de Matemática by Fernando Carapau, Fabio Chalub, Francisco Santos and Nico Stollenwerk, and the 2012 school will again be in Finland.

DM describes the possibilities to organise a future school in Greece; also other possible venues are discussed.

CJ informs the Board about the work of the new ethics committee of EMS, where she represents ESMTB; a major initial undertaking is to write a code of conduct.

CJ has investigated the possibility of starting a blog on the Society website, which could serve for example as a discussion forum associated with the JMB Perspectives. A dedicated editor is vital, perhaps a young colleague could serve as editor.

MH has checked ERC funding possibilities, unfortunately nothing is open to scientific societies or large conferences.

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[1] Appeared as the December 2010 issue of Acta Biotheoretica

WA (in written report) calls for more active support of the Communications. The next issue should appear well in time before ECMTB'11, and should contain the preliminary programme of ECMTB'11, reports by individual Board members, a new section of book reviews, and a historical overview celebrating the 20 years of the Society. Lack of publisher's advertisements in the last issue is a concern.

PJ summarizes new initiatives in Sweden, a report should be solicited for the Communications.

4. Perspectives in Mathematical Biology series in JMB

Helen Byrne continues to be the editor of the Perspectives series, but she needs help especially in soliciting articles and in disseminating information about this new forum; AP will work with Byrne. The visibility of the series and its connection to ESMTB is discussed in detail.

5. ECMTB'11 in Kraków

RR gives a detailed report on the preparations to the ECMTB'11 conference (joint with SMB). Announcement, minisymposia, schedule, fees, mentoring, abstracts/proceedings are discussed in detail. Wolfgang Alt and Vincenzo Capasso will help the Board to organize the celebration of the 20th anniversary of the Society during ESMTB'11. Plans for the celebration include inviting founding members of the Society and honouring past Presidents.

6. Reinhard Heinrich Award

André de Roos has left the Award committee, which now consists of CA, WA, AD, David Rand and Edda Klipp. WA proposed to invite one more member (the Board discusses candidates), and proposes that he would step down after one more year.

AD (as member of the committee) reports that in the last year, 17 applications arrived and the quality of theses is very good. In previous years, often two winners were awarded the prize. WA therefore proposed selecting three candidates to

award e.g. free Society memberships, and one first prize winner each year. After discussion, the Board decides that the prize can be given "ex-aequo" also in the future, but prefers to maintain just one prize with the possibility of the jury distinguishing (with no prize) up to two other candidates.

7. ECMTB'14

Planning starts for the 2014 conference of the Society. A leading proposition is to hold the next conference in Spain, MH comments on this possibility. Other possible countries are Italy or Sweden (AP and PJ to investigate, respectively).

8. Elections of new Board members

The election of the new Board will take place after the ECMTB'11 conference, the list of election candidates will be finalized during the Assembly of the Society. The Board prepares a list of possible candidates recommended by the Board to the Assembly. Although the new Statutes make it possible for a current Board member to run for a second term, no outgoing Board member will do so at this time.

9. Diverse (dealt with before Mats Gyllenberg joins the meeting and the teleconference with Olga Chiarcos takes place).

A request for financial support arrived from a workshop to be held in 2011 in Casablanca; the decision is deferred for insufficient information.

The next Board meeting will take place in Kraków, the day before ECMTB'11.

10. JMB

Teleconference with Olga Chiarcos, Springer Verlag

Olga Chiarcos presents her report on year 2009 of JMB. The total number of submissions (275) continues to be high, there is an increasing number from China and India. The rejection rate was 74%. Online publication within 2-3 weeks from acceptance. Online access to JMB occurs

mainly via package deals with institutions. Full-text downloads remained very high in 2009 (ca 108,000); changed policy of Google caused problems in 2010, Springer works on solutions. Table of Contents requests (2700 in 2009) also grew. The impact factor increased to 1.695 in 2009 (the 5-year impact factor is 1.971), and JMB is ranked by ISI as 18/29 in mathematical and computational biology. Author satisfaction is good (60% very satisfied, another 28% satisfied).

CB asks that Springer updates the Aims and Scope of JMB according to the text agreed in the previous Board meeting (Dresden 2009); that the Perspectives articles indicate their ESMTB origin also in the Table of Contents; and that occasional announcements placed by ESMTB are also visible via the Table of Contents webpage[2]. RR discusses with Olga Chiarcos about Springer's book exhibition and the promotion of JMB and BMB during the ECMTB'11 conference.

Discussion with Mats Gyllenberg, editor-in-chief

Perspectives: Mats Gyllenberg proposes to submit articles for the Perspectives series through the Editorial Manager system of JMB, which he will then assign to Helen Byrne as Perspectives editor. Procedures are discussed to ensure that the decision remains with the Board (with possible veto from the editor-in-chief). EK asks that the submission page links to the Author Guidelines specific to the Perspectives.

Special issues: Two special issues are underway, one in honour of Simon Levin (edited by Alan Hastings) and one on biological imaging (edited by S. Siltanen and M. Lassas). Standards are the same as for regular papers.

Other points: Mats Gyllenberg informs the Board that plagiarism (including also self-plagiarism) is becoming a serious concern. Springer provides the editors with software

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[2] Already done by Springer, except that listing announcements in the electronic ToC is technically impossible for it would interfere with electronic abstracting and indexing (e.g. by ISI).

(Authenticate) to uncover plagiarism, which results in a 5-year ban from all Springer journals and the author's University being informed. Disputed authorship (including coauthors not being informed) and undeclared conflicts of interest also pose problems. DM proposes to put ethical guidelines on the JMB website (MH: which authors must explicitly accept), and raises the question how to help authors with language problems (plagiarism may happen simply to obtain grammatically correct text). JMB's current practice is that although the copyeditor corrects language mistakes, this capacity is naturally limited and papers are rejected for bad English.

CJ asks about the referees: JMB receives two (quite often 3) reviews of papers admitted to the review process, except when the editor himself serves also as one of the reviewers. There are ca 2000 referees in the pool.

CB thanks DM for organising the Board meeting in Crete. The meeting ends at 18.05.

Eva Kisdi
ESMTB Secretary

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EMS-ESMTB summer school series launched with

The Helsinki Summer School on Mathematical Ecology and Evolution 2010
22-29 August, Turku, Finland

ESMTB is pleased to announce a new series of summer schools launched jointly with the European Mathematical Society. The series started with the 2010 edition of The Helsinki Summer School on Mathematical Ecology and Evolution.

Five highly distinguished professors gathered with 45 selected participants to spend the last week of August in Finland. The simple outline of the Helsinki summer schools fills the week with a high speed, concentrated program: five graduate-level courses covering subjects of mathematics outstandingly important in the field and subjects of biology of current interest. The 2010 program featured lectures on evolutionary game theory by Karl Sigmund (University of Vienna), bifurcation analysis by Yuri Kuznetsov (University of Utrecht), stochastic differential equations by Carlos Braumann (University of Evora), population genetics by Reinhard Bürger (University of Vienna) and stochastic epidemic models by Tom Britton (Stockholm University). The program was opened with a lecture by Mats Gyllenberg (University of Helsinki), the director of the school.

I cannot disguise my enthusiasm when writing about the lectures! Starting from basic principles, Karl Sigmund took his audience to the very frontiers of research on cooperation. He covered parts of his new book (*The calculus of selfishness* is a must-read!) and included even unpublished results. Yuri Kuznetsov's lectures unfolded increasingly complex bifurcation structures with the kind of exceptional clarity that uniquely conveys the beauty of mathematics. Coming to the perhaps hardest topic of all, Carlos Braumann explained stochastic differential equations going into depth while staying absolutely clear; we all have learnt a lot, myself included. No mathematical biologist should have his degree without learning population genetics, and I believed I knew its basics reasonably well; but Reinhard Bürger taught us many new things, including results proven in the past 1-2 years, and organised it all into crystal clear lectures assuming no prior knowledge of the subject. The field of epidemiology has seen the rise of stochastic models that can handle realistic small-scale structures like contact networks and households, thus departing from the ideal but often less realistic case of infinitely large, well-mixed populations. This change of view is a major breakthrough and for this reason I was very happy to have Tom Britton lecturing on stochastic models of epidemics.

We were fortunate to have an excellent audience to the excellent lectures. The school received 150 applications (a 50% increase from the previous edition of the Helsinki school), of which we could invite 45 students. The

participants were diverse with respect to their research interests, but as a common basis, everyone had at least an undergraduate degree or equivalent education in mathematics; the school expressly defined PhD students of mathematics as the target audience. On the first day, everyone introduced himself with a few-minute presentation of his research, and everyone put up a mini-poster to help people of similar interests to find each other. The evenings found us socializing around the sauna and the traditional Finnish evening snacks, giving plenty of time for discussions.

From the school's name, don't leap to the conclusion that it takes place in Helsinki – it is in Turku. The Linnasmäki Congress Centre has been an excellent partner providing every service for the school, making it very much worth to move 160 km or so westward along the coast of Finland. The financial support of the Academy of Finland via the Centre of Excellence in Analysis and Dynamics Research enabled the school to cover all local costs so that participation was free of charge.

For some participants, the school did not end Saturday night with the boat trip to the archipelago and dinner on a tiny island among the bonfires lit as Finns part with summer. The lecturers offered topics for take-home essays, and participants whose essays passed at least four of the five courses are awarded 8 ECTS credits. As the school itself, the essays required hard work. But whether or not they took this extra mile, the feedback from the participants was always highly positive. I am deeply grateful to the lecturers and also the participants for making this school such a success.

Now we are looking forward to the 2011 school in Evora, organised under the auspices of the Centro Internacional de Matemática (Portugal) by Fernando Carapau, Fabio Chalub, Francisco Santos, and Nico Stollenwerk on *Dynamical models in life sciences*. In 2012, the series comes to Finland again, with a school dedicated to speciation models and organised in collaboration with the ESF Programme Frontiers of Speciation Research.

The possibility is now open for all to propose and organise a summer school endorsed jointly by ESMTB and EMS, placed in the EMS framework of *Applied Mathematics Summer Schools*. My experience is that this effort is hugely rewarding. The Board of ESMTB welcomes proposals for the 2013 school and onwards!

Visit the home page of the 2010 school: http://wiki.helsinki.fi/display/huippu/mathbio2010

Eva Kisdi, organizer

Helsinki Summer School on Mathematical Ecology and Evolution 2010

8th European Conference on Mathematical and Theoretical Biology 2011

Kraków, June 28 - July 2, 2011

http://www.impan.pl/~ecmtb11/

The triennial meeting of the European Society for Mathematical and Theoretical Biology (ESMTB) and the annual meeting of the Society for Mathematical Biology (SMB) will be held together.

Key topics

- Immunology
- Cancer
- Bio-imaging
- Cellular Systems Biology
- Cell and Tissue Biophysics
- Neurosciences
- Molecular Dynamics
- Medical Physiology
- Regulatory Networks
- Developmental Biology
- Epidemics
- Education
- Conservation Biology
- Bioengineering
- Population Dynamics
- Ecosystems Dynamics
- Evolutionary Ecology
- Population Genetics
- Genetics and Genomics
- Bioinformatics and System Biology
- Miscellaneous

We will have about 770 talks of different types and 130 posters

The deadline for late registration and on-line payment is *June 17-th.*

Information about the conference venue, maps and the transport information can be found at http://www.impan.pl/~ecmtb11/index.php?file=venu.html .

Three different trips are organized on Thursday afternoon, see http://www.impan.pl/~ecmtb11/index.php?file=sche.html&sub=socp.html)
and the registration to these trips is available on-line ONLY! (it will not be possible during the conference).

Best regards and looking forward
to see you in Krakow

*Organizing Committee
of ECMTB 2011*

Reinhart-Heinrich Doctoral Thesis Award

Reinhart-Heinrich Doctoral Thesis Award 2010

For 2010 the awarding committee obtained applications by *8 young scientists*, who had recently finished their PhD thesis. Again, as in previous years, the theses represent a broad and interesting range of actual research topics in our growing field of Mathematical and Theoretical Biology: Regulatory Networks (by *Pavol Bokes*, *Christoph Kaleta* and *Tina Toni*), Computational Neurobiology (by *Bernhard Englitz*), Sensitivity Analysis for Dynamical Models (by *Matieyendu Lamboni*), Tissue Remodelling (by *Václav Klika*), Epidemiology and Ecosystems Theory (by *Sebastian Funk* and *András Szilágyi)*. Thanks for all the applications!

Out of these the committee pre-selected five candidates, whose full theses were probed. They obtained their promotion in various branches at European universities:

Sebastian FUNK (Mathematical Biology)
      Royal Holloway Univ. London
Christoph KALETA (Bioinformatics)
      Univ. Jena, Germany
Václav KLIKA (Mathematical Modelling)
      Technical Univ. Prague
András SZILÀGY (Biological Physics)
      Eötvös Univ. Budapest
Tina TONI (Theoretical Systems Biology)
      Imperial College London

A ranking concluded the final decision: The awarding committee nominates as *winner* of the RH Award 2010

- ***Tina TONI** (MIT Cambridge, USA)*

and, equally, on rank two

- ***Sebastian FUNK** (Zool. Society, London)*
- ***Václav KLIKA** (Tech. Univ., Prague)*

Tina TONI
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MIT Cambridge, MA 02139-4307, U.S.A.
ttoni@mit.edu

Approximate Bayesian computation for parameter inference and model selection in systems biology

Curriculum Vitae:

I obtained my undergraduate degree in Mathematics at the University of Ljubljana, Slovenia, and a Masters degree in Inter-disciplinary Mathematics at the University of

Warwick, UK. My master thesis examined probabilistic models of gene regulatory networks, focusing particularly on Bayesian networks.

For my PhD I worked on systems biology of cellular signaling processes. My main focus was the development of statistical and computational tools that allow us to learn the structure and parameters of signaling networks from biological time-course data. In particular, I have been working with Approximate Bayesian Computation algorithms based on Sequential Monte Carlo (ABC SMC), which I applied to dynamical systems in prokaryotic and eukaryotic signal transduction and stress response pathways.

I defended my PhD thesis in March 2010, and from July 2010 on I am working as a Wellcome Trust-MIT Postdoctoral Fellow at the Department of Biological Engineering at Massachusetts Institute of Technology with Professor Bruce Tidor and Professor Ron Weiss.

Laudatio:

Tina Toni prepared an extremely valuable thesis with ground-breaking ideas for biological model selection and parameter estimation in complex dynamical systems. The chosen approach is to combine mechanistic modelling by (stochastic) differential equations with Bayesian inference for estimation of model parameters including credibility intervals, in order to distinguish among a set of competing models and assess their quality.

This challenging task required significant theoretical and practical difficulties to be overcome. Tina Toni introduces three novel algorithms belonging to the class of approximate Bayesian computation (ABC) methods, which can evaluate posterior distributions without having to calculate likelihoods. The favored algorithm is based on a sequential Monte Carlo framework providing computational advantage over other existing ABC methods.

This new generation of data evaluation methods is applied to a wide variety of biological systems such as prokaryotic and eukaryotic signalling and stress response pathways, gene regulatory networks, and infectious diseases. Posterior parameter distributions are analysed in order to gain further insight into parameter sensitivity and sloppiness of the selected models.

One of the principal articles that arose from this thesis has been published in the *Journal of the Royal Society Interface*: "Approximate Bayesian computation scheme for parameter inference and model selection in dynamical systems". It has already received a significant number of citations and is widely seen as a landmark work in the field.

Beyond the impact of her published work, in her theses Tina Toni has put together a very coherent and well-explained theory, together with a series of elaborated examples, displaying significant insight and innovation in her work.

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Extended Summaries of Theses

Tina TONI

Approximate Bayesian computation for parameter inference and model selection in systems biology

Mathematical modelling has become an important tool in the biological sciences. Due to the overwhelming complexity of biological systems, it is not straightforward to determine the structure of suitable mechanistic models. Moreover, the majority of parameter values are unknown, and despite technological advances, parameters are often difficult to measure experimentally. Therefore, statistical and computational techniques are needed to distinguish the good models from the unsuitable ones and to estimate unknown parameters.

In this thesis we present a novel algorithm for parameter estimation and model selection of dynamical systems. The algorithm belongs to the class of approximate Bayesian computation (ABC) methods, which can evaluate posterior distributions without having to calculate likelihoods. It is based on a sequential Monte Carlo framework, which gives

our method a computational advantage over other existing ABC methods.

The algorithm is applied to a wide variety of biological systems such as prokaryotic and eukaryotic signalling and stress response pathways, gene regulatory networks, and infectious diseases. We illustrate its applicability to deterministic and stochastic models, and draw inferences from different data frameworks. Posterior parameter distributions are analysed in order to gain further insight into parameter sensitivity and sloppiness.

The comprehensive analysis provided in this thesis illustrates the flexibility of our new ABC SMC approach. The algorithm has proven useful for efficient parameter inference, systematic model selection and inference-based modelling, and is a novel and useful addition to the systems biology toolbox.

Background and summary

Recent advances in high-throughput experiments in the biological sciences coupled with the increase in computing power provide a good basis for developing new, more realistic quantitative and predictive mechanistic models of complex systems. To develop and utilize such models, we require the values of all parameters, such as kinetic rates of mRNA production, protein turnover and post-translational modifications (e.g. phosphorylation or dimerization). Due to technological restrictions or high cost, it is, often, impossible to measure all the parameters experimentally. This provides the motivation for the first topic of this thesis - the development of an algorithm for parameter inference of dynamical system models. While parameter estimation has recently become a well studied topic, relatively little attention has been given to the choice of model(s) to use for inference. Despite this, the question "What is the best model to use?" is probably the most critical question for making valid inference from the data [1], and therefore we make model selection the second topic of this thesis.

This thesis focuses on statistical inference of dynamical models, in particular ordinary differential equation and stochastic master equation models. We develop and apply an inference algorithm for estimation of dynamical model parameters and model selection on a set of candidate models. Throughout the thesis we give examples from population and systems biology. In the last two chapters we tackle two currently challenging problems in systems biology: inferring mechanisms of eukaryotic phosphorylation dynamics and modelling stress response in bacteria. In approaching these problems we have worked in collaboration with two experimental groups. The starting premise is to obtain a detailed understanding of the underlying biological problem and to extract the necessary biological information to be included in the model. We then continue by developing a set of candidate models and use ABC SMC to infer the parameters and perform model selection based on experimentally collected data. We finish by analysing the developed models and simulation results.

This thesis takes an interdisciplinary approach to current challenges in systems biology. We combine methods from the areas of dynamical systems, deterministic and stochastic modelling, statistical inference and Petri nets, and go on to suggest future experiments to our experimental collaborators. Our main motivation has been to develop a statistically sound approach that is applicable to real biological problems, which are inherently stochastic, involve unknown parameters, and where most of the experimental data is noisy and incomplete.

Outline by chapters

In Chapter 1 we discuss the current challenges in quantitative dynamic modelling in systems biology and introduce the thesis contents.

In Chapter 2 we give an overview of existing approaches for parameter estimation and model selection. We will only provide a brief overview of the material required for the understanding of the following chapters.

In Chapter 3 we develop ABC SMC (Figure 1), a computationally efficient algorithm for parameter estimation, which is based on approximate Bayesian computation and sequential Monte Carlo [1].
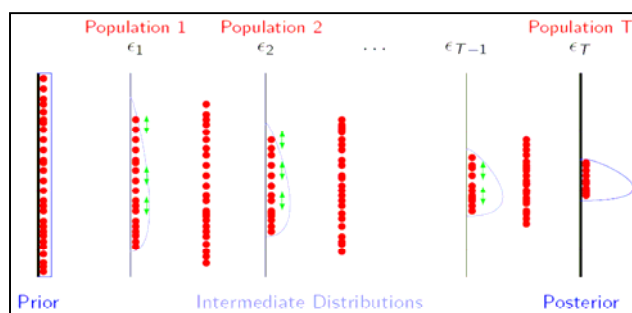
Figure 1: A schematic illustration of the ABC SMC algorithm [2]. Particles (red circles) are propagated through intermediate distributions towards the ABC-approximated posterior distribution.

In Chapter 4 we then apply our ABC SMC algorithm to a range of biological problems, and illustrate how the algorithm performs in practice. Moreover, we explore how the inferred parameter distributions can be further analysed to obtain information on parameter sensitivity, inferability and sloppiness [2,3].

In Chapter 5 we adapt the parameter estimation algorithm and develop ABC SMC for model selection [4]. We derive several versions of the model selection approach and choose the most promising one.

In Chapter 6 we apply the model selection algorithm to several problems in epidemiology and molecular systems biology [5]. Simulated as well as real datasets are used. We discuss the computational performance of the algorithm, and compare its results with analytical solutions and results obtained by a conventional Bayesian approach.

In Chapter 7 we consider a set of dynamic phosphorylation models (Figure 2) in light of experimental ERK signalling pathway data. We are interested in which of these phosphorylation models (or hypotheses) is the best one for modelling the system. We approach this problem using the methods developed above. Crucially, we have been able to provide convincing arguments, and for the first time in vivo that de-phosphorylation of ERK occurs in a distributive manner (Figure 2) [6].

In Chapter 8 we model the phage shock protein response in Escherichia coli [7] with the use of Petri nets and inference-based modelling (Figure 3a-b). We analyse the structure and dynamics of the developed model in stochastic and deterministic frameworks. Here our approach has allowed us to use present qualitative data in order to make quantitative and testable predictions of the temporal behaviour of the important cell-membrane stress response system [8,9]. In particular we have been able to show that current data are commensurate with potentially oscillating responses; this possibility had not before been noticed and is now being explored in targeted experiments that are based on our predictions.

Conclusion and Outlook

In the work for this thesis I have developed a framework for parameter estimation and model selection that can deal with the complexities of mathematical models for biological systems, and the uncertainties inherent to systems biology data. In the final two chapters we used this framework in order to address two important biological applications of cellular signal processing in collaboration with experimental research groups. There is vast scope for applying this approach in systems biology (but also beyond, for example in population biology) [10]. Based on the work in my thesis I am now developing, exploring and applying this methodology further in collaboration with bioengineers and systems and synthetic biologists.
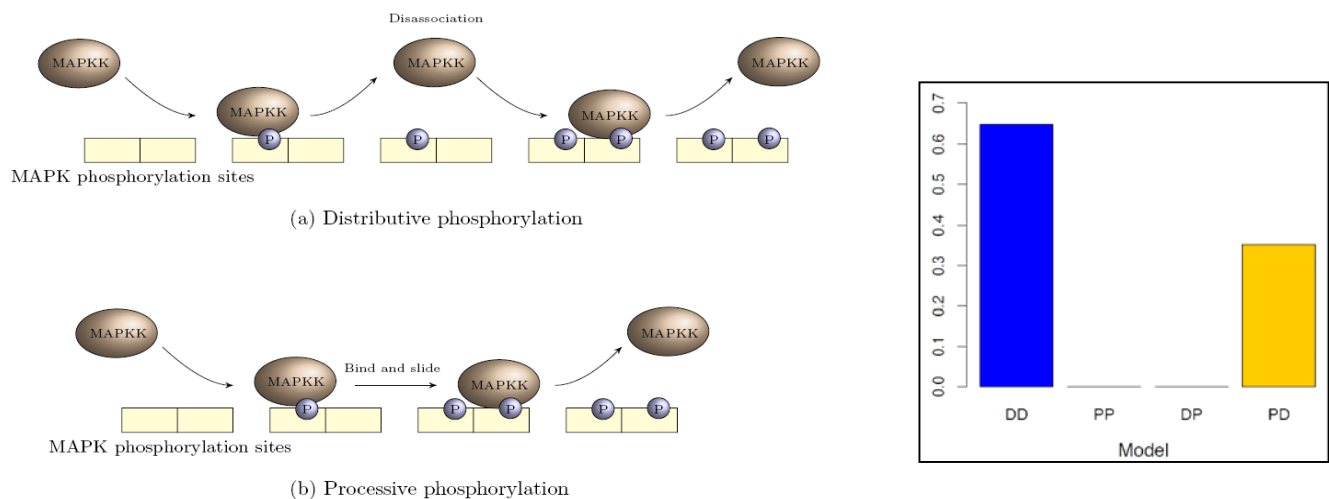

Figure 2: Double phosphorylation and dephosphorylation can be distributive (D) or pro-cessive (P). Model selection on four phos-phorylation and de-phosphorylation models was performed, using *in vivo* Mek-Erk phosphor-ylation data. Shown is the inferred marginal posterior distribution of the model [7].
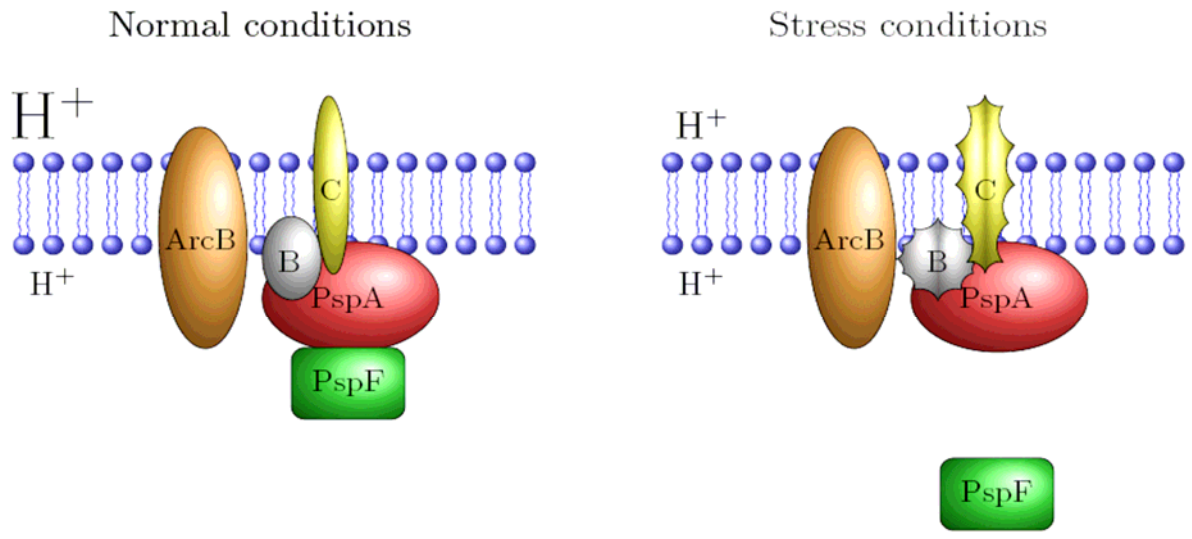
Figure 3:

(a) A schematic illustration of the phage shock proteins PspA, PspB, PspC and PspF under normal and stress conditions [8].
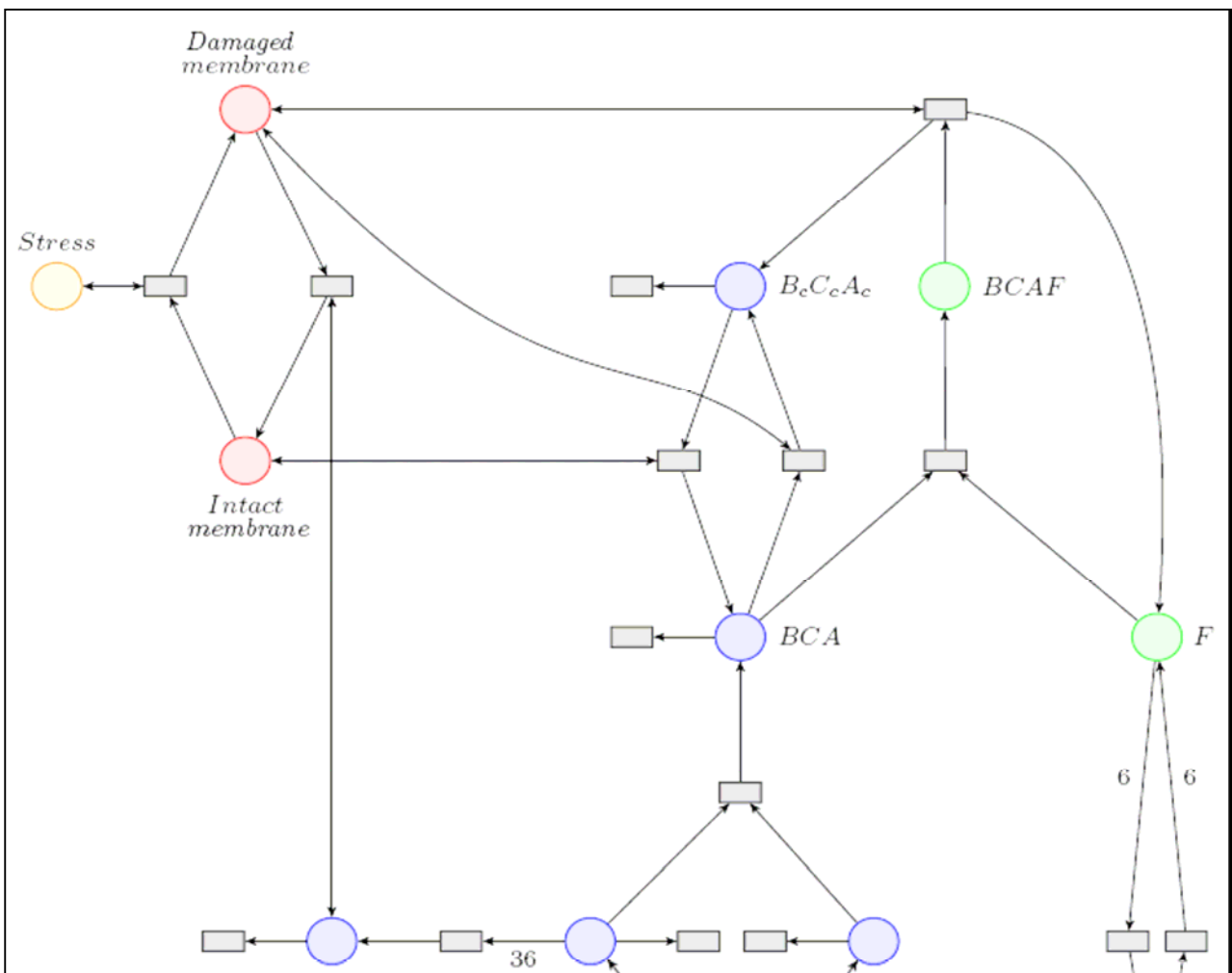
(b) Petri net model of the phage shock protein response in *E. coli* [10].

References

[1] T. Toni, D. Welch, N. Strelkowa, A. Ipsen and M. P. H. Stumpf. Approximate Bayesian computation scheme for parameter inference and model selection in dynamical systems. *Journal of the Royal Society Interface* 6, 187-202, 2009.

[2] T. Toni, J. Liepe, M. Stumpf. Inference of signalling pathway models (with focus on Approximate Bayesian Computation for dynamical systems). Book Chapter in *Handbook of Statistical Systems Biology*, Wiley, 2011.

[3] M. Secrier*, T. Toni*, M. P. H. Stumpf. The ABC of reverse engineering biological signalling systems. *Molecular BioSystems* 5, 1925-1935, 2009.

[4] T. Toni, M. P. H. Stumpf. Simulation-based model selection for dynamical systems in population and systems biology. *Bioinformatics* 26 (1), 104-110, 2010.

[5] T. Toni, M. P. H. Stumpf. Parameter inference and model selection in signal transduction models. Book chapter in *Computational Biology, Methods in Molecular Biology*. Springer 673, 283-295, 2010.

[6] T. Toni, Yu-ichi Ozaki, Paul Kirk, Shinya Kuroda, M. P. H. Stumpf. Elucidating phosphorylation dynamics of the ERK MAP kinase (in preparation).

[7] N. Joly, C. Engl, G. Jovanovic, M. Huvet, T. Toni, X. Sheng, M. P. H. Stumpf, M. Buck. Managing membrane stress: the Phage shock protein (Psp) response, from molecular mechanisms to physiology. *FEMS Microbiology Reviews* 34 (5), 797-827, 2010.

[8] M. Huvet*, T. Toni*, H. Tan, G. Jovanovic, C. Engl, M. Buck, M. P. H. Stumpf. Model-based evolutionary analysis: The natural history of phage shock stress response. *Biochemical Society Transactions* 37, 762-767, 2009.

[9] T. Toni, G. Jovanovic, M. Huvet, M. Buck, M. P. H. Stumpf. From qualitative data to quantitative models: analysis of the phage shock protein response in *Escherichia coli*. *BMC Systems Biology* 5:69, 2011.

[10] J. Liepe, C. Barnes, E. Cule, K. Erguler, P. Kirk, T. Toni, M. P. H. Stumpf. ABC-SysBio - approximate Bayesian computation in Python with GPU support. *Bioinformatics* 26(14), 1797-1799, 2010.

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### *The dynamics of contagious diseases and human behaviour*

This thesis is about modelling the impact of human reactions on the spread of contagious diseases. More specifically, it tries to elucidate the dynamics of the interaction between awareness of a disease and the spreading disease itself by formulating and analysing a suite of mathematical models. To put this into context, it is important to realise that awareness itself can spread in a population, not entirely dissimilar to the way a disease does. This analogy has been proposed more than 50 years ago, and many models for the spread of rumours have since been based on models for the spread of diseases. In this thesis, the interaction between two spreading entities, awareness of a disease and the disease itself, is investigated by considering a set of different models and studying how the basic reproductive number changes under the respective model assumptions.

Awareness of a disease provides the basis for individual reactions and can contain elements of an infectious process itself when it spreads through a population by word of mouth. For example, according to the Chinese Southern Weekend newspaper, the text message "There is a fatal flu in Guangzhou" was sent 126 million times in Guangzhou during the 2003 SARS outbreak, causing people to stay home or wear face masks when going outside. Web-based studies of search trends indicate that the transmission of information played a role both in public perceptions of avian influenza (H5N1) in 2005 and Influenza A (H1N1) in 2009.

In the first model studied in this thesis, the focus is on capturing the ephemeral nature of awareness by letting it deteriorate in its spread through the population. The basic reproductive number derived there reflects this feature and captures the local dynamics. It is shown that the protective behaviour triggered by local awareness can indeed stop a disease outbreak in its tracks, but only within a limit which can be expressed in terms of the basic reproductive number of the disease. This effect does not operate in an unstructured population where awareness can mitigate an outbreak, but does not change the epidemic threshold. In a structured population, on the other hand, awareness is shown to be much more effective if the networks of the spread of awareness and disease are clustered and overlap, in which case the highest levels of awareness occur where it matters most (Figure 1).
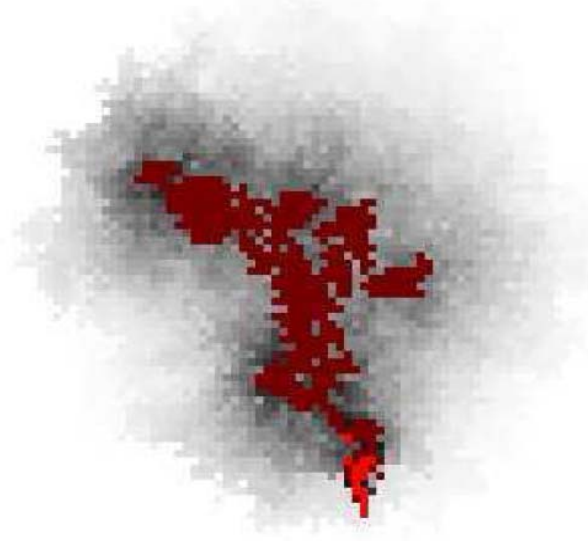
Using another model, a different angle to the same question is taken. In this model, awareness is no longer assumed to diminish as it spread, allowing for a more systematic treatment of different scenarios. In that case, the epidemic threshold does indeed change in an unstructured population, and the extent to which it does so under different types of behavioural change is quantified here. A pair approximation is developed and used to quantify the effect of network overlap on local correlations and their dynamics on regular networks. It is shown that even if awareness cannot spread by itself, there can be a strong impact on the disease dynamics, the divergence from mean-field results being the strongest if the spread of awareness is nearly critical (Figure 2).
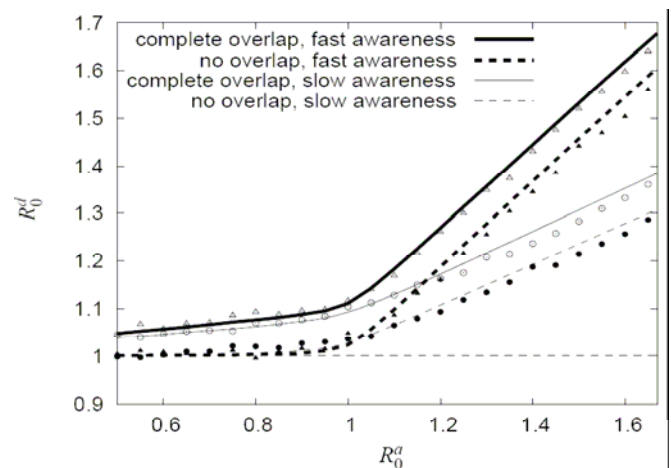
With a last model, the focus turned towards the impact of heterogeneity in network structure and correlations between the degree distributions of the two networks. The model is based on percolation theory and the emergence of giant connected components of infected individuals on infinite random networks. This model is static in nature and, when applied to the interaction of awareness and disease, contains the implicit assumption that awareness spreads so much faster than the disease that timescales do not matter. This allows for a closer look at the impact of network heterogeneities than was possible with the other models. It is shown how the basic reproductive number of a disease is reduced if awareness has immunised part of the nodes, and how this effect changes under different degrees of immunity and overlap. It is found that if awareness spreads first and blocks

part of the network to the disease, it is most effective in containing a disease if the two networks are highly heterogeneous and the degrees between them are positively correlated, so that the hubs on one network are hubs on the other (Figure 3).
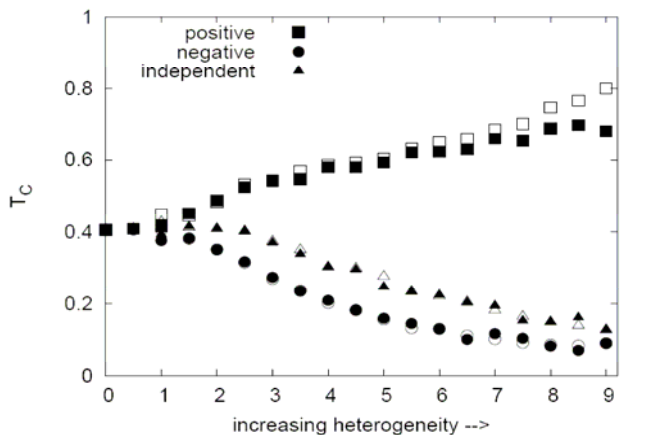
All these findings are united by the overarching theme of studying two processes interacting in their spread on two different networks connecting the same set of individuals. In that sense, the methods developed here are not limited to the scenario of disease and awareness, but could be applied to any situation where diseases or societal processes are transmitted through a population and interact in their spread.

The motivation for this thesis, however, came from the aim to understand the dynamics of the interaction between the spread of awareness of a disease and the disease itself. What, then, is the conclusion? Which of the different expressions for the basic reproductive number or the epidemic threshold in the different chapters is the "correct" one? The different models were all based on a different set of assumptions. Partly, these assumptions were motivated by the desire to understand certain features of the dynamics, but partly they were necessitated by the requirement of mathematical tractability, in itself crucial for understanding the inner workings of a model.

In that sense, the different epidemic thresholds found all constitute part of the answer. The extent to which any of the models is useful in describing a real-world situation can be decided only by testing them against measured data. This is particularly difficult for the behavioural aspect of the problem studied here but not necessarily impossible, as first attempts have shown. All models presented here can, *in principle*, be tested with data. Therein, and in the presentation of a novel way to view the interaction between contagious disease and human behaviour, lies the contribution of this work.

Ultimately, mass human behaviour remains to some extent unpredictable, and particular so in the face of disaster. Still, a concerted approach of observational studies and further mathematical modelling can be expected to lead to valuable insights into the way epidemics spread in human populations.

Acknowledgements

Further reading

Ferguson N. Capturing human behaviour. *Nature* 446 (7137):733–733, 2007.

Funk, S., Gilad, E., Watkins, C., and Jansen, V. A. A. (2009). The spread of awareness and its impact on epidemic outbreaks. *Proc Natl Acad Sci U S A* 106 (16):6872–6877.

Funk, S., Gilad, E., and Jansen, V. A. A. (2010). Endemic disease, awareness, and local behavioural response. *J Theor Biol* doi:10.1016/j.jtbi.2010.02.032.

Funk, S. and Jansen, V. A. A. (2010). Interacting epidemics on overlay networks. *Phys Rev E Stat Nonlin Soft Matter Phys* 81 (3 Pt 2):036118.

Funk, S., Salathé, M., and Jansen, V. A. A. (2010). Modelling the influence of human behaviour on the spread of infectious diseases: a review. *J R Soc Interface* 7 (50):1247–1256.

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Towards long-term prediction of tissue remodeling

Why are we interested in the bone remodelling phenomenon? Besides common reasons for our interest (such as understanding to a process in human body that is responsible for depositing and withdrawing minerals and several growth factors from bone tissue, repairing microdamages that are accumulating in the tissue, or renewing the tissue itself), some examples where the understanding of bone remodelling phenomenon is essential are the following:

1. Bone remodelling is responsible for aseptic loosening of prosthesis in total joint replacement - due to stress shielding (there is the same problem with dental implants).

2. As a consequence of improper loading of vertebrae, they adapt their shape to better resist to it. This adaptation is usually dangerous when the formed osteophytes (protuberance growing from vertebrae) may press against spinal cord or outgoing nerves. This happens usually after treatment of vertebrae fracture, herniated disc or pathological curvatures of spine. These facts motivate us to formulate a model of this process that is able to elucidate or even predict response of bone tissue in the mentioned situations.

This thesis does not explicitly deal with tissue remodelling in general because there are some specific features related only to the chosen tissue that are needed to be taken into account. However, the presented approach used for the bone remodelling phenomena can be perceived as a general framework for tissue remodelling. A recent research in remodelling of arteries shows that very similar mechanisms are present and moreover, some of them are carried out by the same agents. In Chapter 1 the reader is getting acquainted with basic facts about bone and bone remodelling. Further, the importance of such a renewable process in the human body is elucidated, as well as its important implications for daily life. Since a new model for the mentioned phenomenon is presented here, it is necessary to first review the literature. Although there are more than 20 models of bone remodelling, I believe that the presented model has something new to offer.

Chapter 2 - Thermodynamic considerations - formulates a theoretical background for coupling effects in biochemical processes. It shows the importance of mechanical loading and also it offers a theoretical explanation of a known fact that only dynamic loading is of essential relevance for bone remodelling [1], [2]. To support and to elucidate these theoretical conclusions, a simple example of tissue renewal is proposed and studied. Despite its simplicity, it provides stimulatory results for discussion.

In Chapter 3, a new model describing the bone remodelling phenomenon is proposed. A thorough parameter setting is carried out and basic features of the model are shown [3]. Further, the applicability of this model is studied

and extended in the last chapter where, firstly, a rather thorough recherche of biological background related to bone remodelling was carried out, see for example a review by Robling et al. [4]. Bounds of applicability are searched and examples of practical usage and consequences are shown.

As was mentioned, some of the results have a general character and some are specific to bone remodelling. However, if one is able to formulate the (correct) fundamental processes occurring in the chosen remodelling process (the presented model is actually its third version that finally turned out to be a correct one - i.e. it showed a correct qualitative behaviour), he may follow the presented analysis and used techniques that will lead to a tissue remodelling model for a different tissue than bone. We consider bone remodelling process to be mainly controlled by five interactions among particular substances: formation of multi-nucleated osteoclasts (controlled by RANKL-RANK-OPG pathway), resorption of old bone tissue, releasing local factors from bone that consequently attract and activate osteoblasts, which in turn secrete osteoid. The final stage is mineralisation of osteoid that leads to new bone tissue. Actually, these interactions can be interpreted more generally, they epitomise the basal concept of tissue remodelling:

- interaction represents creation/formation of the dissolving agent,
- interaction can be interpreted as removal of old tissue,
- is an activation of cells that are able to form a new tissue, and
- represent a (two-stage) formation of new tissue.

For overview of considered interactions in the proposed bone remodelling algorithm see Fig. 1. Of course, parameters are tissue specific but the presented procedure can be used as a template for finding needed data in literature where almost no experiment can provide these concrete sought data.

We believe that modelling processes in biology really requires an interdisciplinary approach. This needs to comprise biochemistry and often mechanics, or physics in general. We have developed a bio-thermodynamic concept for tissue remodelling that seems to be an appropriate tool for these complex interdisciplinary problems and thus leads to a formulation of meaningful models [5]. It offers a theoretical explanation of the coupling effect phenomenon between mechanical loading and chemical reactions based on non-equilibrium thermodynamics (CIT - classical irreversible thermodynamics). Also the question whether static or dynamic loading influences biochemical processes was addressed - the necessity of dynamic loading as a stimulatory mechanism was shown. Further, the used concept suggests that chemical and mechanical processes do not only facilitate or support one another but they may also play a triggering role for the other coupled process - some biochemical processes may need mechanical stimulation to run and vice versa as well - chemical reactions may provide energy for some mechanical processes. This approach enables to describe reaction kinetics not only as a function of affinities or chemical potentials of components (which actually is the usually used law of mass action) but also as a function of dynamic loading [6].

Moreover, a more detailed control mechanism can further be added into this model when needed, see Chapter 4. We have added the effects of RANKL, RANK, OPG, PTH, estradiol, and NO on bone remodelling which were found to be important for the ability to simulate various disease related to bone [7], [8], see Fig. 4. Because these effects are translated into an appropriate RANKL or OPG molar concentrations, the number of RANKL-RANK bonds (that were present in the original model) manage their impact, see the schematic of interactions in the proposed bone remodelling algorithm including RANKL-RANK-OPG pathway Fig. 1.
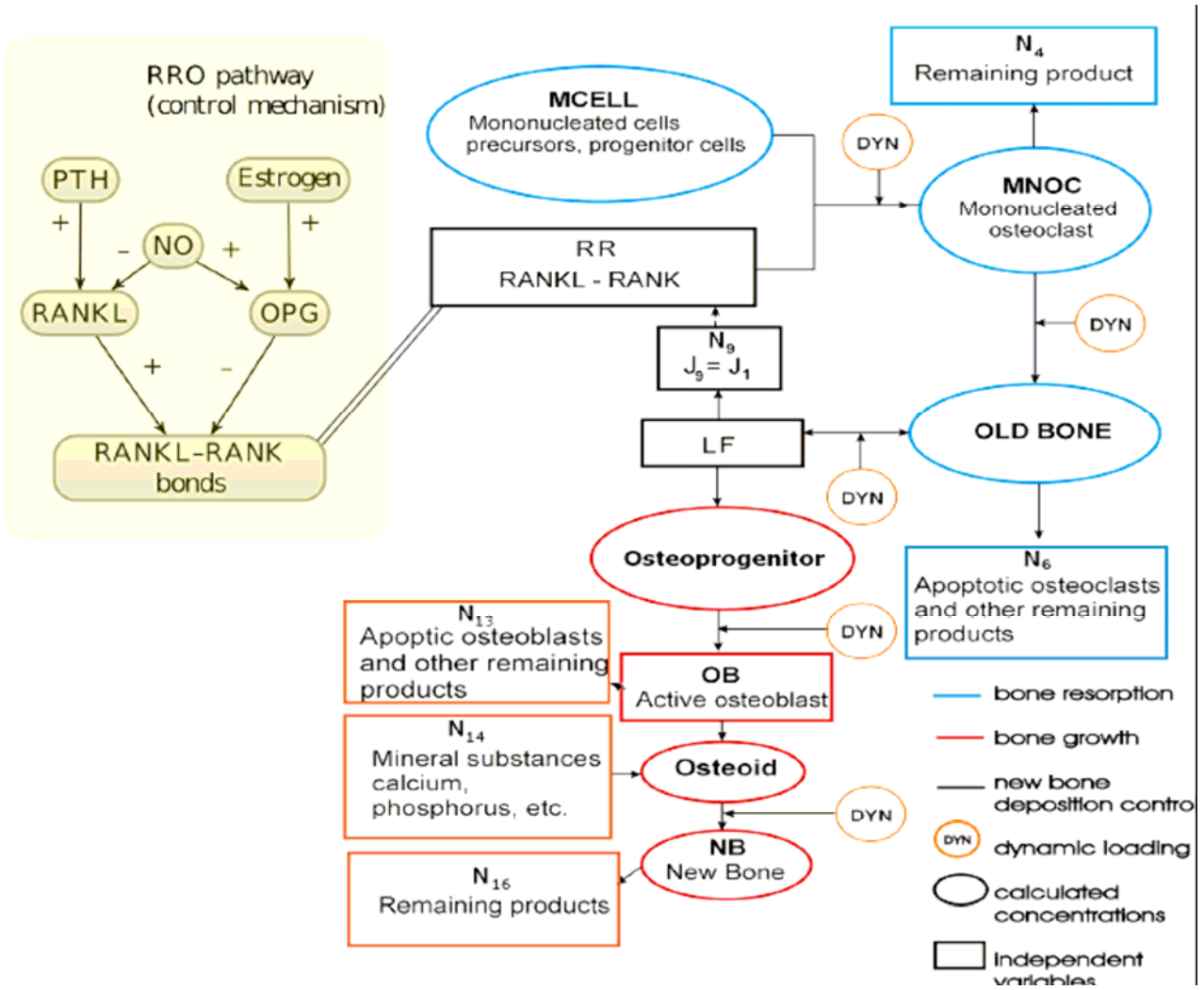
Fig 1. Schematic of interactions in the proposed bone remodelling algorithm with RANKL-RANK-OPG pathway.
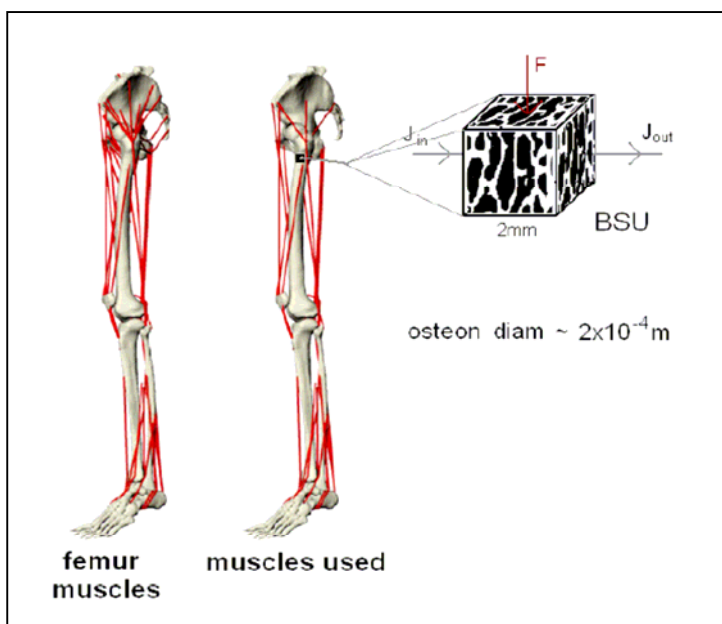

Fig 2. Considered acting forces on a femur in FEM calculations as found in the study by Heller et al. [1].

Reaction kinetics in space can be described according to the above mentioned bio-thermodynamic concept using system of reaction-diffusion equations. However, the vast majority of agents, nutrients, etc. are transported through arteries in bone tissue (unlike in cartilage). Thus, we do not consider the effects of spatial diffusion to be significant and neglect them. A typical usage of the mentioned model would be with the finite elements method. Bone is divided into finite elements (actually into bone structural units that are not arbitrarily small) with appropriate boundary conditions for considered muscle forces, see Fig. 2, further-more, bone is subjected to loading from the hip joint resulting from body locomotion. Consequently, in each of these elements all the considered chemical processes describing bone remodelling are running (we assume a premixed, ideally stirred mixture of substances; further, the processes are considered to be isothermic at body temperature) but with different mechanical stimulation that varies throughout the bone.

This mechanical stimulation, dynamic straining, is computed using FEM from a standard mechanical problem and is used as an input for the model. When this procedure is applied to a femur 3D geometry with homogeneous distribution of tissue density as an initial state, a new distribution of density appears where clear dense and sparse region can be seen. Moreover, their spatial distribution corresponds to cortical (dense areas) and spongy bone (sparse areas) found in human femur. We may now study effects of both distinct control mechanisms - mechanical stimulation and biochemical conditions.

As an example demonstrating the capability of the model to predict the effect of various loading condition, disuse of femur was simulated as there is clear and quantified evidence that bone tissue resorbs under reduced mechanical stimulation, see Fig. 3.
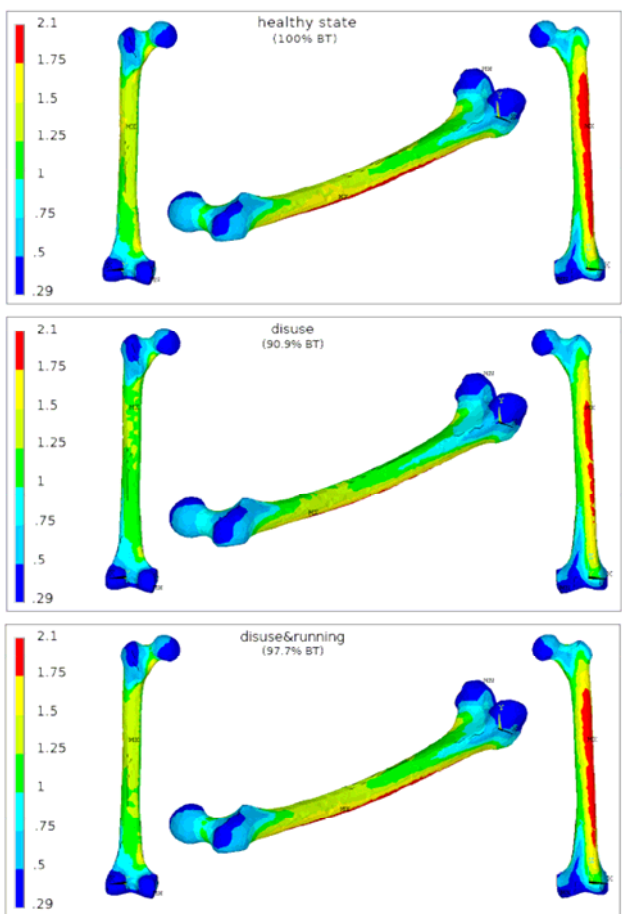

Fig 3. Prediction of disuse effect on bone quality - simulation of insufficient loading (half of the recommended daily stimulation), treatment proposal - running (30 minutes every other day), and its simulation. Notice the change of bone mass (BM) of the whole femur.

Another possible outcome is displayed on Fig. 4, depicting a calculated prediction of the presented model. As an example, the most common disease related to bone remodelling was chosen, menopause. Similarly, predictions of bone quality after disuse and with hyperparathyroidism are shown in the thesis. During menopause, a decline in estradiol levels occur. In some women, the decrease is very dramatic (a drop below $5\frac{pg}{ml}$ is observed, whereas a standard serum level is $40\text{-}60\frac{pg}{ml}$) while in some not (serum level remains above $20\frac{pg}{ml}$). Furthermore, it was observed that, together with estradiol, there is a decline in nitric oxide levels (see chapter 4). An example of a woman who is physically active (correct mechanical stimuli on

regular daily basis, i.e. approximately 20000 steps per day) but in a consequence of menopause has decreased serum levels of estradiol and nitric oxide (as mentioned above - estradiol: $2.5 \frac{pg}{ml}$, NO level correspond to $0.02 \frac{mg}{kg}$ per day of nitroglycerin) is depicted in Fig. 4. The presented model predicts a decrease of 8% in bone tissue density, which does not seem to be osteoporosis yet. This may be because menopause is accompanied by more effects than these two mentioned and also most probably because they are less physically active (may be caused by pain). If we combine the 8% decrease (Fig. 4) caused by menopause alone with another 9% decline caused by improper loading (predicted by the model), we get a significant drop by almost 20% in the overall bone density of the femur, which can be considered as osteoporotic state. One possible treatment of bone loss connected with menopause is treated with hormone therapy (HRT). Simulation of such a treatment that increased estradiol serum levels to $20 \frac{pg}{ml}$ (or by $0.107 \frac{mg}{kg}$ per day of nitroglycerin treatment which is actually less expensive) is given in Fig. 4. Again, the importance of mechanical stimulation shown when increased physical activity (running 30 minutes every other day) increases bone density in similar fashion as HRT treatment (the same figure). And best results are reached when both effects are combined and even the original bone tissue density can be restored – see Fig. 4.

Because of the complexity of studied field, we are in close contact with orthopaedists and surgeons - mainly the needed simplification of the studied process was consulted with them. Further, the model predictions about the effects of stem insertion on quality of bone as a consequence of bone remodelling were validated using X-ray images of their patients. Currently, the model can be used for simulation of particular diseases of bones related to remodelling (see the enclosed figure) and even for proposing a possible treatment: a coupled effect of mechanical stimulation and biochemical control. In cooperation with medical doctors, a validation of these predictions should start in near future. Because every model is from its very essence always only a simplification of studied process, it is needed to know the bounds of applicability of such a model. This investigation may also reveal other interesting features and results of the proposed model. In our case, these long-term predictions of bone remodelling in humans are the biggest asset that the presented model brings to this field, which has been studied for more than 20 years.

References

[1] Heller, M. O., Bergmann, G., Kassi, J.-P., Claes, L., Haas, N. P., Duda, G. N., 2005. Determination of muscle loading at the hip joint for use in pre-clinical testing. *Journal of Biomechanics* 38, 1155--1163.

[2] Klika, V., 2010. Comparison of the effects of possible mechanical stimuli on the rate of biochemical reactions. *Journal of Physical Chemistry* B 114 (32), 10567--10572.

[3] Klika, V., Maršík, F., 2009. Coupling effect between mechanical loading and chemical reactions. *Journal of Physical Chemistry* B 113, 14689--14697.

[4] Klika, V., Maršík, F., 2010. A thermodynamic model of bone remodelling: The influence of dynamic loading together with biochemical control. *Journal of Musculo-skeletal and Neuronal Interaction* 10 (3), 220--230.

[5] Klika, V., Maršík, F., July 2011. Biomechanics. Vol. 1. INTECH, Vienna, Ch. Feasible simulation of diseases related to bone remodelling and of their treatment, ISBN 978-953-307-312-5, [online] http://www.sciyo.com .

[6] Klika, V., Maršík, F., 2011. Feasible predictions of bone remodelling using modelling techniques. *Locomotor Apparatus* 1+2, 26--41, [online] http://www.pojivo.cz.

[7] Klika, V., Maršík, F., Maršík, I., February 2010. Dynamic Modelling. INTECH, Vienna, Ch. Influencing the Effect of Treatment of Disease Related to Bone Remodelling by Dynamic Loading, ISBN 978-953-7619-68-8, [online] http://www.sciyo.com .

[8] Robling, A. G., Castillo, A. B., Turner, C. H., 2006. Biomechanical and molecular regulation of bone remodeling. *Annual Review of Biomedical Engineering* 8, 455--498.

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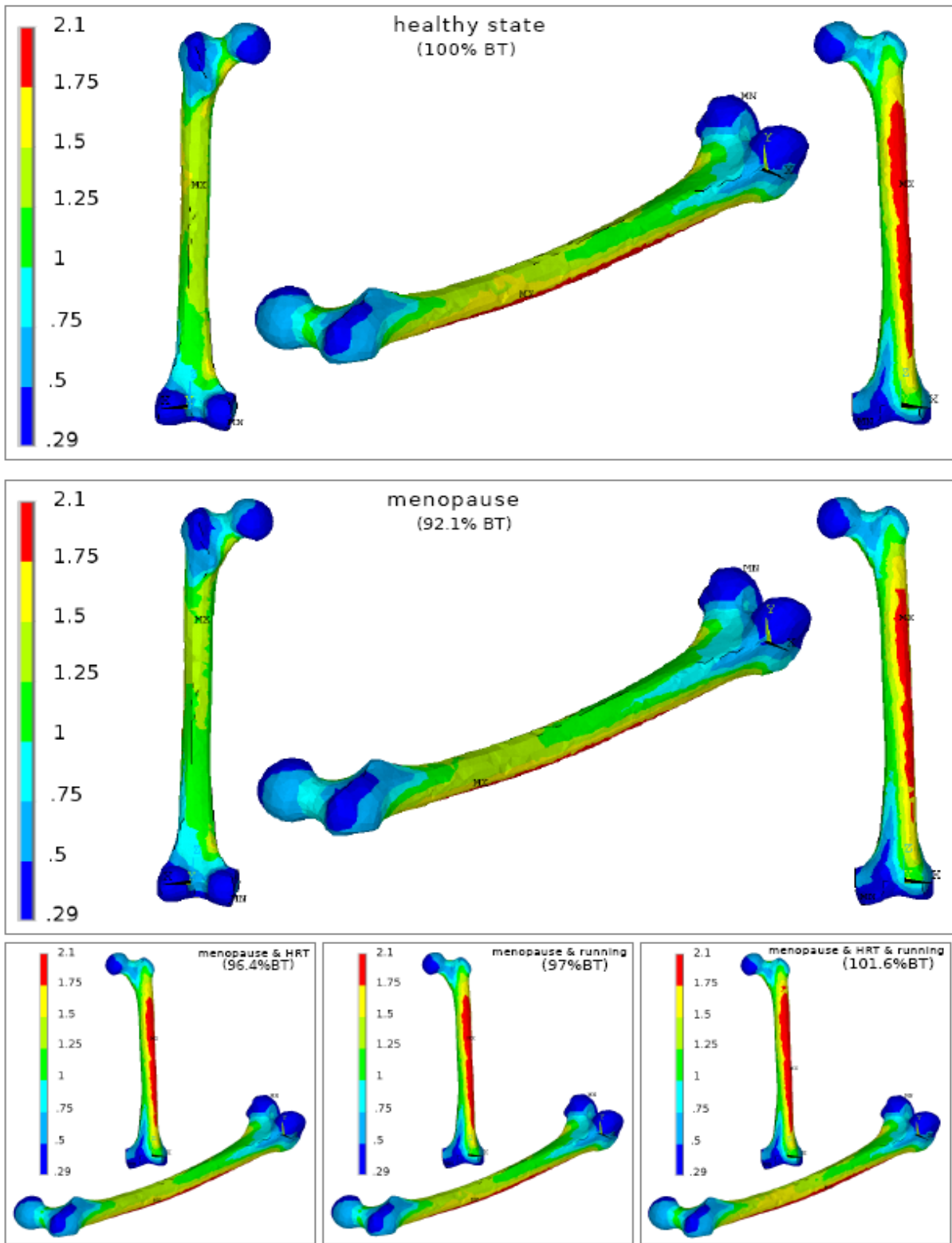CR-12000 Prague

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Fig 4. Prediction of the menopause effect on bone quality (estradiol levels decreased to $2.5\frac{pg}{ml}$ and NO to half of its normal level), treatment proposal, and its simulation - hormonal treatment (HRT), running (30 minutes every other day). Notice the change of bone mass (BM) of the whole femur.

Memories on the 20th anniversary of the foundation of ESMTB 1991

I wish to start by thanking the scientific community of Mathematical and Theoretical Biologists for having at first accepted the challenge of establishing a common European forum via a European Society, and later, for having made it full of content both in research and in education. Part of my memories are taken by my previous Editorial that appeared 2000 in the first issue of the Communications of the ESMTB, and I thank the Editors of them for having given room on that occasion and, in the present volume, to my memories. Further information I have taken from other articles in the same Communications.

It is with great satisfaction that I am now called to attract the attention of our community after 20 years from birth of the *"European Society for Mathematical and Theoretical Biology"* (ESMTB) in 1991; both pregnancy and birth had not been so easy, considering that at that time Europe itself was in a very early stage of its political unification, the most important event having been the opening of dramatic artificial barriers that had been raised between East and West Europe as a consequence of the most horrible war in history. Somehow, pregnancy of th ESMTB had anticipated such an event. It has always been my strong opinion that Science and Education can unify and, thus, anticipate political unifications more than just economic treaties (http://ec.europa.eu/research/era/).

Indeed, during 1988 it happened that I was Visiting Professor at the Centre for Mathematical Biology of Oxford University, invited by its founder, Jim Murray. To my great chance also Simon Levin (at that time President of SMB) and Mayan Mimura (already an important figure in Japan) were there at the same time. The main European scientific programmes had already been launched by the European

Union, and in my opinion it was a pity that – while various actions had already been taken by other groups in Applied and Computational Mathematics to be supported by Bruxelles (also under the strong inf1uence of the now well known "David Report" (1984), "Renewing US Mathematics. CriticaI Resource for the future" on the role of Mathematics in Science and Technology http://books.nap.edu/openbook.php?isbn=0309042283&page=R1.
 – no kind of coordinated action had been undertaken by Mathematical and Theoretical Biologists. This happened in spite of the fact that in the same report and later updates (appeared in the Notices of the American Mathematical Society), our areas of interest had been recognized as crucial for the future development of Biotechnology, control of infectious diseases, environmental protection, modelling of the immune system, cancer, etc. Further, at the academic level there was no sign of concrete recognition of the cultural relevance of our discipline both, in Mathematics Departments and in Biomedical ones, always being considered ancillary for their research and professional context. I am sorry to say that notwithstanding our efforts, in many recent conferences and workshops we are still discussing about an increasing attention of the biomedical community to mathematical or even to more general quantitative approaches to Biomedical research *(CBE—Life Sciences Education Vol. 9, 248–265, Fall 2010; Journal of Mathematical Biology "Perspectives").*

At that time the Society for Mathematical Biology already existed; a second good chance was that then its President was Simon Levin, who had considered as important an action in Europe, recognized by the European scientific community and by the Commission in Bruxelles. So Levin, Mimura, Murray and myself agreed that we might have activated a process of awareness by establishing "a permanent forum for all those, who are genuinely interested in the

scientific development of the subject", the first action being the organization of a European Conference on Mathematical and Theoretical Biology cosponsored by SMB and the analogous Japanese Association. Levin submitted to the Board of SMB (who welcomed the initiative) a letter of mine, expressing my intention of organizing the Conference. The same letter was forwarded to a first list of "delegates" of different national activity groups in Europe: I am glad to report that Lee Segel himself had proposed a participation of the Israeli community. After an exchange of letters during the years 1988-1989 (and a series of visits to Simon at Cornell that I spent during my Christmas holidays of those years) a "Steering Committee" was set up to act as the Scientific Committee of the *First European Conference on "Mathematics Applied to Biology and Medicine"* to be held somewhere in Europe. Bari, my home town, had been identified as a natural choice, after the successful experience of a world-wide conference on the same topics organized by myself, the late Enea Grosso (a pioneer of the local School of Medicine), and Stefano Paveri-Fontana in 1983, but I liked to accept the proposal by Jacques Demongeot, who offered hospitality and organizational support in Grenoble at l'Alpes d'Huez, so to make it an action independent of the small group of initiators. I have to acknowledge the substantial additional support of the Italian National Research Council (CNR) via the Institute for Research in Applied Mathematics (IRMA), of which I had been the Director at that time.

This first committee included, in addition to myself, J. Demongeot (France), O. Diekmann (The Netherlands / Math), I. Dvorak (Czechoslovakia), A. Goldbeter (Belgium), W. Jaeger (Germany), N. Keiding (Denmark), G. I. Marchuk (Soviet Union), J. A. Metz (The Netherlands / Bio), J. D. Murray (United Kingdom), L. Segel (Israel), who represented most of the European countries, as well as S. Kauffman and S. Levin as delegates of SMB. The first conference, January 7-11, 1991, at *l'Alpes d'Huez* was a great success and a lot of enthusiastic participation was shown from all over the world, especial1y by the very many young delegates.
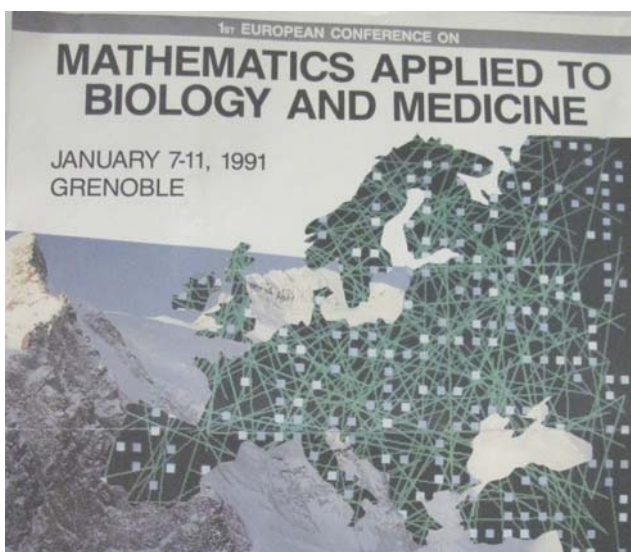
In the meanwhile (December 1990) Karl Hadeler had favourably supported the idea of establishing a European organization of "Mathematical and Theoretical Biology" in the editorial of the *Biomathematics Newsletter* (n.5), which he had recently established in collaboration with Wolfgang Alt. It appeared natural to take the opportunity of gathering so many participants at this conference to call them to an *Assembly for the possible constitution of a European Society*. As a biblical condemnation to human beings, the joy of a birth is anticipated by some physical pain (throes of childbirth); lively discussions arose about many issues, as about the terms "Mathematical" and "Theoretical", about the role of women in scientific societies (how can one forget the "vivid" participation of Zvia Agur) etc. – but the overall atmosphere was so good in substance that a provisional Board was acclaimed including myself, Jacques Demongeot, Karl P. Hadeler, Willi Jaeger, and Jim Murray (President) that would have prepared

the Statutes of a *European Society for Mathematical and Theoretical Biology* and run the first election of the Board of the Society. The Statutes were presented to the Prefet de Grenoble on March 16, 1992, signed by myself (in representation of the President) and by J. Demongeot (as Secretary): http://www.esmtb.org/downloads/ecmtb/ecmtb4.pdf ; the history after that is all published in the Biomathematics Newsletter and the subsequent Communications of ESMTB.
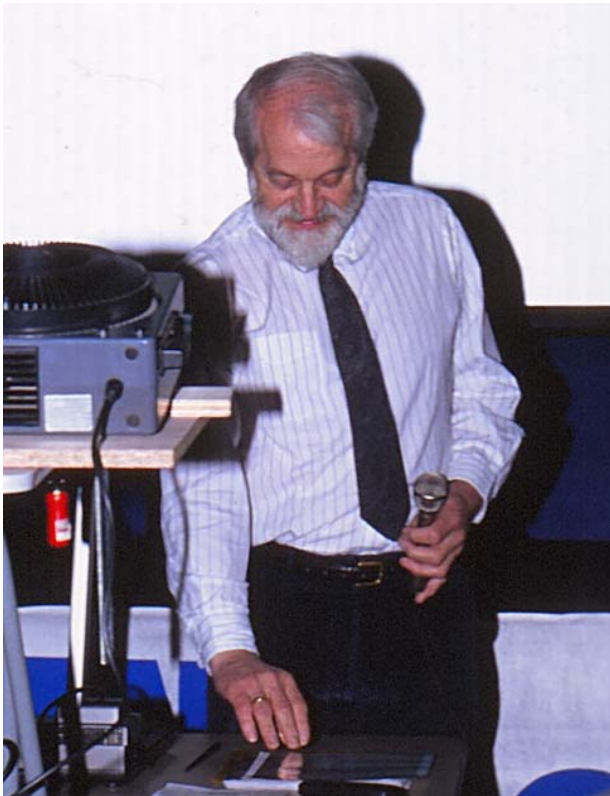
James D. Murray

ESMTB has had seven Presidents, *James D. Murray* (UK), *Karl Hadeler* (Germany), *Jacques Demongeot* (France), *Vincenzo Capasso* (Italy), *Mats Gyllenberg* (Finland), *Wolfgang Alt* (Germany), and *Carlos Braumann* (Portugal); the last two have got an extension from originally five to now ten members of the Board, including two advisors.

From the letter that I wrote to the potential members of the Society after the First Conference in January 1991, on behalf of the provisional Board, I like to report the following statements:

Karl Hadeler and Lee Segel

"In addition to the classical analytical approaches, new computational methods have been facilitated by the advent of the "computer revolution", which has made available to every scientist enormous computer power and has enhanced the role of mathematics in the description of complex systems which are refractory to direct analysis. A better integration across disciplines is essential for the elucidation of biological phenomena through mathematical and computational approaches, and to explore complicated nonlinear phenomena.

Communication itself, on a global scale, has been enhanced immeasurably through computer networks, and has made possible collaboration on broad international scales, far beyond what was possible just a few years ago... On the other hand we cannot ignore, and in fact we wish to participate in, the process of integration of Europe, without forgetting international cooperation on a larger scale."

I am glad to say that a lot has happened in the last two decades along what had been anticipated in the above letter. Still, we have to admit that many challenging problems remain unsolved for the full understanding of complex biological problems (see JMB Perpectives, PITAC Report http://www.nitrd.gov/pitac/reports/20050609_computational/computational.pdf); consequently, with great sadness, dramatic diseases still remain open challenges to the overall scientific community.

On the scientific side, various initiatives have been successfully supported by the European Community. Among those we may recall the ESF-Network on *Immune System and Tumor Growth* (coordinated by Nicola Bellomo and Luigi Preziosi; the Special Interest Group on *Shape and Size in Biotechnology and Medicine,* coordinated by V. Capasso within the EU Network of Excellence MACSI (http://www.macsinet.org/newsletter/4.pdf), and still operational within ECMI (the European Consortium for Mathematics in Industry) http://www.mat.unimi.it/users/shape/; the Marie-Curie Research Training Networks on *Modeling, Mathematical Methods and Computer Simulation of Tumour Growth and Therapy* (coordinated by N. Bellomo), and on *Biology-inspired Techniques for Selforganization in Dynamical Networks* (coordinated by A. Deutsch).

I had the honour and the responsibility to be President of ESMTB in 2000, after about ten years from foundation; I have to thank the whole community for having accepted my enzymatic role at the embryonic stages of the Society, and for having later participated very actively to its further revival. I have been very lucky to receive the strong support of all main scientific leaders at birth, and the proactive collaboration of the Board members during my period of presidency. Among those you may read below the names of the Vice President Mats Gyllenberg, the Secretary/Treasurer Mark Chaplain, the Summer School Committee Ovide Arino and Philip Maini, the Editor of the Communications Wolfgang Alt, in addition to Hans Heesterbeek and Philippe Tracqui, and others. Without them, ESMTB would not have been capable of establishing the roots of its important achievements. All of them have played and still play major roles in the international community.

By considering the relevance of education for the formation of a new generation of scientists, capable of integrating mathematical expertise and competence in Biology and Medicine, under the initiative of Ovide Arino (prematurely died in 2003) the ESMTB engaged in 2000 a sub-Committee initially with Arino and Philip Maini, for organizing a permanent *European Summer School*, the first edition of which was held 2000 in Martina Franca (Apulia, Italy) with significant financial support by the European Union

http://www.mat.unimi.it/users/miriam/ESMTB/MARTINA-SS/summer_school.html.
This initiative, now dedicated to the late Ovide Arino, is still running under diverse local responsibilities all over Europe.

Thanks to our members, various curricula dedicated to Mathematics in the Life Sciences have been activated at various places in Europe.

Also in 2000, the Board engaged a sub-committee with Marc Chaplain, Hans Heesterbeek and Philippe Tracqui, in order to establish a **Student Travel Font** allowing PhD students and young post-docs to participate in Conferences and Workshops.

ESMTB has always considered of great importance to keep and establish solid links with national societies in Europe at large, and "sister" societies such as SMB (with which we have since long a joint member-ship programme) and the JSMB, the Japanese Society that was founded as *"Association for Mathematical Biology"* already in 1989.

Mayan Mimura

More than that, action has been taken to become associate members of international organizations in Europe, and in the world; in particular, the European Mathematical Society (EMS) and ICIAM (International Council for Industrial and Applied Mathematics) have welcomed our association to both of them, and delegates of ESMTB have a seat in their Board/Council. ESMTB has always played an active role at the ICIAM quadrennial conferences, with dedicated sessions and a series of main lectures, including the ones by Wolfgang Alt and by Jim Murray. For the 2011 conference to be held in Vancouver, ESMTB has contributed in a significant way to shape its scientific programme.

ESMTB has been actively participating in further international initiatives such as the International Conferences on Population Dynamics, the so-called DESTOBIO; etc.

As far as the editorial activity is concerned, the *Biomathematics Newsletter* with its first issue in June 1988 has evolved into the annually appearing *European Communications in Mathematical and Theoretical Biology*, and the *Journal of Mathematical Biology* (JMB) by Springer has been adopted as the Official Journal of our Society (one of the two current Editors in Chief of the Journal being Mats Gyllenberg, past President of ESMTB). JMB hosts the ESMTB pages dedicated to "perspectives" in the fields of our interest; let me recommend members of our community, especially the young ones, to read such pages, which offer an overview on possible developments of the discipline.

In addition, many ESMTB members participate in the editorial boards of important journals dedicated to our discipline at large.

It had been a pity, as stressed by Karl Hadeler and myself in an open letter in the Biomathematics Newsletter, that in 1994 Springer had decided to discontinue, with issue 100, the publication of the *Lecture Notes in Biomathematics*, a pillar in the development of our areas of interest, which have included volumes that now are classics of the international scientific literature; not to forget the equally named book series, out of which singles out the book by Jim Murray, one of the most influential volumes in the whole field of Mathematics applied to Biology. I am aware of various attempts to re-establish such a series with different publishing companies, and I wish that soon we may have a similar authoritative series of volumes.

Meanwhile, scientific literature dedicated to Mathematics in the Life Sciences has enormously increased both in quantity and even better in quality, and direct collaboration of Mathematicians with Biologists, though difficult, has shown significant results.

One of the most prominent activities of our Society is the organization of the internationally well-known

European Conferences on Mathematical and Theoretical Biology, since 1998 most of them jointly organized with SMB, see

http://www.esmtb.org/conferences

After the first one held in **Grenoble-Alpes D'Huez** in 1991, the flag had been passed to

The **2nd** **European Conference on "Mathematics Applied to Biology and Medicine"**
December 15-18, 1993
at Ecole Normale Supérieure de **Lyon**, France
Organizers: *Pierre Auger & Jacques Demongeot*

The **3rd** **European Conference on "Mathematics Applied to Biology and Medicine"**
October 6-10, 1996
at University of **Heidelberg**, Germany
Organizer: *Willi Jäger*

Willi Jäger and Vincenzo Capasso

The **4th** **European and International Conference on "Theory & Mathematics in Biology & Medicine"**
June 29 – July 3, 1999
at Frije Universiteit **Amsterdam**, The Netherlands
Organizer: *André de Roos*

The **5th** **European Conference on "Mathematical Modeling & Computing in Biology and Medicine"**
July 2-6, 2002
at Università di **Milano**, Italy
Organizer: *Vincenzo Capasso*

It is a pleasure to mention that this conference, substantially supported by the European Union, had been recognized as one of the few Success Stories within the Fifth Framework Programme, the only one related to Mathematics (http://ec.europa.eu/research/fp6/mariecurie-actions/pdf/hls_en.pdf)

The **6th** **European Conference on Mathematical and Theoretical Biology**
July 18-22, 2005
at the Technical University of **Dresden**, Germany,
Organizer: *Andreas Deutsch*

The **7th European Conference on Mathematical and Theoretical Biology**
June 29 – July 4, 2008
at the University of **Edinburgh**, Scotland
Organizer: *Marc Chaplain.*

The **8th European Conference on Mathematical and Theoretical Biology**
will take place
June 28 – July 2, 2011
at the University of **Krakow**, Poland
Organizer: *Ryszard Rudnicki.*

The numbers of participants during these Conferences have steadily increased; more than 500 in Amsterdam (1999); there were almost 700 in Milano (2002); at the Conference in Dresden (2005) the organizers counted **810** participants coming from all over the world.

In addition to the above, with great satisfaction it is to mention the major role played by members of our community in establishing centres of excellence, dedicated to the interaction between Mathematics and Life Sciences; among many of them I am aware of CIMAB (Italian National Centre for Mathematics for Biology, Environmental Sciences and Medicine), including the major Italian institutions at Italian Universities and National Research Council; the Centres for Mathematical Biology in Oxford, Nottingham, Bath and Dundee, BIOMS in Heidelberg, RICAM in Austria, also the Institute for Theoretical Biology at Humboldt University in Berlin and others of similar kind.

I would like to mention that even the IHES (Institute des Hautes Etudes) in Paris, usually dedicated to pure mathematics and theoretical physics, is nowadays actively involved in a programme on Mathematics and Molecular Biology (the Abel Prize recipient Misha Gromov being one of the major scientific animators of such a programme) http://www.ihes.fr/jsp/site/Portal.jsp?document_id=1988&portlet_id=1044.

This year I have been given the responsibility of the Presidency of the *European Academy of Sciences* (www.eurasc.org), as a concrete recognition of my continued efforts in building up a European community of Scientists,

including the foundation of ESMTB. The reader may like to know that the first important action that I have launched for the EURASC has been the Kepler Prize for Young European Scientists (KEYS) offered to a multidisciplinary and multinational group of young graduates; in fact, the first Kepler Workshop has been dedicated to Mathematics with Biology and Medicine, and been supported by BIOMS and IWR (i.e. Willi Jäger, once again) at the University of Heidelberg, and the Heidelberg Academy of Sciences, see below (**page 34**) and
http://www.eurasc.org/kepler/Kepler2010.asp

I have been glad to realize that authoritative scientists of our community are also members of EURASC, including Mats Gyllenberg, Peter Jagers, Willi Jäger (also Blaise Pascal Medallist of EURASC), etc. I look forward to organize further events in collaboration with ESMTB.

Vincenzo Capasso,
Universita' degli Studi di Milano

Kepler Prize Workshop on Complex Living Systems
Managing Complexity, Reducing Perplexity
Heidelberg, May 16-20, 2011

This workshop has been held as a part of the 2010-11 KEPLER AWARD for European Young Scientists (KEYS), established by the European Academy of Sciences (EURASC). Recipients of the award have been *Marcello Delitala* (Italy), *Giulia Ajmone Marsan* (France), and *Andrea Picco* (Germany), leading a group of a dozen of young European scientists with a PhD in either Mathematics or Biology, or Medicine.

The workshop, financially supported by the BIOMS programme of the University of Heidelberg (part of the BioQuant initiative), and the IWR of the same University has taken place at the historical Heidelberg Academy of Sciences and Humanities (during May 16-18), and at the interdisciplinary BioQuant center of the University of Heidelberg (during May 19-20).

The meeting has been devoted to the modelling and simulation in life sciences, focussing on some of the most challenging current topics in biology and medicine and related mathematical methods, with the aim of achieving a deeper insight into those biological phenomena and, ultimately, a better understanding, simulation and control of them.

Interdisciplinarity has been the leading issue of the workshop; the ability to interpret scientific problems from different points of views is evidently more and more important, besides the technical knowledge needed to face them.

The workshop main topics have been: complexity in life sciences and in biosystems, regulatory networks, cell motility, multiscale modelling and simulation of cancer, morphogenesis and formation of biological structures, and evolution and adaptation.

These topics have been developed by researchers from various disciplines and different scientific communities (biologists / mathematicians / physicists), sharing a common interest in life sciences.

Intense discussions among participants and stimulating interchange between senior and young researchers in a very collaborative atmosphere have been a specific feature of the workshop. Several round tables were organized to discuss the topics of the day, highlighting possible new lines of research and methodology, and giving suggestions for the scientific development and careers of young researchers.

A key issue emerged during discussions has been the need of more and more direct interaction between Mathematicians and Biologists, along the following keywords:

Data Driven ⟷ *Model Driven*
Modelling *Experiments*

The workshop has been surely instrumental in furthering interactions for joint research and exchange of information among groups beyond disciplinary silos and political boundaries. Ultimately, it has been a way to identify a common ground for further collaborations and a seed of future collaborations.

More than 50 researchers participated in the workshop. The scientific programme included 10 keynotes talks, delivered by senior speakers – *D. Brunner* (Zurich), *F. Bussolino* (Turin), *V. Capasso* (Milan), *A. Dell* (London), *T. Hillen* (Alberta), *L. Hufnagel* (EMBL, Heidelberg), *W. Jäger* (Heidelberg), *U. Klingmüller* (DKFZ, Heidelberg), *V. Quaranta* (Nashville), *D. Sherrington* (Oxford) - and almost 20 invited talks delivered by young scientists from many different European institutions.

Interaction has been favored by an intense social programme, including a welcome party in the historical halls of the Academy, a well attended and vivid Social Dinner at an historical Heidelberg Brauerei, and an agreeable boat trip on the Neckar River, with interesting discussions on the top roof of the boat, thanks also to a sunny afternoon. An expected important outcome will be the enhancement of a European Community through scientific cooperation.
During the workshop, it has been planned to edit

a booklet reporting the contributions, in terms of extended abstracts and presentations of the speakers. The book will be regularly registered as a publication, for further dissemination, possibly by an authoritative international publisher.

We wish to thank here all those who contributed directly or indirectly to the successful organization of the Workshop: participants, speakers, the President of the European Academy of Sciences for the initiative of the Award, the Directors of BIOMS and of IWR at the Heidelberg University , for the generous financial support and the local organization, together with the local Academy of Sciences and Humanities who have offered such a great opportunity to young researchers.

Particular thanks are due to the Local Committee of the University of Heidelberg (Willi Jäger, Maria Neuss-Radu, Anna Marciniak-Czochra, Ina Scheid) for their essential support to the workshop successful outcomes.

All information regarding the workshop can be found at the web site of the conference:
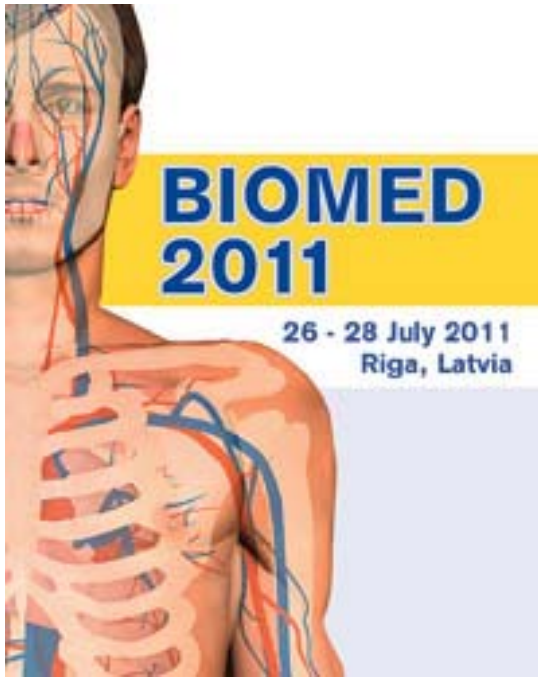
http://www.eurasc.org/kepler2010

where a gallery of pictures will soon appear.

Marcello Delitala
(on behalf of the
Kepler Prize Recipients)
Turin, May, 2011

Kepler Prize Winners and Selection Committee

Ninth International Conference on Modelling in Medicine and Biology

26 - 28 July 2011
Riga, Latvia

Organisers: University of Lativa, Latvia, Riga Technical University, Latvia, Riga Stradins University, Latvia & Wessex Institute of Technology, UK
Sponsored by WIT Transactions on Biomedicine and Health

View the conference website, which has full details about the conference objectives, topics and submission requirements at:
http://www.wessex.ac.uk/biomed2011news3.html

This ninth International Conference on Modelling in Medicine and Biology is a well established and recognised forum for dissemination of the latest research and applications in this important field.

Advances in medical and biological technology are transforming medical care and treatment; in great part this is the result of the interaction and collaboration between medical sciences and engineering. This has resulted in substantial progress in health care and in the quality of life of the population.

Computer models in particular have been increasingly successful in simulating biological phenomena. These are lending support to many applications, including cardiovascular systems, the study of orthopaedics and biomechanics and electrical simulation amongst others.

Another important contribution, due to the wide availability of computational facilities and the development of better numerical algorithms, is the ability to acquire, analyse, manage and visualise massive amounts of data.

The conference topics cover a broad spectrum including the application of computers to simulate biomedical problems, ranging from cardiovascular modelling to virtual reality and simulation in surgery.

This important conference started in Southampton in 1991, followed by a meeting in Bath (1993) and others in Milano (1995), Aquasparta (1997), Ljubljana (2003), Bologna (2005), New Forest (2007) and Crete (2009). The papers presented at these meetings are archived in the WIT eLibrary
(http://library.witpress.com), where they are immediately and easily accessible to the international scientific community.

Conference Topics

- Cardiovascular system
- Biomechanics
- Simulation of physiological processes
- Computational fluid dynamics in biomedicine
- Orthopaedics and bone mechanics
- Data acquisition and analysis
- Virtual reality in medicine
- System Biology

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 four years of broad response (with more than 10 applicants on the average) and successful selection of winners, see the documentations in the annual *European Communications (ECMTB No. 10 - 13),* 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 currently consisting of:

> Andreas Deutsch
> Carlos Braumann
> Philip Maini
> David Rand
> Peter Schuster

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 *Andreas.Deutsch@tu-dresden.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 **31st December** of each year, by which time the nominated thesis should have received final acceptance by the doctoral granting institution. Names of potential applicants may also be suggested by any ESMTB member (by writing to Andreas.Deutsch@tu-dresden.de).

Shortlisted applicants will be asked to send their full thesis.

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The picture on the front cover is taken from

Figure 4 in the Extended Thesis Summary by Václav Klika
Simulation of bone remodeling

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