
Editorial

Dear readers,

Welcome to the October 2002 issue of the European Communications for Mathematical and Theoretical Biology, the communications journal of the European Society for Mathematical and Theoretical Biology (ESMTB). This is the 4th issue in the new style and fortunately we were able to prevent another delay this time.

In this issue there is more news from the ESMTB than previously. You will find the new ESMTB statutes on the next page, the minutes of several board meetings and of the general assembly starting on page 4, ESMTB's finances (p.6), ESMTB board candidates' statements (p. 8) and a report on the conference in Milano (page 28).

In this issue you will not find, in contrast to the previous issues, reviewed scientific papers by young authors. We have decided to stop publishing these papers. There are several reasons for this. First of all, it is not good to work in competition with established scientific journals. Furthermore, the refereeing and rewriting process has led, on more than one occasion, to severe delays (notably for the 3rd issue).

As you will read in the section on Society news, the ESMTB has reached agreement with the publisher Springer Verlag about adopting their *Journal of Mathematical Biology* (JMB) as the official scientific journal associated with the ESMTB. This is a very good development for both the members of ESMTB and for the journal. The agreement will have some repercussions for the Communications. In every issue of JMB (monthly), the ESMTB will get two pages that can be used for informing its members. One of us, who is also a member of the ESMTB board, has written down suggestions for the kind of information that could be provided (see page 7). We would value the opinion of our readers on this. Please send your comments and suggestions to Hans Heesterbeek (address below) and also indicate if you wish to take on part of the work involved.

After finishing this issue, Andrea de Gaetano will leave ECMTB's Editorial Board due to personal reasons. The remaining editors regret this. We thank him very much for all his hard work for the newsletter in recent years. In particular, we owe him the Communications' look which so much improved on its predecessor, the Biomathematics Newsletter.

This service to ESMTB members can be maintained only if the editorial team is now strengthened. We urgently need additional people to take care of specific tasks, each of which requires only little work once every six months. To give an example, one task is to contact organizers of workshops, conferences and summer schools and ask them to submit a brief report for the Communications, and then to make sure these arrive in time and to put them in a standard format (and edit them if needed). There are several tasks like this. If you want more information on the kind of tasks we need help for, please contact one of the editors by e-mail. Otherwise, this issue may be the last issue!

We hope you find this issue worth reading and valuable.

The editors: Wolfgang Alt, Andrea de Gaetano, Edith Geigant, Hans Heesterbeek

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

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

The email address for questions and suggestions is

esmtb@mis.mpg.de

*The closing date for submissions to the next issue COMMUNICATIONS # 4 will be **March 31st, 2003**. Please send, preferably by e-mail, information, scientific reports and other material to one of the editors:*

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Statutes of ESMTB

Approved by the General Assembly, Milan, July 5, 2002.

The old text is written in normal font

Additions are written in **bold font**

Deletions are written using ~~striketrough font~~

EUROPEAN SOCIETY FOR MATHEMATICAL AND THEORETICAL BIOLOGY

SOCIETE EUROPEENNE DE MATHEMATIQUES ET DE BIOLOGIE MATHEMATIQUE ET THEORIQUE

STATUTES

1. Name and Residence

A1. The name of the Society is: "European Society for Mathematical and Theoretical Biology (ESMTB)". The Society has its registered office in Grenoble (France) **and is subject to French law.**

2. Purpose

A2.1. ESMTB is a nonprofit organisation. The purpose of the Society is to promote theoretical approaches and mathematical tools in biology in a European **and wider** context.

A2.2. The Society will achieve its purpose stimulating scientific research and education in the field of Mathematical and Theoretical Biology by:

organizing conferences

organizing courses and summer schools

promoting the distribution of scientific papers

promoting scientific exchanges

collaborating with other existing organizations in the same or related field at a national, continental and world scale

promoting further unification of European and world societies

any other means...

3. Members

A3.1. The Society is composed of full members (persons and institutions), honorary members, and student mem-

~~bers. Registration as a member of the Society is carried out by the Board after verification that this person has sufficiently shown competence and well-grounded interest in the field of activity of the Society.~~

A3.2. Membership shall end by written resignation **by the member or by cancellation, due to failure to pay annual membership fees and may be cancelled after consideration by the Board.**

A3.3. The Board shall keep a register in which the names and addresses of the members are recorded.

A3.4. Reciprocity membership at reduced rate will be considered after approval by the board with similar national organizations.

4. Admission

~~A4.1. Free admission for the founders members (see A11.4)~~

~~A4.2. Free admission disappears once the society is created~~

~~A4.3. New members will have to be proposed by 2 full members.~~

5. Board

A5.1. Only full members, ~~who are permanent residents of Europe and Israel~~ can be members of the Board. The Board consists of ten persons, elected by secret mail ballot, voted by the majority of the full and honorary members (one member = one vote). The term of each Board member is six years. The terms should overlap such that every three years five new Board members are elected. Board members cannot be elected for more than six consecutive years. **The term begins on January 1st the year after the election.**

A5.2. The Board chooses a President, a Vice-President, a Secretary and a Treasurer among its own ranks. The posts of Secretary and Treasurer may be held by the same person.

The President directs the activities of the Society. He/she is the official representative of the society. If the President is temporarily prevented from fulfilling his/her duties the Vice-President shall temporarily take his/her place.

The Secretary maintains the records of the Society in cooperation with the President and in accordance with the decisions made by the Board.

The treasurer is responsible towards the Board for the funds and annually presents a written report on these to the Board.

A5.3. The Board meets as often as necessary, **but at least once a year**. It is convened by ~~its~~ **the President** or at the request of at least ~~three~~ **five** of its members. The presence of ~~three~~ **the President and at least four other** members of the Board is necessary for the deliberations to be valid. Minutes shall be taken during each sitting and they shall be signed by the President and the Secretary.

A5.4. Decisions are made by an ~~absolute~~ **simple** majority of votes. Material decisions may be made by oral ballot. Decisions concerning persons shall be made by secret ballot. **The President has a tie breaking vote in material decisions. In decisions concerning persons ties are resolved by casting lots.**

A5.5. The expenditures are regulated by the President. The Society is represented in courts of law and in all legal domains and **financial matters** by the President or his designated representative. The representative of the Society must enjoy full possession of all legal rights.

A5.6. The Board is responsible for regular accounting of its budget and shall present the latter at General Assembly meetings.

A5.7 The Board applies and interprets the statutes

6. General Assembly

A6.1. The General Assembly is composed of all ~~full and honorary~~ members. An institutional member has only one vote. The General Assembly meets **at least** every ~~two~~ **three** years. It is convened by the Board or at the request of at least one third of its members. Its agenda is proposed by the Board. **The announcement and the agenda must be made public at least one month before the meeting.** The President of the Society chairs the meeting.

A6.2. The General Assembly approves reports on the management of the Society, the financial situation, the state of the Society and other related areas.

A6.3. The General Assembly approves the accounts of the previous ~~fiscal period~~ **three years** and deliberates issues on the agenda.

A6.4. No procuration will be accepted for votes.

7. Advisory Council

A7.1. For specific tasks (such as summer schools, congress, European Commission), the board may appoint advisory councils. It is the duty of the advisory council to give advices to the Board on request or according to its own will. It can for example constitute the scientific committee for the periodic Scientific Congress of the Society.

A7.2. The members of an advisory council are appointed for a period of not more than four years; after this period, they may be reappointed for only one consecutive term.

A7.3. The advisory council is chaired by a President appointed by the Board.

8. Scientific Committees

A8. The Board is authorized to create scientific committees on specific topics, which report directly to the Board, the members of so-called scientific committees being appointed and dismissed by the Board.

9. Financial Resources

A9.1. The financial resources of the Society come from:

fees contributed by the members,
subsidies,
acquisitions by testamentary succession and gifts,
other assets.

A9.2. The Board determines the annual membership fees.

A9.3. Books and records are kept of the financial state of the Society in such a manner that its assets and obligations may be established at all times.

A9.3.1. The Board annually appoints two cash auditors (outside and independent of the Board) who, for a period of one year, audit the accounts and give a written report to the General Assembly.

A9.4. The General Assembly's approval of the accounts releases the ~~Treasurer~~ **Board** of the Society from all liability with regard to ~~his~~ **its** management for the former ~~two~~ **three** years.

10. By-laws

A10. The Board draws up by-laws necessary to efficiently run the Society.

11. Modifications and dissolution

A11.1. The statutes of the Society may be modified ~~by the vote of at least half of the present members at the general assembly (no procuration accepted for all matters related to elections and votes)~~ **by simple majority of voting members through mail ballot.**

A11.2. The dissolution of the Society may be decided by vote, only by the approval of at least two thirds of all of its members **through mail ballot.** The General Assembly should then appoint one or several committees charged with the duty of liquidating the assets of the Society. The Board makes use of the net assets of the Society according to law and to the purposes of the Society.

~~A11.3. The Board applies and interprets the statutes.~~

~~A11.4. The following persons are the founders of the Society: the persons having explicitly and personally expressed their will to found the Society during L'Alpe d'Huez meeting, on January 10, 91.~~

~~A11.5. The following persons constitute the provisory Board of the Society:~~

~~V. Capasso — Education
J. Demongeot — Secretary
K.P.Hadeler — Communication and EEC relationship
W. Jäger — Organization of the Heidelberg meeting
J. Murray — President~~

~~Grenoble, December 10, 1991.~~

12. The new statutes become effective on January 1st 2003.

Society News

ESMTB Board Meeting

Tuesday, July 2nd, 2002 at the Department of Mathematics, University of Milano

Present: V. Capasso, M. Gyllenberg, M. Kaufmann, V. Krivan, A. Stevens, P. Traqui

Guests:

for the discussion about Communications and Summer Schools: W. Alt, A. DeGaetano

for the discussion of reciprocity memberships: M. Mimura (Japanese association of mathematical biology) C. Panetta, L. Sattenspiel (SMB)

1) Apologies for absence

Z. Agur, O. Arino, M. Chaplain, H. Heesterbeek.

It was agreed upon to shift some points of the agenda.

2) Reciprocity memberships

M. Mimura reported about the Japanese association of mathematical biology: It exists since 1989 and has about 300 members. Once or twice a year bigger meetings take place. The last one was in Hawaii, jointly with SMB. A Japanese society of mathematical biology should be founded soon (in 1 or 2 years). There is the hope to have a joint conference with ESMTB in 2004/2005.

ESMTB expects to have about 300 members by 2003. There are more efforts to convince Brussels now to accept mathematics in the life sciences.

L. Sattenspiel: SIAM has formed a new group in life sciences. SMB is very interested in reciprocity memberships. Several scientists are members of ESMTB and

SMB. There is a hope for more members. It has to be discussed how to deal with the two official Journals of SMB and ESMTB.

JMB is now the official Journal of ESMTB. Scientifically it is and will be open to scientists from all nations. Joint conferences should take place, like in Amsterdam in 1999. Specific joint committees will discuss details of financial arrangements for the reciprocity memberships and concerning the two Journals later.

The board thanked M. Mimura, C. Panetta and L. Sattenspiel

3) Communications

Wolfgang Alt excuses the delay of publication of the last Communications. There were many practical problems. In the future the workload has to be distributed. New volunteers are needed.

JMB will have only 24 pages per year free for publication of society news. Also JMB does not allow for special issues. Therefore the Communications are very important. Its regular appearance is of utmost importance. A publication twice a year is optimal.

The Communications should contain reports on activities, announcements of future activities, a list of recent publications of people, who are interested in the Communications, longer abstracts of theses, research announcements. There was a discussion whether scientific papers should be published in the Communications or not. For young people it could be better to publish in regular journals.

Short term announcements like jobs or conferences, advertisements of jobs and institutions should be put on the society web-page. The Communications should contain medium and long term information. Written reports of financial issues of ESMTB should appear.

The president of the society should be in touch with the editorial board of the Communications. Also an editorial board within the board should be formed which discusses the information to be put into the 24 pages in JMB per year, in the Communications and on the web.

Another issue of the Communications should appear in October. Among all other information it should contain short statements of the possible new board members. The opening lecture of the ECMTB2002 by M. Iannelli and the closing lecture by W. Jäger should be published. Information on the 6th framework program of the EU should be given.

From next year on the Communications will have the subtitle: Forum of the ESMTB.

Financial handling for the Communications will be done in Rome for the next issue.

4) Summer Schools

DeGaetano: Summer schools have taken place in Saint Flour (1997), Termoli (1999) with EU grant, Martina Franca ESMTB school (2000) with EU grant, Siguenza ESMTB school (2001), Urbino ESMTB school (2002), with EU grant. There is the wish to re-confirm O. Arino as organizer of the schools.

Clear accounts of the schools should be made. A membership list should be kept. The information of the board about the planning of summer schools should be better. The board should have an input into the themes of the school. More modern fields should be included. ESMTB members should be asked what their interests are.

The board thanked W. Alt and A. DeGaetano for their reports.

5) Minutes of previous meeting

The Minutes of the Prague meeting were accepted.

6) Balance of 2001, 2002

The balance of 2001, 2002 was approved.

The secretary of ESMTB should provide an updated list of members.

People who have not paid yet should be reminded to pay.

7) Discussion of the new statuses

Compare separate information by Mats Gyllenberg.

7a) Elections

Compare minutes of the Assembly of ESMTB (following below).

8) Update about the Conference

See report on the 5th ESMTB Conference on Mathematics & Computing in Biology and Medicine (ECMTB2002) by Daniela Morale in Past Activities (on page 28).

9) Preparation of the General Assembly

10) Proposal for the next Conference

Alcala/Madrid Spain, Rafael Bravo as local coordinator.

11) Other business

None.

The Board thanked V. Capasso very much for being the host of the board meeting in Milano during the 5th European Conference of the ESMTB.

Report by Angela Stevens (for the ECMTB board).

Minutes of the General Assembly of the ESMTB

Milano, July 5th, 2002, at the 5th Conference of the ESMTB

Present: 18 members of the ESMTB (including 4 board members - Capasso, Gyllenberg, Krivan, Stevens) (Boukal, Cerrai, Jaeger, Kirkilionis, Koski, Logofet, Marciniak-Czochra, Morale, Paveri-Fontana, Preziosi, Pugliese, Schuster, Swat, Westerhoff).

Report about ESMTB activities concerning EU funding is added to the agenda. With this change the agenda was approved.

1. Presidents report

20-25 new ESMTB members were attracted during the Milano conference. Overall ESMTB has about 300 members but only about 150 have paid.

ESMTB is member of EMS and has a seat in the council of EMS. Mats Gyllenberg is the delegate. The special committee for applied mathematics of the EMS has been confirmed and its role strengthened after the meeting of EMS in Berlingen (CH). V. Capasso and M. Gyllenberg participated in the meeting. V. Capasso has been confirmed as a member of the committee for the next term.

Last year in Berlin at the joint meeting of SIAM and EMS mathematics in life sciences was very much present. V. Capasso was part of the program committee.

ESMTB is a member of ICIAM and has a seat in its council. V. Capasso is the delegate of ESMTB. A call for mini-symposia is out for the ICIAM at Sydney. Members of ESMTB are encouraged to contribute.

Remark from the audience: Molecular aspects in biology should be considered more.

For the ECMTB 27 mini-symposia were organized. 75 fellowships were given from Brussels for the conference. Also funding for East Europeans was available, partially disregarding age.

ESMTB is organizing regular summer schools, has Communications, a web-page, adopted JMB as official journal of the society, a list of other journals is offered at a reduced prize.

From 2003 on JMB is the official journal of ESMTB. The present editors in chief stay during the next term. Every 4 years the editors in chief may change. Normally one of the two editors in chief is from North America. The editorial board should be international and attract papers also from emerging fields

Remark from the audience: The editors must be independent from any society.

Remark from the audience: Some journals act differently.

ESMTB pays a flat fee of 10.000 Euro per year for JMB. The electronic version of JMB is free for paying members of ESMTB. They also receive the Communications, have reduced rates for summer schools, get two other journals for a lower prize. 24 pages in JMB (2 pages per issue) are free per year for advertisements of the society. Institutional members of ESMTB might also use these. Five members of an institution which is an institutional member of ESMTB can take advantage of the benefits. There is no free electronic access to JMB for institutional members.

SMB and the Japanese association of mathematical biology were both positive about a possible reciprocity membership and the joint organization of workshops. Details of membership fees have to be discussed. The budget and fees of ESMTB should be decided upon by the board. Fees have to be raised next year.

Remark: A detailed discussion about ESMTB membership fees followed. It ended with a consulting vote of the assembly:

In order to not discourage membership, the fee for 2003 should not exceed 60 Euro for regular members. The membership fee for normal members who pay for 3 years in advance should be 3x60 Euro. (accepted by all present persons)

The editors of the Communications ask for help (Alt, DeGaetano, Geigant, Heesterbeek) The Communications are a forum for the society. The web page is for real time information, like conferences, positions. The Communications should contain medium and long-term information. The ESMTB board will form a general editorial board to decide where to put which information (JMB, Communications, web-page).

Summer schools were held in St. Flour, Termoli, Martina Franca (1st ESMTB school), Siguenza (2nd ESMTB school), Urbino (3rd ESMTB school).

Members of the society should be informed by e-mail about the school. In future there should be fewer lectures with a longer duration each (e.g. 3/4 lectures for 5/6 lecturers each) during the schools and they might only last for a week.

The student travel fund of ESMTB should be advertised in a better way.

2) Balance:

The balance of 2001, 2002 was approved by the assembly.

3) Elections:

5 board members out of 10 step down every 3 years, after they have served 6 years. This time:

Z. Agur, O. Arino, V. Capasso, M. Chaplain, A. Stevens. They have to be replaced. People have to be considered who dedicate their work fully to mathematical and/or theoretical biology. Many fields should be represented within the board, many nations, the gender balance

should be take care of. Most important is quality of research and dedication to the development of the society.

Until end of August all members of ESMTB have the right to suggest new candidates. M. Chaplain, H. Westerhoff, A. Pugliese and A. Stevens take care of this procedure as election committee.

In the future, 2 month before the general assembly an e-mail to all members of the society will be sent and ask for suggestions of new candidates for the board. One month later suggestions have to be sent in, so that 1 month before the assembly a list with those 10 candidates with the largest numbers of supporters can be prepared and sent to the members of ESMTB.

4) New Statutes:

The new statutes were presented and discussed. All people in the assembly agreed to them. The new statutes will be sent to all members of the ESMTB and will become effective on January 1st, 2003.

5) 6th framework program of the EU

ESMTB should consider proposing its own network.

6) Discussion:

ESMTB should connect with biological societies. Bioinformatics should be included, molecular biology too.

7) Suggestion for the letter to the ESMTB members:

Elections of the new board for the period 2003-2005 will be held during fall by mail ballot. All members of the society are active and passive voters.

Candidates are invited to send a short scientific profile of themselves and their aims to the editors of the ESMTB Communications and also to the secretary of ESMTB by the end of August 2002, according to the format of previous candidatures (compare the first issue of the communications) The next elections will be for five new members of the board.

The five confirmed board members are:

M. Gyllenberg FI, H. Heesterbeek NL, M. Kaufmann BE, V. Krivan CZ, P. Traqui FR

Report taken by Angela Stevens (for the ECMTB board).

Report of the Secretary/Treasurer

M.A.J. Chaplain, Secretary and Treasurer of ESMTB, University of Dundee

Membership: Currently the membership of the Society stands at 303. This figure includes all those individuals who, at one time or other during the period January 1998 – June 2002 have paid annual membership fees at least once. This represents a large increase in the membership since 1998 when the figure was 85. However, there remains a difference in “members” and those who actually pay their annual fee (see below).

Annual Fees: The collection of the annual membership fee has always been problematic. The Society’s bank account is currently located in the UK and payment must be made in pounds sterling. Given current financial practice there is always some “loss of money” in bank charges when transferring money between two countries

with different currencies. Prior to the introduction of the EURO earlier this year the problems were complicated for all involved. However, the most efficient way up until now to receive the annual fee of €40 is by cash and this has been largely successful. It is anticipated that the new treasurer will be based in a country within the EUROZONE and that a new Society account will be set up later this year in EUROS. This will facilitate the transfer of future annual fees for all members (except those of the UK!!). Up until now, due to the “small” number of members it was not possible to pay using credit card as this would have introduced a very large annual fee (£1000, €1700) payable to the bank which the Society was unable to afford. Should the membership continue to rise this may be a viable payment option in future.

A letter reminding members to pay their forthcoming annual fee is normally sent out in November/December. However, it should be noted that there is a (large) difference in the membership number (303) and those who regularly pay their annual fee. The current number for those who have paid their 2002 annual fee is 125 (this is expected to rise slightly after the ESMTB Conference, Milano July 2002, and also the ESMTB Summer School in Urbino). This has been a “historical problem” for the Society and it is hoped that setting up a EURO bank account later in the year will enable more members to pay their annual fee quickly and easily. It is hoped that more “institutions” will join the Society over the forthcoming years.

Financial accounts: The current balance of the Society’s accounts stands at €9340. This is expected to increase to over €10,000 by the end of the year since there will be more membership fees paid in by then. Thus the Society will be in a position to meet the cost of paying Springer Verlag in early 2003 for the new Journal agreement from the current funds (It should be noted that I inherited the Society’s accounts with zero money in them!!).

Overall summary: The Society is currently in a healthy position financially, but will need all the current reserves to pay the first annual fee to Springer. However, it is hoped that the new benefits of having a world-class international journal as the Society’s official journal will lead to an increase in membership. Coupled with easier payment methods when the new treasurer takes over, I believe that the financial future is good. Of course all concerned with the Society – ordinary members and Board members – must continue to work hard to ensure the Society’s continued growth and success over the next few years.

Journal of Mathematical Biology becomes the official journal of the ESMTB

Mats Gyllenberg, Vice President of ESMTB

The Board of ESMTB and Springer-Verlag have signed an agreement concerning their future collaboration over the publication of the Journal of Mathematical Biology (JMB). According to this agreement JMB becomes the official journal of ESMTB as of January 1, 2003 (Volume 46/1).

The agreement gives benefits both to individual members and to the Society as a whole. All individual members who have paid their membership fee will have electronic access to the full content of JMB without any extra charges. Members will be informed of how to register online with LINK to access the full-text version of JMB. ESMTB will pay an annual lump sum of EUR 10 000 for this electronic access.

ESMTB will assume responsibility for future scientific guidance of JMB. It will identify new or emerging areas of research in mathematical biology that should be represented in the scope of JMB. In cooperation with the Editors-in-Chief and in consultation with Springer, it will take appropriate steps to adapt the published Aims & Scope of JMB and the composition of the Editorial Board, as and when necessary, to reflect such developments. The Society will in cooperation with the Editors-in-Chief then in office and in consultation with Springer, appoint the Editors-in-Chief next to take office. Normally one of the Editors-in-Chief will have a North American affiliation. The present Editors-in-Chief will remain in office for a further (renewable) four year term. In each issue of JMB, two pages will be available to material produced by ESMTB. These pages will contain for instance announcements of ESMTB events and other activities.

Suggested content for the ESMTB-pages in JMB

Hans Heesterbeek (Member of ESMTB board)

When the *Journal of Mathematical Biology* (JMB) becomes the official journal of the ESMTB, as of January 1st 2003, we will be responsible for two pages per issue. The journal has two volumes of six issues each per year, leading to a total of 24 pages of information from ESMTB.

1. Generating the content must run like clockwork. Publication of the issues cannot be delayed. A single coordinator must ensure that two pages are delivered to Springer every month.
2. The information given on the ESMTB-pages must be of interest to our members, but also to other readers of JMB. Ideally, the pages must generate interest in the society amongst non-members reading the journal.
3. The information must be diverse, but must not compete with the *Communications* (formerly *Biomathematics Newsletter*) of the ESMTB. Information specific for members (e.g. minutes of board meetings) and information taking up more space and providing more details will be given only in the *Communications*. Given the much more speedy publication of the JMB-pages, the possibility exists to contact members fast.
4. Contributions have to be fixed and commissioned far in advance and back-up material needs to be present in order to prevent empty pages (even partly) from arising.
5. Sections of different types of information could be rotated through the year so that readers know what to expect and so that the coordinator can have several people responsible for one or two pages per year.

Suggested content:

1. Every issue has to contain brief information about the ESMTB: its aims and activities, current board (+ list of past presidents), how to contact the board, web-address + Communications address, where to send material of interest to the members, conditions for membership (+ reciprocal membership and benefits) and how to become a member or institutional member. **This must be possible in ½ page, every issue.**

2. Fast communication with ESMTB members (and also to show these activities to other readers). **Maximum ½ page per issue**, not to be used if no such information is available. Examples of use: details of ESMTB conferences, summer schools and other activities (such as travel grants, awards etc). If this part is not used, one of the parts below can expand for that particular issue.

3. Notifications of new books: title, author(s), publisher, isbn-number(s), price, publication date, and number of pages. **One page, three per year, e.g. every February, July and September.**

4. Notifications of conferences, summer schools: name of activity, place and dates, contact person + address, web-site address. **One page, three per year, e.g. every January and June and October.**

5. Recent advances: short notifications of papers from other journals (biology, medicine, mathematics, computational sciences, ...) that could be of interest to readers of JMB. Title, author(s), journal reference + few sentence explanation of its value (a sort of Perspectives/News and Views as in Science/Nature but very brief). This is more work and needs careful coordination and help from people from various backgrounds in suggesting material. I feel, however, that it is also a very worthwhile undertaking. **One page, twice per year, e.g. every April and December**

6. Research announcements: title, author(s), one paragraph description of research topic and approach. A similar possibility, but then a few paragraphs to several pages, existed previously in JMB. Announcements must be of interest to readers of JMB. It is possible to include a request for mathematical or biological collaboration on the topic highlighted. Also this category of information must be carefully coordinated. **One page, twice per year, e.g. every May and November.**

7. Perspectives on teaching mathematical and theoretical biology/medicine: One page contributions, commissioned by the coordinator. **One page, e.g. every March**

8. Research groups in Europe: ½ page contributions, commissioned by the coordinator, highlighting research groups in theoretical/mathematical biology/medicine; two per page. **One page, e.g. every August.**

Candidates' Election Statements

Wolfgang Alt

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der Universität Bonn, Germany
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Since having been proposed as (another German) candidate, I am ready to serve for these elections, even though I already had been on the Board during the first 5 years

of the Society, and now could well let further colleagues take over.

My main engagement would be within the envisaged 'Editorial Board' -- responsible for collecting and distributing news, announcements, requests, reports, presentations and, particularly, critical and historical notes on Theoretical Biology and Biomathematics in the European Society. Besides the web site and journal pages in JMB, I would further endorse a regular paper publication of the 'European Communications' as a public 'forum for exchange of ideas and concepts'.

An important topic should be more interdisciplinary contacts between bioscientists and mathematicians: in every-day research, in teaching programs as well as on workshops and congresses. In particular, transparent and adaptable *biomath curricula* might be collected and compared (from already realized local programs in different European countries) and, eventually, implemented and tested. Each Applied Math student, graduated or not, should easily be able to visit Biology courses or labs and, vice versa, mathematical modelling seminars and practical simulation courses have to be designed for easy participation by Biology students.

Scientific profile:

As leader of a small interdisciplinary group on *Theoretical Biology* and of two research projects within the SFB 611 on 'Singular phenomena and scaling in mathematical models' I like teaching to biology students, e.g. methods of stochastic processes and spatial differential equations, and working with biologists, physicists, mathematicians and even philosophers on the principles of motion and interaction in biological systems.

Rafael Bravo de la Parra

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I would like the Society to be so attractive that every, or almost every, member of the European biomathematical community feels worthy to join it. To get this I would suggest that the Society begins by supporting all the activities in the field of mathematical and theoretical biology in Europe, whether they are organised by its members or not.

It would be also important to make easier the beginning of the careers of young scientists in the field and it is indispensable to provide a very fluid exchange of information.

I will try to move the Society in that direction. Till now I have collaborated in the organization of some conferences and schools and I hope I can help on this.

Scientific profile:

I'm assistant professor in the Department of Mathematics of the University of Alcalá. I lecture the mathematics courses of the Faculty of Environmental Sciences. My research interests are the application of dynamical systems theory in population dynamics especially in the area of mathematical ecology.

Helen Byrne

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If elected to the Board of the European Society of Mathematical and Theoretical Biology, my main aim would be to raise the Society's profile throughout the mathematical and biomedical communities in Europe and internationally. I believe that this is extremely important as collaboration plays a key role in ensuring that our research is biologically relevant and that the results are exploited fully.

Ways in which we could achieve this include inviting more experimentalists to our meeting and organising smaller, satellite meetings which focus on specific biological or medical problems and which are attended by experimental biologists and mathematicians. (I have experience of organising such events in Nottingham.)

I would also like to encourage more young researchers to enter the field of mathematical biology and to work at the exciting interface between theory and practice.

Scientific profile:

I am a Reader in Mathematical Medicine at the University of Nottingham and hold an Advanced Fellowship which enables me to concentrate full-time on my research. To date, this has focused on modelling different aspects of solid tumour growth, although I have also worked on other problems involving placental development, macrophage infiltration and tissue engineering.

I am motivated by the biomedical applications of the problems and believe that collaboration with experimentalists is important in ensuring that the problems studied are biologically relevant and the results exploited fully.

Andreas Deutsch

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As an ESMTB board member I would concentrate on the following objectives.

a.) *Interaction with experimental biologists:* my impression is that the activities of the ESMTB have already triggered fruitful dialogues and cooperations within the mathematical/theoretical biology community. However, in the future more emphasis should be laid on the strengthening of links with experimental biologists. Possible activities include the invitation of experimental biologists to workshops and schools organized by the ESMTB.

b.) *Mathematization of biology:* the application of mathematics to biological problems is not only attractive for students and researchers at universities but also school children. Own experiences with school children have shown that they are extremely motivated if they learn about “wet” biological applications of seemingly “dry” math. Mathematical biology should not only be considered in university curricula but activities should be extended to inform school teachers and school children about math biology applications. In addition, during the next ESMTB conference one could think about a public

evening which presents a popular science talk with a math biology topic.

c.) *Profile shaping:* I would try to shape the “corporate identity” of the ESMTB. The ESMTB should not “run after” or compete with the numerous financially well equipped bioinformatics activities but instead demonstrate the broad spectrum of math biology ranging from very abstract reasoning (“proof-oriented”) to very applied topics (“simulation-oriented”). This spectrum is still not well known by experimental biologists and often not even by the theoreticians themselves. Also for this aim the next ESMTB conference is a very good forum since one could demonstrate the richness of mathematics applied to biology by distinguished lectures focusing on different “mathematical perspectives”.

Scientific profile:

I'm the head of the newly founded department “Methods of Innovative Computing” at the Center for High Performance Computing at the Dresden University of Technology (for an introduction to the activities of the new department please see the separate article in these communications). I studied mathematics and, received my PhD in biology and my habilitation in theoretical biology.

My research group is focussing on mathematical modelling topics with applications in cancer growth, immune system dynamics and microbial pattern formation.

Also, I'm one of the initiators and organizers of the interdisciplinary MTBio network (Modelling and Theory in the Biosciences, www.mtbio.de).

Reinhart Heinrich

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Aims: My objectives as a Board member of ESMTB are the following:

(1) Although Mathematical and Theoretical Biology is a fast growing field, there is still an enormous gap between theoretical and experimental work. For example, many theoreticians are, to a large extent, unaware about recent achievements of experimental research in the field of molecular cell biology. Moreover, it is my experience that most experimentalists still ignore completely the results of theoretical work. To bridge this gap it will be, for example, necessary to include also biologists in the regular meetings of the society and to organize joint workshops.

(2) Having experience in various research and teaching programs for graduate students I will help to organize International Summer Schools which bring together young scientists and teachers from all over the world. It will be a challenge to focus these schools on combining research in bioinformatics, such as gene expression analysis, with research in the fields of nonlinear dynamics of complex cellular processes. I will work for joining the corresponding activities of ESMTB and the Society of Mathematical Biology (SMB).

(3) There is an increasing need to incorporate Mathematical Biology in the curricula of biology, biophysics, mathematics, and informatics. Based on my experience

in teaching theoretical biophysics over many years I will strongly support efforts in this direction. Although a number of specialized monographs do exist, excellent textbooks are missing which give a broad account of standard methods and results in our field. The ESMTB should coordinate activities in preparing and publishing such textbooks.

Scientific profile:

I'm leader of a research group on theoretical biophysics at Humboldt-University Berlin and director of a Graduate program "Dynamics of Cellular Processes" of the German Research Council (DFG).

My research is mainly focused on the following topics: (1) Mathematical modelling of metabolic networks, (2) Modelling of signal transduction pathways, (3) Nonlinear dynamics and of biochemical reaction systems and cellular transport, (4) Evolutionary optimization in the field of molecular cell biology, and (5) Metabolic Control Analysis.

I'm author of about 120 original papers on these topics (for recent work see: <http://www.biologie.hu-berlin.de/~theorybp/publications/publications.html>) and author of the monograph: The Regulation of Cellular Systems (Chapman and Hall, New York, 1996, with Stefan Schuster). I worked as visiting professor at the University Bordeaux 2 (1990) and recently (2000/2001) as visiting professor at the Department of Cell Biology (Harvard Medical School, Boston). I'm a founding member of the European Society of Mathematical and Theoretical Biology.

Christine Jacob

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I would like to improve the diffusion of mathematical methods, to encourage the generalizations of the models and methods that are built in particular problems. I think that stochastic models and rigorous statistical estimations must be more encouraged. All this could be done during the conferences by giving the invited lectures as courses and by increasing the number of lectures on stochasticity, comparison of stochastic models and their deterministic counterparts, and statistics. This also could be done through a forum where members of ESMTB could ask for methodological problems. European interdisciplinary projects should also be encouraged. The forum could also be used for this objective.

Scientific profile:

I am a research director at INRA (National (french) Agronomical Research Institute) in the Biometrics and Artificial Intelligence department. I am responsible with a colleague for a team dealing with epidemiological risks and food risks. This team has about ten people. I worked in many biological and mathematical fields: in mathematics, my State Thesis was on biological rhythms detection and on confiners, the stochastic equivalent of attractors. Now, my main research interests concern branching processes (behaviour, statistical estimation, approximation by dynamical systems) and their biological applications: modelling, study of the behaviour and estimation of the amplification process in the Q-PCR

biomolecular technology, modelling, study of the behaviour and estimation of the evolution of diseases in open populations, idem concerning the evolution of mosquitoes populations which are vectors for some diseases. I have also worked for several years on the prediction of the functional structure of RNA by modelling its folding by a jump process. I always try to generalize the models and theories that I build in order that they can be applied to other problems.

Luigi Preziosi

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I believe that investing on young researchers is the best policy to have a growing society. Through international schools and workshops the ESMTB already promotes interdisciplinary contacts among young researchers in biology, medicine, bio-engineering, bio-physics, informatics, and mathematics.

I think it is fundamental to encourage young researchers, especially from different fields, to work on the same project. This can be achieved, for instance, by organising study groups and "bio-mathematics modelling weeks", or by supporting joint Ph.D. research projects involving both a researcher in bio-medicine and a mathematician/physicist.

I'd also explore the possibility of having an on-line journal freely accessible to ESMTB members, possibly charging downloads to non-members.

Scientific profile:

Laurea in Mathematics cum laude at the Università di Napoli. Ph.D. in Mechanics with minor in Mathematics at the University of Minnesota. Ph.D. in Mathematics at the Università di Napoli. Professor of Advanced Mechanics and Analytic Mechanics at the Engineering Faculty of the Politecnico di Torino.

Contact person of a European Community Project relative to a Research Training Network on "Using Mathematical Modelling and Computer Simulation to Improve Cancer Therapy" (RTN1-1999-00294, downloadable from <http://calvino.polito.it/~preziosi/-rtnprop.ps>)

Author of more than 60 publications in the international literature in several fields Mathematical Physics and Applied Mathematics, such as

- dynamics of immiscible fluid and viscoelasticity,
- kinetic models in gasdynamics and population dynamics,
- kinetic and continuous models of tumour growth,
- deformable porous media applied to bio-mathematics, composite materials manufacturing processes, and soil mechanics.

Author of 3 scientific books in the international literature on mathematical modeling and methods in kinetic theory, in mechanics and in the applied sciences in general.

More information can be found on the WEB page <http://calvino.polito.it/~preziosi>.

Hans Westerhoff

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On the European Society for Mathematical and Theoretical Biology:

The turn of this millennium has witnessed one of the greatest successes of mankind: We know the base pair sequence of our DNA, therewith the amino acid sequence of all our proteins, and therewith something about (almost) everything that matters for life. Why then is it that we do not know how life works, and how we can rid ourselves of disease and famine? I think that this is because the essence of life is not *in* those amino acid sequences and proteins but *between* them, i.e. *in their interactions*. And, the multitude and nonlinearities of these interactions, i.e. their complexity, cannot be understood without the application of mathematical methods and theoretical concepts. However, among the molecular biologists that govern functional genomics there is a complete lack of appreciation of what mathematics and theoretical biology can bring to biology and medicine. And, among mathematicians there is a fear of becoming engaged in something that is as genuine and demanding as life itself.

I see it as the mission of the European Society of Mathematical and Theoretical Biology to establish maximum synergism between Mathematics and Biology.

We should aim (i) to ensure that a major part of the flux of euros of the framework 6 program flows where it should, i.e. to Mathematical and Theoretical Biologists engaged in Systems Biology, (ii) that large groups of experimental biologists become acquainted with the power and beauty of mathematical biology and (iii) that large groups of mathematicians become fascinated with the scientific beauty of Biology and indeed of 'life itself'.

I will work for getting Brussels engaged and for organizing schools and workshops teaching the practicalities of this mission.

Scientific profile:

On 19530114 I began life outside the womb. Since 1975 I have been able to translate his fascination with life into experimental and mathematical biochemistry. This ranged from bioenergetics through molecular biology to ecology and tumor biology, and from nonequilibrium thermodynamics and statistical mechanics to metabolic, hierarchical and ecological control theory, always applied to fascinating biological examples. Presently I hold two Chairs, one in Microbial Physiology (Free University, Amsterdam, EU) and one in Mathematical Biochemistry (University of Amsterdam, EU) (<http://www.bio.vu.nl/hwconf/>). I am also director of the Center for Research on bioComplex Systems (CRCS) at the former University. I coordinate the European Systems Biology Initiative for Genomics and Health (www.systembiology.net) and drive the silicon cell initiative (<http://www.siliconcell.net/>).

Communications

The EU's Sixth Framework Programme

Period from 2002 to 2006

The EU's Sixth Framework Programme for research was adopted by the Council of Ministers in June 2002, and will officially be launched during a conference in Brussels from 11 to 13 November 2002. The Sixth Framework Programme will cover the period from 2002 to 2006. The conference will be a major forum to present the objectives and priorities of the Framework Pro-

gramme and to explain rules for participation. At the same time the conference is meant to create opportunities for scientific debate and exchange of best practice beyond those subjects addressed in the Framework Programme.

Information on CORDIS (Community research and development information service) and the Sixth Framework Programme, news, and instructions appear regularly at the web site <http://www.cordis.lu/en/home.html>.

Research Announcements

Closing Lecture of the ECMBM by Willi Jäger (Heidelberg, Germany)

July 6th, 2002, Milano.

Notes taken by A. Stevens.

Multiscale problems in biosciences: Flow, transport and reactions in tissues

The last lecture of a conference is specially challenging. During this conference we talked a lot about the future of mathematics in biosciences, and within biosciences that means biology and medicine. Biological phenomena in modern research fields, like molecular genetics, brain research, bio-engineering, or environmental sciences, cannot longer be treated qualitatively but have to be analysed quantitatively. Even in bio-informatics a lot of quantitative statistics is involved. New statistical methods that are based on quantitative modelling need to be explored.

The challenges for mathematics in biosciences are caused by the complexity of biological systems and by the range of scales involved. Multi-scale analysis is one of the necessary tools to overcome the complexity, namely to pass from a detailed, fine granular description to a rougher, but more effective model; to replace a huge network by a reduced system that describes the main effects. It is necessary to consider all scales that occur in biological phenomena. They range from molecular complexes, macromolecules, cells, tissues, organisms, ecosystems, up to the biosphere and the environment. These are spatial scales from microstructures to macroscopic systems and temporal scales from pico- and nanoseconds to centuries. We need to develop appropriate modelling and simulation techniques.

In the following I will give some examples of problems that I consider as challenging in the field.

Starting from the micro scale, it is important to understand the processes that take place within cells. New theoretical methods are needed to become able to study transport, flow and reaction in these systems. Classical methods alone do not work here. Mathematics in biosciences is not an auxiliary science, but the science where these new techniques have to be developed. Nowadays fluorescence microscopy, for example, is giving better and better resolved spatio-temporal information on intracellular processes. For instance, one has to study quantitative information about transport in the living cell, e.g. the traffic between nucleus and cytoplasm. Looking at the membrane of the nucleus, one should more closely analyse features of active transport across the nuclear boundary. Some small molecules do not pass this boundary but large molecules do. Which kinds of interactions play a role in these processes? Another problem is the simulation of geometric structures of chromosomes and

of molecular processes that take place during genome transcription.

These and other challenging topics in molecular biology have to be explored, also by researchers of this society (ESMTB). And they have to enter this field quickly. The German Government has initiated a very well funded program BIOFUTURE for young scientists in biotechnology and mainly in molecular biosciences. Right now only 1% of the researchers involved in this field are mathematicians, otherwise mainly physicists, nearly no bio-informaticians and computer scientists. This field is very interesting for mathematicians and challenges all applied disciplines of mathematics computer science.

Calcium and other secondary messengers are transported via vesicles at a synapse. Simulate e.g. a single neuron and clusters of neurons in 3D and try to reproduce the details in a realistic manner! Discretizations of such complex structures and models for the fine structure are needed.

There are excellent 3 D data for tumours and large systems of vascular capillaries, but not enough methods to deal with processes like flows and reactions in such systems, which have to be considered as random media. However, these are important to understand the observed branching phenomena. Look also at the structure of leaves and their vessel systems.

Usually, available information on the observed patterns is not used in models and the stochastic geometry is not taken into account well enough. In fact, we have to deal with stochastic processes on a stochastic geometry. It is a great challenge to investigate this situation, even in other contexts, not only in biology. Consider root networks and root hairs. How are the mechanisms of nutrient uptake regulated? This is important to know for agricultural or industrial applications e.g. in designing and controlling root reactors, a new type of bioreactors. You have to understand the process before you can optimise it. Analysing networks of channels and capillaries is very challenging. Systems of channels have not yet been understood. Usually one has to assume certain length-diameter relationships which are not satisfied in many situations.

Look at the brain as an organ. It is a porous medium. The pressure in the brain is not the same everywhere. Look at the skin and try to identify the glucose content of the skin by the reflection of light. Consider the lung or other organs and analyse the transport of blood or oxygen through them. In alveoles, the walls are flexible. This is another challenge for a mathematical description. One cannot apply the usual technique of homogenisation. One has to find correct descriptions of blood flow through tumours. Organs like brain, heart, lung, and kidney have been modelled, but not the liver. This is astonishing, since every drug is transported through it. So it is very important to understand processes there. It is a system that cannot be understood just by image analysis.

One has to study the different scales of the problem to connect microscopic models with macroscopic descriptions.

Now I want to focus on the techniques that are needed to tackle the above-mentioned problems. These are image and data analysis, the analysis of random media with asymptotic analysis techniques - we have to deal with channels, membranes, and cells - nonlinear partial differential equations and optimization. We have to consider discrete and stochastic particle systems. Processes in cells may depend sometimes on single molecules. There is transmission of information between different scales. One has to derive effective models and understand how the model solutions depend on different scales. Also error estimates have to be performed, in order to understand when the model is valid, since every scaling is in a sense arbitrary, and can only be justified by the quality of approximations obtained, e.g. by scale expansions.

The complexity of different model systems has to be reduced for a real understanding. It has to be understood which processes are fast and which are slow. One has to find the “epsilons” in the processes and how to solve the reduced problems. Different scales might have to be found by computational tools, by methods in stochastic geometry, and by homogenisation.

In biology, we have to deal with complex geometric structures, different cell sizes, pore sizes, etc. One needs microscopically precise information and must use suitable limit procedures and rescaling. However, the error has to be controlled; so one ends up with e.g. scaled limits, effective systems like Darcy’s law, and system data, like the permeability tensor. One has to show that the

limit problem is in good agreement with the experimentally observed phenomenon.

The transport through an array of cells with a semi-permeable membrane is related to analysing diffusion in random structures. One has to look for effective diffusion coefficients. We need receptor-based models to understand cell behaviour and to model growth and pattern formation of tissue. The distribution of receptors on the cell surface plays a role. Homogenization might be the right tool to derive effective model equations. If you have to deal with transmission conditions at interfaces, or to formulate effective boundary conditions, asymptotic analysis methods are needed. Consider e.g. rough surfaces, like the sharkskin problem in bio-fluid dynamics. You have to deal with oscillatory boundaries and boundary layers. The question is how to determine the correct boundary conditions on a smoothed boundary. One has to evaluate drag forces that are related to the skin friction. The flow pattern of swimming sharks is clearly in the turbulent region. If every turbulent flow has a layer around the boundary, which is viscous, then assume for a first model e.g. that the roughness of the skin is small with respect to this viscous layer; by doing this, one is able to show that a sensitive reduction of friction can be obtained by a proper roughness pattern.

I stop here and hope you are motivated to tackle some of the multi-scale problems in biosciences. Take your chances on these problems. If you don’t take them, others will take over.

Thank you very much for your attention - mille grazie!

History of Mathematical and Theoretical Biology

“Sebbene di un interesse di giorno in giorno crescente le applicazioni delle matematiche alle scienze biologiche ci appaiono esse pure al loro inizio.”⁽¹⁾

One hundred years after the words by Vito Volterra at the opening lecture in Rome on the year 1901.

By Mimmo Iannelli (University of Trento)

Opening lecture at the 5th ESMTB Conference, Milano, July 2-6, 2002

In the year 1901 Vito Volterra opened the academic year of the University of Rome with a lecture focused on the application of Mathematics to biological and social problems⁽¹⁾. This was a passionate analysis on the role of Mathematics in the description of nature, and the words that I quote in the title sound premonitory of that special season that, about twenty-five years later, would produce the basis of mathematical population theory.

One century has passed since that lecture, when Biomathematics did not exist as a word nor as field of research. In fact, in that lecture Volterra focused his attention on the applications of Mathematics to fields that were not in the main stream but that he considered very important in his vision of the discipline. At that date “applications of Mathematics to biological sciences seemed to be at an initial stage”: now that time has passed and Biomathematics is an established research field, I think it is interesting to step back to look at the vision that Volterra put forward in that lecture, to follow the first steps of the applications of Mathematics to the biological sciences, to follow the development and the difficulties along the years up to our days and maybe put the same questions as one hundred years ago about the relationship of Mathematics to the other sciences.

It is an honour for me to play this role. I will try to put forward some personal thoughts and unanswered questions on Mathematics and its applications in Biology, together with some anecdotes and memories ... I apologize in advance for my non-professional historical comments, for my naïve views, and for my limited knowledge of the world ... This talk will, however, be a way to give the welcome to everybody at the Conference ...

Vito Volterra: a short biography

To know Volterra as a man helps to understand the scientist. Thus I will start with a few information about his biography ⁽²⁾.



Vito Volterra

- 1860, May 3: He was born in Ancona
- 1878-1880: He attends University in Florence
- 1880-1882: He attends Scuola Normale Superiore in Pisa
- 1882: He gets his Laurea in Physics
- 1883-1892: He becomes Professor of Mathematics in Pisa
- 1892-1900: He becomes Professor of Mathematics in Torino
- 1900: He becomes Professor of Mathematics in Rome
- 1905: He is nominated Senatore del Regno
- 1923: He is the first president of CNR
- 1923-1926: He is Presidente of Accademia dei Lincei
- 1932: He is expelled from all Italian scientific institutions.
- 1938: He is expelled from the Italian population
- 1940, October 11: He dies in Rome.

This is just a selection of events that may help to place him in a historical context and to illustrate his personality. A few comments are in order. His birth date shows that he was born at the time when Italy completed its unification. Thus Volterra was born together with Italy and this helps to understand his political engagement to build an Italian scientific culture. Among the details of

his life before his academic studies, it is worth mentioning that, his family being very poor, he attended a high school (Istituto Tecnico) that should have provided him a work soon after the graduation. Volterra instead was noticed as a very smart student and was provided a fellowship that allowed him to attend courses at the University of Florence and to complete his studies in Pisa at the Scuola Normale Superiore (he had teachers such as E. Betti and U. Dini).

We can see that, right after his Laurea, he had a very fast academic career. Though he graduated in Physics he started as a Professor in Mathematics. Actually in those times there was no real distinction between the two disciplines, or at least they were more intimately related than it may appear at our days. Thus, Mathematics was at the same time Pure and Applied Mathematics, and applications used to come from physical problems. The young Volterra forms his scientific vision on this ground and his late passionate work to extend the action of Mathematics into the field of Biology stems from this early experience.

His fast career takes him to Rome where, at the age of forty, he is one of the most important scientists, having already given great contributions to Mathematics. In particular we must mention his contribution to the foundation of Functional Analysis, in fact, his work “Sopra le funzioni che dipendono da altre funzioni”⁽³⁾, published in 1887, actually points to the concept of a real functional.

In Rome he spends himself in the cultural fight that Italian scientists are conducting against the “world of philosophers” who on their side claim the primacy of humanistic culture. For his cultural and scientific merits, he is nominated Senatore and later on he actively contributes to the foundation of the CNR (the Italian National Science Foundation) becoming its first President.

In those years, however, his political commitment becomes incompatible with the take over of Fascism. It is not only that he fights on the side of liberal-democrats in the Italian Parliament, it is his whole cultural vision that obliges him to resist to the continuous (open and hidden) attacks that Fascism leads against the Italian Institutions. Thus, when somebody proposes to nominate Mussolini as an honorary member of the Accademia dei Lincei he, as President of the Accademia, does not allow even that the proposal be discussed.

The rest of the story is part of that dark period of Italian history: in 1932 he is expelled from all Italian Institutions because he refuses an oath of allegiance to Fascism, in 1938 he is expelled from the Italian population because of the Fascist laws for the “defence of the race”. He was in fact part of the Italian Jewish community.

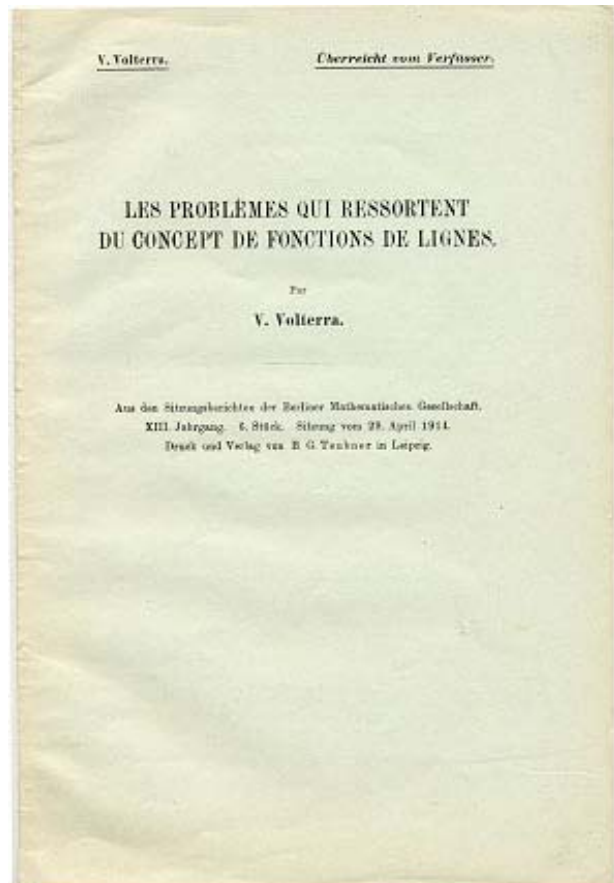
He dies in 1940 subtracting himself to deportation: in fact, three years after his death, on October 1943, the Nazi-SS knocks at his door to seize him ...

On the attempts of applying Mathematics ...

Yes, Volterra was not an easy man ... and his political and cultural stature was not small either ... and all his life is the proof that he believed in what he was doing. His lecture in Rome is a kind of cultural-political talk,

showing the effort of Volterra and other Italian mathematicians of that period, to propagate an idea of Mathematics as an all-pervading method, able to explain all natural phenomena. Again, by Volterra’s words:

The mathematician owns a wonderful tool, created by the efforts of the many ingenious people, cumulated through the centuries. He has the key that can open a way to the many mysteries of the Universe and obtain, by a few symbols, a synthesis that cover and connects many and diverse results of different sciences⁽¹⁾.



He felt the task of supporting this view as a precise duty, it was not just rhetorics for an elegant speech. Actually, Volterra and the other Italian scientists of his times, were engaged in a cultural fight against the dominating cultural trend (“idealism”) led by the philosopher Benedetto Croce who strongly influenced the Italian society. Croce’s view claimed the primacy of humanistic culture and had a diminishing opinion on the role of science and, especially, on the role of Mathematics. In fact, in a letter commenting Volterra’s lecture, Croce declares:

There is no doubt that the use of Mathematics is useful in solving or simplifying complex problems of practical nature. But it cannot produce any effect on the nature of philosophical sciences and, if it can, the effect will be bad Mathematics is numbering and measuring, but in economics any event is choice and will ...⁽⁴⁾

We can see that the role of Mathematics is reduced to solving practical problems applying some sort of refined recipes, while the real events of the world are not intelligible by man and are not subject to natural laws but they are due to man himself through the action of *choice* and *will*.

Actually, at the beginning of the twentieth century, the illuminist view of Volterra was contrasted everywhere in Europe, but in other countries scientific tradition was stronger than in Italy. Here the lack of a diffuse scientific culture made it difficult to resist: in the just born kingdom of Italy, the scientific world had to fight a “constitutive” battle⁽⁵⁾.

Going back to his lecture, here Volterra, in agreement with his general view of Mathematics as a “wonderful tool to understand the mysteries of the Universe”, claims the importance of going beyond the applications in Physics:

But, our intense curiosity is focused on those sciences - biological sciences and social sciences - to which, only recently, Mathematics has turned its interest. In fact we have the strong desire of becoming sure that the classical methods, that have produced great results in the field of mechanics, can be successfully used in the new fields that are opening in front of us.

Biological sciences are not yet ready as a field for the intervention of Mathematics, but Economics does ... The following piece from the talk casts some light upon Volterra’s conviction about the way Mathematics should enter in the description of phenomena in Economics:

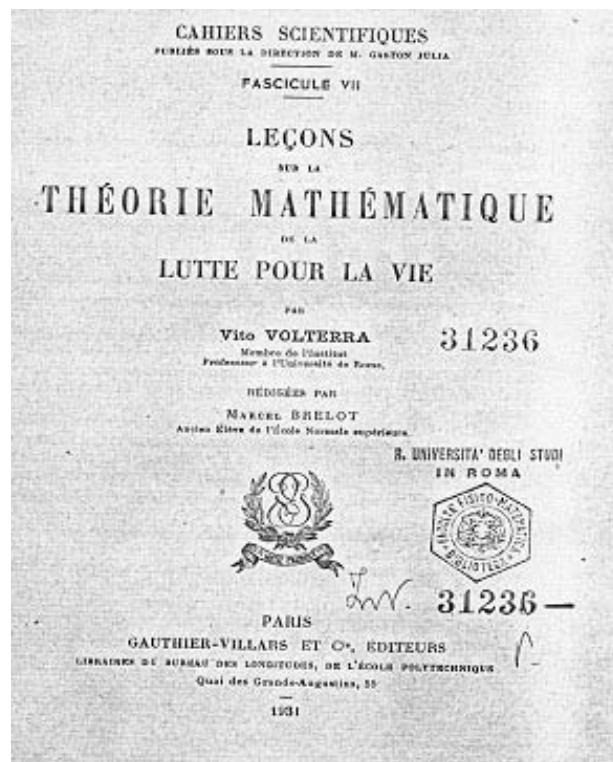
The concept of *homo oeconomicus* ... is very natural to our mechanician and he is surprised by the reactions of the other scientists. For him the concept of *homo oeconomicus* is similar to the other concepts he is used to. In fact he is used to consider ideal surfaces in absence of friction, ... he is used to replace the natural fluids with perfect fluids and perfect gases.

He uses the term “mechanician” that in Italian denotes the scientist expert of “Rational Mechanics”, thus he sets forward a mechanistic view of the world inspired by the traditional approach to physical phenomena. Further on, in the lecture he supports this view in a passionate way:

To formulate concepts in order to introduce a measure; to measure and to deduce laws; to formulate hypotheses; to deduce from these a science of abstract objects; then to compare with the real world; to reject or transform those assumptions if the results of calculus are in contradiction with the real world; to be able to guess new facts and new analogies; or, starting from present data, to discuss the past and the future; this is, in a few simple words how

should evolve a science based on Mathematics.

Thus, Mathematics is involved in a complete circle that goes from the real world to the mathematical objects and again to the real world. This is a fundamental epistemological paradigm that any scientist should be aware of. Volterra is sure that Economics has already moved to the right direction and is confident that Biology would follow soon ...



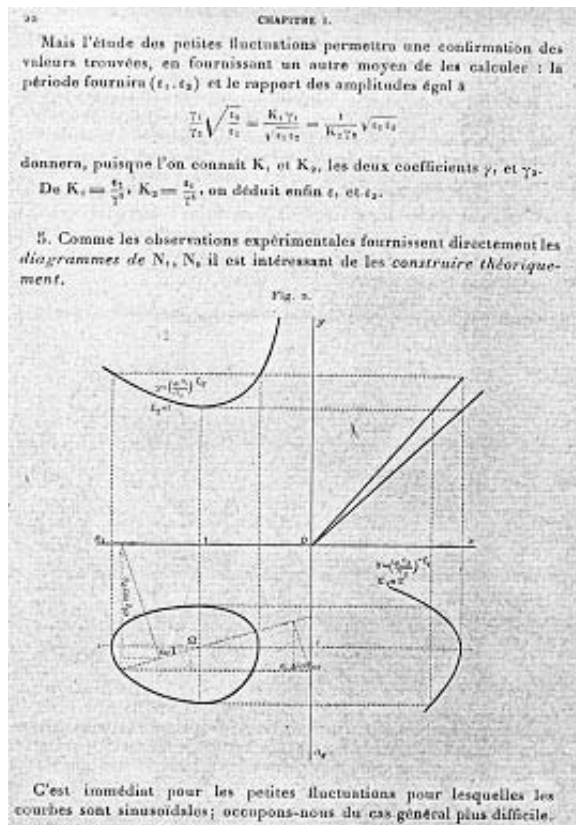
Here I present some studies ...

We are now in 1927, many years after the lecture we have commented above. Volterra has worked hard, as a mathematician and as a political man. He has participated in the first World War at an age of above fifty, and he has given great contributions to the research in Mathematics. In 1927 Volterra publishes his work “Variazioni e fluttuazioni del numero di individui in specie animali conviventi” as a memory of the “Regio Comitato Talassografico Italiano”. Here he stresses again his view, this time in connection with biological phenomena:

Here I present some studies on coexisting species ... To treat the problem from a mathematical standpoint we start from assumptions that, though far from reality, nevertheless give an approximate image of it. Here is how to proceed: we first try to put into words how the phenomena goes on; then we translate this words into the language of Mathematics. This translation leads to differential equations. Then, if we use the methods of mathematical analysis we can go much further than ordi-

nary language and arguments could take us ...

It is well known how Volterra started his interest in this field. In 1925, his son in law, Umberto D'ancona attracted his attention on the data concerning the abundance of fish species in the Adriatic sea, and Volterra formulated his famous system describing the prey-predator interaction so to explain the apparently anomalous shifting of the proportion of predator fish, under the reduced fishery during the war.



Volterra's graphical construction of the prey-predator cycles

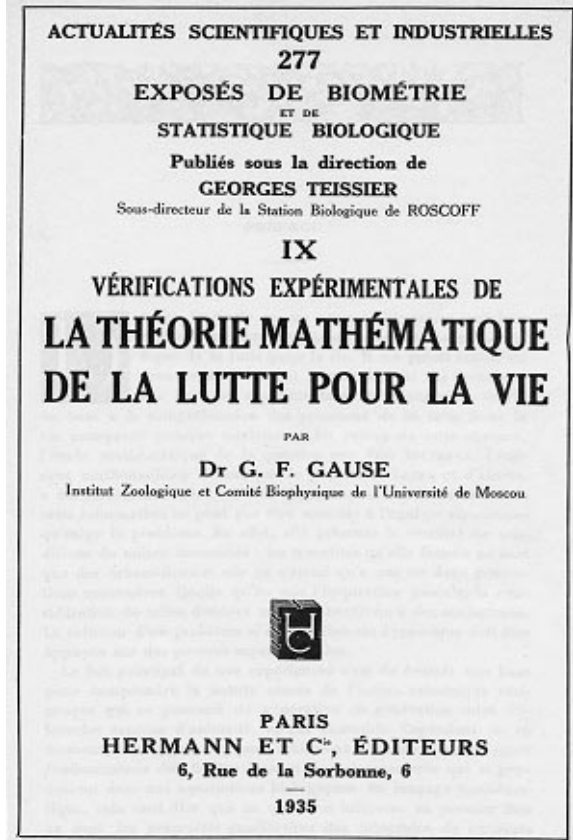
Volterra gets deeply involved into the problems related to Population Biology where he finds a new opportunity of testing and assessing his mechanistic view of the world. He builds up a theory in the style of "Rational Mechanics" where he speaks the language of that "mechanician" who "is used to replace the natural fluids with perfect fluids and perfect gases".

In his book "lecons sur la théorie mathématique de la lutte pour la vie", published in 1931, he summarizes his theory and speaks about existing experimental work that seems to support the results. But he wants more ... he wants to go through what he calls the "applied phase" that should follow the "rational phase" that has already been developed. In fact, in the introduction to the book he writes:

We will present only the researches relative to what we can call the rational phase of the study of the biological associations. Those who will work on the experimental verifications of the theoretical results and will enter into the applied phase will be concerned with a

careful discussion of the assumptions and of the biological validity of the arguments, mainly based on experiments, observations and statistics.

The book is published when the debate on the applications of Mathematics to Population Biology is intense at the international level. Volterra is in contact with all the researchers in the field and is also involved in a priority quarrel with Alfred Lotka whose work he did not know and did not quote in his early papers. However, the models that are now denoted as Lotka-Volterra equations were at the centre of the debate and their role in the interpretation of natural phenomena was extensively discussed by experimentalists.



Volterra is interested in an extended verification of the theory and he is in contact with other experimentalists beyond D'Ancona. He entertains a correspondence with R.N. Chapman, S.A. Graham and W.R. Thompson in the USA, with J. Regnier and G. Teissier in France and with G.F. Gause and V. A. Kostizin in Russia. He follows their work, expecting a feedback to his theory.

In particular Gause publishes a book collecting results from experiments, explicitly designed to assess the theory.

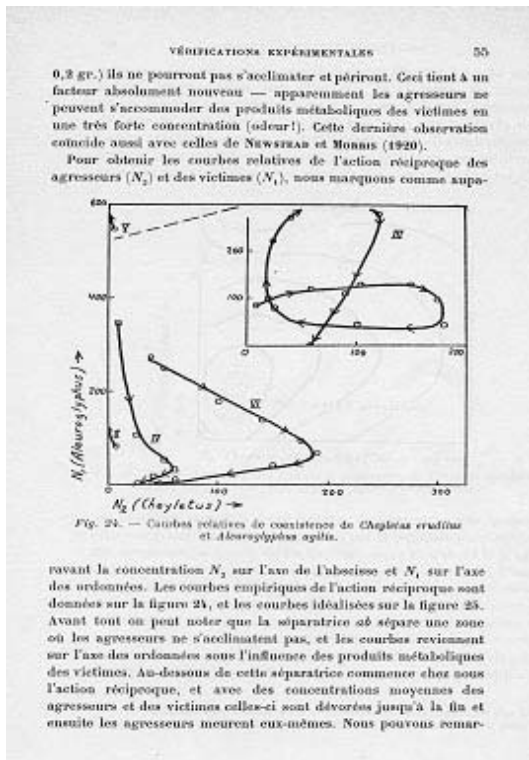
With D'Ancona he starts writing a new book, more biologically oriented. It will appear in 1935 with the title "Les associations biologiques au point de view mathématique" (Hermann, Paris), but something goes wrong during the preparation of the volume and a sort of disagreement between the two scientists arises.

We can trace the terms of their quarrel in their correspondence of that period. In fact D'Ancona writes to Volterra:

Concerning your opinion about the work of Régnier and Gause, I do not know if it is worth adding a whole chapter focused on the work of these two authors ...

... I think that your work is important in itself as a theoretical approach to the problem of coexistence, even independently of possible experimental verification ..

... I do not think that either Régnier or Gause have given a demonstration of the essential part of your theory ...⁽⁶⁾



Gause experiments

It seems that D'Ancona has doubts about the validity of the experimental researches and in the possibility of assessing the theory. In another letter he insists:

I understand that you think I am somewhat jealous of these two authors and that I want to stress my own researches ...

... I think we have to be very careful in accepting these experimental researches as proofs [of the theory]. Your theory is not minimally touched by all these questions. It is a theory logically constructed and sufficiently convincing, in agreement with many data⁽⁶⁾

Finally the book is published, but the collaboration with D'Ancona ends. Later on in 1937, when L. Von Bertalanffy proposes to edit a new book, Volterra refuses to

collaborate with D'Ancona and the latter writes it alone. It will be published in German in 1939⁽⁷⁾.



In the years following the book with D'Ancona, Volterra continued his interest in the experimental work concerning his theory but also went back to the "rational" phase and tried to complete the analogy with mechanics, working at a variational setting for the mathematical description of population interaction. In fact, in 1936 he writes a sequence of short notes where this setting is developed systematically:

Les équations des fluctuation biologiques et le calcul des variations, Comptes Rendus de l'Académie des Sciences, t. CCII, 1936

Les équations canoniques des fluctuation biologiques, Comptes Rendus de l'Académie des Sciences, t. CCII, 1936₁

Sur l'intégration des équations des fluctuation biologiques, Comptes Rendus de l'Académie des Sciences, t. CCII, 1936₁

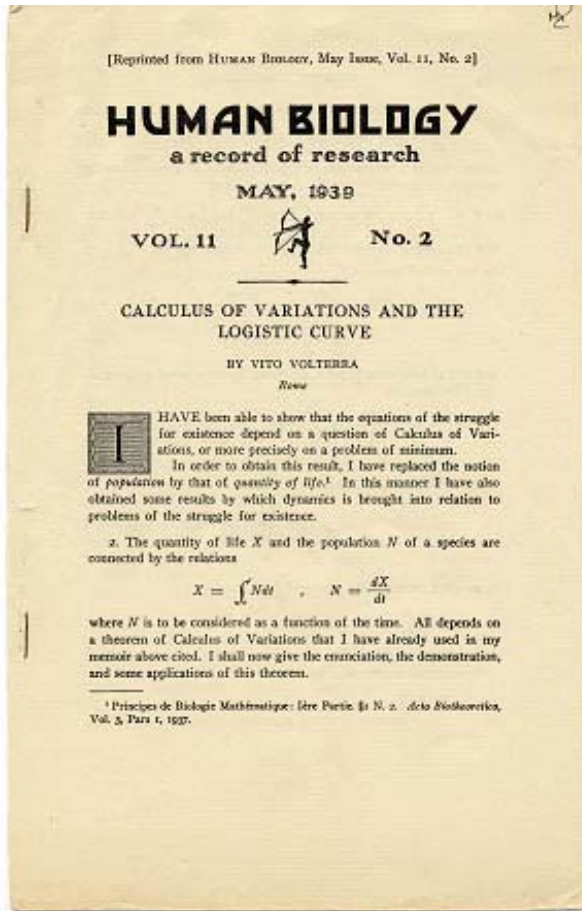
Le principe de la moindre action en biologie, Comptes Rendus de l'Académie des Sciences, t. CCIII, 1936₂

Sur la moindre action vitale, Comptes Rendus de l'Académie des Sciences, t. CCIII, 1936₂

This formulation is actually adopted in all his late presentations of the theory and his very last work on mathematical Biology is concerned with this subject (*Calculus of variations and the logistic curve*, Human Biology, vol. II, n. II, 1939)

When he dies, he leaves an heritage of human and scientific coherence. We are impressed by his rigorous style

in the effort of developing his scientific program until the end and, in his late activity, we still trace the echo of his talk at the beginning of the century with the same passionate thrust in the role of Mathematics in scientific knowledge.



Nevertheless we are somewhat puzzled by his discussion with D’Ancona because it does not seem to be due to personal reasons, but it rather seems to touch the relationship between Mathematics and empirical knowledge. Why could not Volterra understand the objections by D’Ancona? Why did D’Ancona hesitate to interpret data using Volterra’s theory? Was Volterra’s mechanistic view inadequate and optimistic? Were the experimental data not sufficiently extended?

Actually, their quarrel seems to concern the essence of mathematical modelling in Biology and the questions raised should be considered in an epistemological and historical context. In fact, it has been observed⁽⁸⁾ that Volterra’s vision was somewhat “conservative” and too much depending on the scientific heritage coming from Physics, while a different concept of a model was taking over in those years. Probably Volterra was stuck to his principles, while D’Ancona was, instead, more open to the rising criticism to the traditional view, and he felt Volterra’s scheme somewhat embarrassing ...

We may leave to historians the task of expressing a judgment on this point, but we can’t avoid observing that, still at our days, the discussion about modelling and about the significant methods to be used in the investigation of biological facts is not settled at all. Thus, the story of Volterra and D’Ancona is somewhat paradigmatic

and we trace in it many questions that nowadays concern our very active world of Biomathematics ...

Nowadays Biomathematics

When Volterra dies, the questions I listed above are somewhat forgotten. Biomathematics itself seems to disappear. Lotka-Volterra equations and applications of Mathematics to Biology are washed out of the interest of mathematicians. We can guess that this is caused by the devastating experience of the World War. We know that scientists were involved in matters very different from ecological problems: during the war all efforts were concentrated on military problems, in the years after the war the attention was focused on industrial growth and economic development. Thus the period going from 1940 to 1970 is a rather blank page for Biomathematics.

Things start changing about 1970. First slowly, then at a higher and higher speed. Biological journals host more and more mathematically oriented papers and the attention of mathematicians is more and more attracted by biological models. New journals arise, dedicated to the field, new book series are started (the Springer lectures Notes in Biomathematics starts in 1974), Conferences and meetings are organized all around the world.

It has to be remarked that in those years, Applied Mathematics enjoys a general development and Biomathematics takes advantage of the general situation. Nevertheless, Biomathematics has some peculiar features that feed the interest of mathematicians. Mathematical theories such as qualitative analysis of O.D.E.’s and P.D.E.’s, Integral equations, non-linear analysis in general, respond to the need of biological modelling providing language and tools. On the other hand the theories themselves are stimulated and motivated by specific problems and are inspired by general principles that have to find a mathematical shape and setting.

Within this active scenario a sort of philosophical discussion arises about the fundamental principles standing under the modelling procedure and the role of Mathematics. The quarrel between Volterra and D’Ancona seems to come back to light. Thus today, after about thirty years since the beginning of this new era for Biomathematics, and one hundred years after the lecture that Volterra gave in Rome, our questions are still going around the same problems.

These thirty years have produced a composed and multi-faceted scientific community that meets several times a year and is made of some very different scientists, with very different interests and aims. Inside this community you can find mathematicians who are interested only in some class of equations with no concern about the possibility of using these equations to address significant problems, and you can find scientists only interested in simulations with no concern for mathematical rigor and theorems. The quarrel has changed in its form but still concerns the contrast between a diffidence toward Mathematics and an unlimited thrust on its power. It seems that there is still a problem for the “rational” and the “applied” to live together with the same purpose of producing a significant insight into complex phenomena.

But “rational” and “applied” must continue to live together for no other reason that, whatever be the personal taste of any of us, “rational” and “applied” need each other. Let me express this view by sharing with you a piece of literature⁽⁹⁾. Actually a piece that I find to be a nice metaphor of the existential condition of the scientist. The lines below follow the thoughts of Edmond Dantes, imprisoned in the castle of If ... he tries to reconstruct the shape of the fortress ... to build a model of it in order to find a way to escape ... The abbe Faria tries instead to find this way empirically ... digging and digging tunnels ...

From my cell I can't say much about the shape of the castle of If, where I have been imprisoned for so many years ...

I do not know how many times Faria has tried to evade: every time he tried he has worked for months

Me too, I have thought and I continuously think about a way to evade. I have made many conjectures about the topography of the fortress, about the shortest and safest way to reach the outmost tower to jump into the sea. At this point I am not any more able to distinguish between my conjectures and the data provided by the experience ...

Is Edmond Dantes hopelessly confused, or is he instead positively enriched? ...

A non-concluding conclusion

Well ... it is time to conclude this talk ... though I am far from being able to draw any conclusion ... Once we leave Volterra to his historical perspective we are left with our effort to investigate the shape of the fortress ... again, the words by Edmond Dantes may help to continue:

Thus we are continuously dealing with the fortress ... Faria tries to find the weak points of the walls, fighting against new resistances, I reflect on his failures to conjecture new patterns to add to the map of my conjectured fortress.

If I will succeed in building a model of the fortress ...

NOTES:

(1)

“Though of continuously increasing interest, the applications of Mathematics to biological science seem to be at an initial stage”

Vito Volterra: *Sui tentativi di applicazione delle matematiche alle scienze biologiche e sociali*, Annuario dell'Università di Roma anno accademico 1901-1902

(2)

For an extended biography see the first volume of:

Vito Volterra, *Opere Matematiche, memorie e note*.

Edited by Accademia Nazionale dei Lincei, Roma 1954.

(3)

“On the functions that depend upon other functions” Rendiconti R. Accademia dei Lincei, s. IV, vol III, 1887.

In the figure I show the front page of a later paper on the same subject, published in 1917,. This is a reprint that I received from Mrs. Luisa Volterra many years ago when I was starting my interest in Volterra's work. Mrs. Luisa was Volterra's daughter and the wife of D'Ancona, she sent me other papers by her father, in particular a reprint of his last paper in Biomathematics and a copy of the book by her husband. These are shown later in this note.

(4)

letter by B. Croce to G. Vailati. See the introduction to the volume: Vito Volterra, *Saggi Scientifici*, Zanichelli 1990

(5)

For discussions on this point see “Volterra, D'Ancona e la Biologia Matematica” by G. Israel, this is an introduction to the Italian version of the book by D'Ancona and Volterra, “Les associations biologiques au point de view mathématique” (series “I fondamenti della scienza”, edizioni TEKNOS, Roma 1995)

(6)

This correspondence is reported in the reference quoted above in note (5). However for the complete correspondence see

G. Israel, A. Milán Gasca, *The Biology of Numbers. The Correspondence of Vito Volterra on Mathematical Biology*, Basel-Boston-Berlin, Birkhäuser Verlag, Science Networks Historical Studies vol. 26, 2002,

(7)

An English version of this book was published in 1954 with the title “The struggle for Existence”, Biblioteca Biotheoretica

(8)

G. Israel, "Volterra's "analytical mechanics" of biological associations" (in two parts), *Archives Internationales d'Histoire des Sciences*, Vol. 41, Nos. 126-127, 1991, pp. 57-104; 306-351.

- G. Israel, "The Emergence of Biomathematics and the Case of Population Dynamics. A Revival of Mechanical Reductionism and Darwinism", *Science in Context*, Vol. 6, No. 2, 1993, pp. 469-509.

(9)

Italo Calvino : *Il conte di Montecristo*, in *Ti con zero* , Einaudi 1967

Past Activities

From individual to collective behaviour in biological systems

Organisers: H Othmer (Minnesota), N. Monk (Sheffield), P K Maini (Oxford), T J Pedley (Cambridge), B D Sleeman (Leeds)

Isaac Newton Institute for Mathematical Sciences, Cambridge, UK, September to December, 2001

In the last thirty years there has been an enormous increase in our knowledge of biological processes, especially at the molecular and cellular level, but understanding the behaviour of individual enzymes, cells or organisms in isolation is only a first step in understanding the collective behaviour of a population of such individuals. Incorporating individual aspects of behaviour into macroscopic descriptions of population behaviour is a challenging problem, even if only deterministic aspects are considered. The four-month program 'From individual to collective behaviour in biological systems' was devoted to the question of how microscopic information can be incorporated into macroscopic or population-level descriptions in developmental biology, physiology, ecology, immunology and epidemiology. It consisted of a small number of long-term visitors housed in the Newton Institute, together with several short-term visitors. In all, there were 4 workshops held during the program. The program itself was divided into 2 parts:

Part I: Developmental biology and physiology

The first half of the programme focussed on developmental biology and physiology. The former concentrated on pattern formation, gene networks, and developmental mechanics, while the latter was devoted to various aspects related to cardiac physiology, including calcium dynamics, analysis of ion channels in excitable systems, muscle mechanics and integrated models of the heart. A notable aspect of this component of the program was the strong and deep interaction between theoreticians and experimentalists on the fundamental questions from both perspectives. For instance, the detailed presentations by experimentalists such as Paul Kulesa, Kees Weijer and Ray Keller stimulated numerous discussions and several new collaborations between experimentalists and theoreticians. The work here has also highlighted many questions relating to stromal cell development and organisation and the aggregation and pattern formation behaviour of *Dictyostelium*. An important feature of the programme was that in-depth tutorials on both experimental and theoretical aspects were given prior to the workshop and continued throughout the program. For instance, programme participants benefited greatly from the tutorials on modelling of the heart given by Peter Hunter and his associates, since it pointed to the possible use of mathematical techniques developed there in tissue modelling in other areas.

Part II: Ecology, immunology and epidemiology

The second half of the programme was devoted to spatial ecology, immunology and epidemiology. One significant outcome of discussions in these areas was the realisation that the mathematical models developed in one area are often similar to those in another area (e.g. compare immunology and epidemiology). This cross fertilisation of ideas may well have important implications for future research. On the more mathematical front the complementary ideas on stochastic modelling and reinforced random walks discussed by Dirk Drasdo, Andreas Deutch, Angela Stevens and Hans Othmer has opened up a number of novel ways in which phenomena at the cell level may be scaled up to the population level. Open problems include how the limiting processes involved should be interpreted and validated. There is also the excluded volume problem relating to taking account of cell size.

The workshops lasted from 2 to 5 days:

First workshop: Vertical integration in biology: from molecules to organisms

The principal theme of this workshop was vertical integration, focusing on specific examples from developmental biology and physiology, viz., gene networks, cell signalling, morphogenesis, neural networks, neurophysiology and cardiology. Three criteria were used to select these particular areas: (1) there exist extensive studies of behaviour at both the individual and collective levels; (2) well-founded mathematical modelling frameworks are in place for each of these levels; (3) there is a pressing need for a directed attempt to combine modelling and experimental investigations to elucidate the mechanisms of vertical integration, bridging the gap between the two levels of understanding.

To foster efforts aimed at providing insight into vertical integration, it is important to

- (a) bring together researchers from different backgrounds who would not normally find the opportunity to meet to discuss this general issue,
- (b) to train truly interdisciplinary researchers.

The workshop has succeeded in this by

- (i) bringing together experimentalists and theoreticians, as well as those who have successfully combined the two approaches;
- (ii) inviting researchers whose focus is primarily on either the individual or collective levels, which proved productive because the modelling techniques applicable to the two levels are often quite distinct, and
- (iii) inviting a significant number of young researchers to expose them to a wide range of presentations in the interactive environment fostered by the Newton Institute, thereby giving them access to some of the most active researchers in these different fields.

Second workshop: Euromech satellite meeting (Leeds)

The workshop on 'Pattern Formation by Swimming Micro-Organisms and Cells' was hosted by the Department of Applied Mathematics at the University of Leeds on 3rd to 5th December. Professor Nick Hill (Glasgow) chaired the meeting with Dr Martin Bees (Surrey) as the co-chairman. It was organised as an international meeting (Euromech Colloquium 422) under the auspices of the European Mechanics Society, and was funded jointly by the Isaac Newton Institute and the London Mathematical Society. The sixty participants contributed a total of 45 presentations including a lively poster session. Prizes for the best student posters were awarded to Rachel Bearon (University of Cambridge) and Richard Hillary (University of Surrey).

A notable feature of the workshop was bringing together of mathematical modellers in plankton population dynamics, where dispersion is mainly caused by oceanic currents, and those in bioconvection with theorists in the growth of bacterial colonies and the behaviour of slime moulds. The standard of the talks was excellent, and there was much energetic discussion enhanced by keynote experimental and biological presentations. The vigorous state of mathematical biology in the UK and worldwide was demonstrated by the wide range of new mathematical models and mathematical results which were presented, e.g. on travelling waves, Taylor dispersion in suspensions of swimming micro-organisms, angiogenesis, and the fluid mechanics of swarming bacterial colonies.

The very successful theme of a workshop devoted to mechanics applied to biology was a timely new venture for Euromech, and points the way forward for future developments of the Society's interests.

Third workshop: From Worker to Colony: Understanding the Organisation of Insect Societies

Preliminaries to the workshop

This workshop was run by David Sumpter.

For the two weeks running up to the 'worker to colony' meeting, informal discussions were hosted outlining the important research questions in social insects. Over these two weeks the institute had short-term visits from nine experimental biologists, two researchers involved in computer tracking and automatic analysis of insect behaviour and two computer scientists involved in ant algorithms (novel methods of solution, inspired by ants, for solving computationally complex problems). These visitors interacted with the mathematicians already resident at the institute and others who also visited for a short time.

As well as having seminars and informal problem presentations by the visitors, a discussion group on 'robustness in insect societies', was organised taking as inspiration some of the talks earlier in the programme on robustness in other biological systems.

The workshop

The 'worker to colony' workshop was the largest meeting dedicated to the study of insect societies in the UK

for at least five years. There were 90 attendees (70 of whom were short term or 'on the day' participants), who heard both extended one hour research talks by leading international researchers and shorter presentations of particular projects. One main theme was construction and digging by ants: in one talk Theraulaz presented, to the great interest of attendant mathematical biologists, convincing evidence for Turing mechanisms underlying ant cemeteries and other constructions. Another theme was nest choice by ants and bees, with excellent and detailed talks by Seeley, Franks and Pratt. During the breaks between talks there were poster presentations, where younger members got an opportunity to present their work and get some input on possible mathematical modelling. Many new collaborations were formed as biologists found out what mathematics could contribute to the study of insect societies and mathematicians discovered that these societies are a perfect example of individual to collective behaviour in biology.

Fourth workshop: Macroscopic organisation from microscopic behaviour in immunology, ecology and epidemiology

The purpose of the workshop was to bring together experimentalists and theoreticians working in immunology, ecology and epidemiology with the aim of fostering interaction and research.

Approaches using classical deterministic mathematical models have had some limited success in describing these spatial ecological processes. However, there is a growing realization, amongst ecologists and theoreticians alike, that stochastic factors, both demographic and environmental, play a fundamental role in determining ecological outcomes.

Because of new technology the quantification of cellular populations is now routine in immunology laboratories. This has led to a steadily increasing stream of kinetic data on the population dynamics of various types of immune cells. With this accumulation of data comes a realization that a proper understanding of the underlying dynamical systems will only be achieved when the data are considered within the organising framework of a formal theoretical model. Mathematical immunologists have energetically responded to this newly felt need, forming a growing number of close collaborations between theoretical and laboratory immunologists. Some of these collaborations have been rich sources of new insights; not only into biological processes, but also in showing the usefulness of mathematical modelling to large branches of a biological community.

Fundamental to such interactions is the question of how one manages the wealth of molecular detail, and where appropriate, how this detail might be incorporated into a macroscopic or population level description. In seeking answers to these questions a major objective was to attempt to identify mathematical and computational methods common to these areas, whether the individuals are molecules, cells or organisms.

Summary

The consensus of those who attended the programme, either as a short-term visitor or a long-term participant, is

that the programme was very successful in achieving the stated objective of bringing together leading theoreticians and experimentalists to discuss major biological problems that may benefit from mathematical modelling and analysis. In addition the programme successfully attracted a very young group of researchers (of 238 participants, 55 were in the 22-30 age group, 99 in the 31-40 range, 52 in the 41-50 range, 26 in the 51-60 range, and 6 in the 61-70 range), of which 52 were female.

Future directions

The programme highlighted a number of important issues and directions for the future development of research at the interface between biology and mathematics. Some of these are as follows.

1. Biological organization at every level, from molecular to population, is based on complex networks for signal detection, transduction, processing and response, and at present there are few suitable mathematical techniques for analyzing and understanding these systems. One conclusion from numerous talks and discussions is that the level of complexity observed may reflect the need for robust performance in the face of fluctuating inputs. Heretofore the mathematical focus has been on how complex the dynamical behavior of a network can be, but from a biological standpoint a better question is how complex must the network be to function robustly in a given environment. A major objective should be to identify canonical structures in networks that produce stereotypical outputs, {em i.e.} to identify the resistors and transistors of biological networks. This requires detailed modeling of well-characterized systems to provide the basis for the development of new mathematical techniques.

2. Training issues: Future success in interdisciplinary research can only be realized by increasing the pool of suitably trained young scientists. This will require cross-disciplinary training of students at a much earlier age than is currently done, and retraining of faculty for this purpose. In addition, sustained support at later stages, including postgraduate training and research is needed.

Fuller details can be found at

www.newton.cam.ac.uk/programs/ICB/

Modeling and simulating biological processes in the genomic era

Autrans (France), March 2002

Two dozen researchers with various scientific backgrounds started in January 2001 to face the challenges of high-throughput biology in a stimulating year-round workshop that was initiated and supported by genopole® in Evry, France. Some of these scientists were initially more familiar with the field of modelling / simulation, while others were involved in various aspects of (post-)genomics. After 14 months of work, they held near Grenoble a small multidisciplinary seminar that brought together 60 participants.

Lectures

Physico-chemical approaches:

The talks of Jacques Prost, Jean-Baptiste Fournier, Camille Ripoll and Yves Bouligand had physico-chemical approaches to the dynamics of intracellular structures as a common theme. Different sorts of modeling and simulation also played a large part in their work.

Prost insisted on the importance of the mesoscopic scale as one of the relevant scales in biological descriptions. He brought together mathematical modeling and physical experimentation in explaining how bacteria such as *Listeria monocytogenes* travel within and between human cells by locally polymerising actin using a bacterial protein, ActA. He showed how ActA-coated beads could move in a similar way and discussed symmetry breaking and persistence lengths. In the field of intracellular transport, he showed how motor proteins travelling along microtubules could tug tubes of lipids.

Fournier developed a physico-chemical model based on long-range elastic interactions to explore how the curvature of membranes by proteins influences their distribution. He applied this numerical model to the recruitment of dynamins by clathrin coats during endocytosis. There is a general principle here that may underpin the behaviour of many proteins that are integral or peripheral to the membrane.

Ripoll applied physico-chemical theories about the condensation of counter-ions onto linear, negatively charged, cytoskeletal structures to explain a whole range of disparate findings about calcium control of cellular processes. He proposed that condensation and decondensation of ions orchestrate kinases and phosphatases which in turn feed back on structures. This potentially provides a powerful integrative mechanism.

Bouligand took us through the history of liquid crystals in biology and showed us how cholesteric liquid crystals form *in vitro* and *in vivo*. He discussed how liquid crystals in DNA may affect the transcription of genes and the replication and partitioning of chromosomes. One of the many questions his talk raised is whether genome sequences could be used to determine which regions are in a liquid crystalline state.

Metabolic modelling

The next group, Athel Cornish-Bowden, Jean-Pierre Mazat, Christophe Chassagnole and Julie Fiévet, focused on metabolism – and the necessity of using metabolic control analysis to exploit experimental data by computer-modeling.

Metabolism is what cells do, Cornish-Bowden reminded us, and attempts to exploit genomic data that ignore metabolism are doomed. African sleeping sickness is caused by *Trypanosoma brucei* which has its glycolytic enzymes compartmentalised in a glycosome. To identify targets for drug therapy, he used metabolic simulations to determine which of the glycosomal enzymes would be good candidates and which would be useless.

Mazat showed how computer-modeling might be used to create and investigate a virtual mitochondrion, with the prospect of better understanding mitochondrial diseases. The first steps involve using the kinetic parameters of enzymes to predict metabolic fluxes within mitochondria which vary according to cell type. Many mitochondrial

DNAs have now been sequenced and he held out the prospect of deriving metabolic maps from genetic ones.

Chassagnole modeled how pollutants such as heavy metals affect the flux through the threonine pathway. He determined the control points and showed that the multiple effects of these pollutants can only be understood by modeling the whole pathway.

Fiévet gave a different dimension to metabolism by introducing constraints due to molecular crowding and the cost of protein synthesis. She introduced the concept of combined response coefficient which takes into account the necessity for cells to evolve a particular distribution of enzymes to optimise the flux through a given pathway.

In these presentations of metabolic modelling, there was little joy for proponents of the genome or proteome as the source of all wisdom – the emphasis was placed on control coefficients and on an integrative understanding of pathways.

Interaction networks

Cellular life is all about patterns of interactions. Interpretations of these patterns were proposed by Derek Raine, Jacques Ricard, Marcelline Kaufman and Jacques Demongeot.

Raine gave us the history of power laws, self-organised criticality and small world networks in metabolism and gene regulation. He derived a parameter related to information entropy to assess the complexity of a network based on the ratio of the clustering or cliquishness to the average path-length between two elements. He examined gene expression during the cell cycle of *Caulobacter crescentus* in terms of this complexity parameter.

Ricard told us more about information. He pointed out that metabolic networks may contain more information than genetic ones. He argued that in metabolic networks the nodes could usefully be considered to be the reactions themselves. Then, beginning with Shannon's theory of information, he derived expressions for metabolic networks in which the values correspond to either integrated systems or emergent systems.

Kaufman took us through the logical analysis method for determining the dynamics of regulatory networks that include gene-protein and protein-protein interaction networks. This essentially discrete approach has been developed to allow asynchronous events in a network to be analysed. This approach permits multi-stationarity states and periodicity to be predicted relatively easily from complex experimental data.

Demongeot continued in the vein of logical analysis by discussing interaction matrices, which represent how, for example, one gene regulates another. He raised the problem of the relationship between the number of steady states of the system and the number of regulatory circuits in the interaction matrix. Whilst these analytical techniques should prove suitable for interpreting the wealth of transcriptome data now available, Demongeot showed us that these data are far from perfect and presented a statistical method that helps improve them.

The preceding four talks were all of relevance to the interactions occurring in large intracellular networks, an

understanding of which is critical if we are to exploit genome sequencing and the transcriptome.

Miscellaneous

The last series of talks, by Pierre Auger, Yannick Kergosien and Vincent Schächter, were more general.

Auger began by arguing that a progression up through the levels in biology is accompanied by a reduction in the time required for the units to interact and by an increase in the size of the units. This allowed him to apply an aggregation method to hierarchical biological systems and so obtain a simple model in which only a few global variables are important.

Kergosien explored the relationship between adaptation and branching using a simple robust algorithm that is of general relevance to epigenesis or to other situations where multidimensional tree graphs are drawn. He showed us how repeated, abortive attempts at branching might precede a major branch point.

Finally, Schächter gave us a salutary tour of the problems associated with trying to make sense of biological data. These ranged from serious problems with the quality of the experimental data to the inadequacy or limited applicability of models. Schächter's talk highlighted the importance of developing better and more integrative models and simulation techniques.

There was no shortage of candidate methods of simulation presented at the meeting on different occasions (posters, discussions) by the multidisciplinary audience. These ranged from multi-agent systems and cellular automata to L-systems, P-systems, MGS and SiliCell.

Workshops

Each of the four year-round workgroups convened an afternoon workshop devoted to its topics. Two of them, on Hyperstructures and on Endomembrane dynamics, revolved around biological models that are representative of a wide class of processes and are challenging for modeling/simulation. The other two workshops, on Observability and Organization, dealt with conceptual innovations in the overall methodology of biological modeling.

Hyperstructures

Biological objects are often "constructive dynamical systems" whose structures evolve as a consequence of their internal dynamics, which in turn is affected by the overall structure. Because very few tools are presently adapted to tackle constructive dynamical systems, they constitute fascinating challenges for modeling/simulation.

A typical case of a constructive dynamical system in cells would be hyperstructures, defined by Vic Norris and Michel Thellier as supramolecular assemblies that may comprise heterogeneous elements such as protein, lipid, ion, RNA, DNA. They appear during the operation of a particular cellular function and dissociate when the function is no longer required. Some of them are stable cellular substructures. Many of them are dissipative structures that only exist during active, energy-consuming functioning. Such hyperstructures may form if the affinities among their constituents change during functioning to provide higher stability of the whole. The

concept of hyperstructure provides an intermediate level between the molecule and the cell and interconnects various remote scientific fields. Because this concept is not easily amenable to experimental testing at the bench, computer simulation is needed to investigate hyperstructure properties and to test whether the concept is coherent. A three-dimensional model of a metabolic hyperstructure has been created. It demonstrates that it is possible to find simple general rules to generate hyperstructures whose existence and stability depend on a flux of material.

The discussion that followed resolved some issues related to the materiality of hyperstructures, their typical time scales and thermodynamic properties. The concept of hyperstructures has the virtue of emphasizing the dynamics in structural assembly/disassembly, and the multiplicity of functions for a given protein. The major criticisms bore on the very heterogeneous nature of hyperstructures, and the lack of experimental work in this field, which requires caution in the choice of an appropriate formalism that would not automatically generate the expected result.

Endomembranes

In cell biology, the secretory process in eukaryotic cells also corresponds to a constructive dynamical system, as it appears to autonomously generate new structures as a result of its molecular dynamics. François Képès reviewed the only documented case of a membrane-bounded intracellular compartment whose very existence strictly depends on its continued functioning, as for non membrane-bounded dissipative structures. Indeed, the Golgi apparatus of baker's yeast appears at steady-state as a continuously renewed set of transitory membrane-bounded structures that self-mature, rather than as a permanent entity. On the basis of this case and of recent advances in related molecular studies, a detailed model was proposed, that encompasses the birth of a yeast Golgi element and bridges its molecular and morphogenetic aspects. This model was extended to three successive evolutionary "inventions", from bakers' yeast to a methylotrophic yeast, to plant, and then to animal cells: stacking, stabilizing and aggregating the primary Golgi elements.

During the discussion, it was clearly stated that there are other possible mechanisms that may explain the morphogenesis observed in the Golgi apparatus. On the one hand, Jacques Prost pointed out in his talk (see above) that membrane bending can be caused not only by self-assembly of molecular coats, as in the clathrin-mediated vesiculation, but also by the action of microtubules or motors that can pull the membranes. On the other hand, it is known that asymmetric bilayers can easily undergo a bending process, due to forces depending on local curvature. If those forces can accentuate the curvature, a sufficiently large random fluctuation can start a bending process. Moreover, the morphogenesis can be explained by several mechanisms, each intervening at a specific time. It would therefore be interesting to determine the time scale of the migration described in the physico-chemical model presented by Jean-Baptiste Fournier (see above). Jean-Marc Delosme suggested that an order of magnitude may suffice to have an idea of the

range of validity of this model in the morphogenesis of the Golgi apparatus.

Observability

For a variety of reasons, one may not be able to observe enough about a biological system to immediately determine whether a property holds; this is the notion of "observability". In Popperian terms, to be able to refute a property, one must be able to construct experiments which bring the model system in some desired state that provide enough information for conclusive validation or refutation; this is the notion of "operability" (basically the notion of "controllability" in systems theory). As Gilles Bernot reminded us, one would like to deal with properties that display both operability and observability.

The case study proposed by Janine Guespin is the hypothesis that there may be populations of *Pseudomonas aeruginosa* bacteria that keep on producing mucus in the lungs of cystic fibrosis patients because of a stable, epigenetic change that occur in the course of the infection. A formalism must be selected and a model of the object under study must be constructed using that formalism. The formalism used for the case study was adapted from that presented by Marcelline Kaufman (see above). It uses multivalued logical variables and a simple temporal logic, and has been modified to explicitly allow the notion of future. A model consists in modes of relations between components or parameters whose number is typically sufficiently large that one cannot readily figure out its behaviors. The model, together with statements about model behavior, may be viewed as a means of describing a complex hypothesis. Separating model and statements about the model (such as feedback loops in the model for the case study and a statement about which loop is functional) makes things cleaner, albeit all are hypotheses and could be merged into the model.

Organization

This workshop is about theoretical tools for simulation and analysis in genomics. Simulation corresponds to a corpus of tools which simulate the behavior of biological process. Analysis corresponds to tools for the finding of structural and dynamical properties from a topological representation.

During the session, Jean Louis Giavitto summarized the advances achieved by the workgroup. Christophe Godin introduced tools for the simulation of plant growth. Franck Molina presented work on the definition of a language dedicated to the design of ontologies. Finally, Franck Delaplace showed how emergent properties could be analysed in biological networks. These talks and the general discussion emphasized the relationships between models and computational frameworks, and between biological complexity and languages.

Conclusion

Among the messages that we took away, a couple were particularly strong. Firstly, to be successful in exploiting the results offered by the investment in the genome, a truly integrative modelling has to take into account physical chemistry of the sort presented at the seminar. In the theatre of the cell, these principles provide the script that a host of molecular actors have learnt over the aeons to interpret. Secondly, the gap between biological

and physical approaches to complex systems is being bridged. New concepts are being generated and those interested in integrative simulation now have the exciting task of learning to exploit them. Thirdly, the dialogue between simulation and bench experimentation has been initiated and should be emphasized in the near future.

Further reading:

An Autrans seminar book was edited by Patrick Amar, François Képès, Vic Norris and Philippe Tracqui. It contains the meeting abstracts, original papers and courses that relate to the above topics, and detailed accounts of the workshops. It is available from Dr. Hélène Pollard, Directrice-Genopole-Recherche

(Helene.Pollard@genopole.com).

François Képès, Franck Delaplace, Jean-Marc Delosme, Janine Guespin, Roberto Incitti & Vic Norris.

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(*This is a slightly shortened version of a report that will appear in "Biology International" in October or November 2002, see: <http://www.iubs.org/test/bioint/frbi41.htm> The editors.*)

Gatherings in Biosemiotics 2

Tartu–Puhtu–Tallin, n Estonia, June 14–17, 2002.

The international annual meetings in biosemiotics as an initiative of the Tartu and Copenhagen biosemiotic groups started with the first Gathering held in May 24–27, 2001, in Copenhagen. After a decade of numerous sessions under the cover of various bigger meetings either in semiotics or biology, this series of conferences intends to be a regular framework for discussions and scholarly exchange of ideas and views in semiotic biology. A report on the First Gathering is available in *Sign Systems Studies* vol. 29(1): 369–376, 2001 (by Claus Emmeche). A collection of papers of the event has been published in *Sign Systems Studies* vol. 30(1), 2002 (see the table of contents and ordering information at <http://www.ut.ee/SOSE/sss30.1.htm>).

The aim of the Gatherings in Biosemiotics is quite ambitious — to work for the formation of biology that would use as a basic approach the methods of semiotics. The importance of this project comes from the understanding that the inclusion of the problem of the origin of sign, as well as the analysis of meaningful communication in living systems requires a more general methodology than that of biophysics. Thus it can be seen as a paradigm in theoretical biology.

The meeting of 2002 included three days of talks in Tartu, a visit to Karl Ernst von Baer House, a session in Puhtu Biological Station (the place of work of Jakob von Uexküll in 1930s), brief walkings on an Estonian wooded meadow and on a raised bog, and the final session in Tallinn Zoo. There were about 40 participants from 15 countries.

The papers were presented by Jesper Hoffmeyer (why the genome is so small), Marcello Barbieri, (organic codes), Anton Markos (addressee of the genetic text),

Stefan Artmann (Jacobian biopragmatics), Frederik Stjernfelt (the core hypotheses of biosemiotics), Kalevi Kull (biosemiosis and intentionality), Wolfgang Hofkirchner (differentia specifica of biosemiosis and a theory of evolutionary systems), Yagmur Denizhan (semiotics and metasystem transition theory), John Collier (information expression and cohesive levels), Claus Emmeche (biosemiotics and experiential biology), Tom Ziemke (affordance vs. functional tone: a comparison of Gibson's and Uexküll's theories), Donald Favareau (collapsing the wave function of meaning: the contextualizing resources of talk-in-interaction), Toshiyuki Nakajima (construction of umwelt to control probabilities of events in living), Tommi Vehkavaara (an outline of basic semiotic concepts for bio- and robosemiotics and the emergence of umwelt), Andres Luure (the role of relations in semiotics), Sergey Chebanov (bilateral biosemiotics: a problem of sense on a super-triplet level), Elisabeth Johansson (biosemiotic perspectives in gasflux models), Edwina Taborsky (a pansemiotic architecture), Soren Brier (the third culture), Luis Bruni (the global phenotype), Alexander Sedov (part-whole interactions), Myrdene Anderson (neoteny and its role in taming and domestication), Mette Böll (evolution of empathy), Dominique Lestel (on the expression of negation among animals), Gottfried Suessenbacher (mythology and evolutionary psychology), Aleksei Turovski (semimetabolism of animal associations), Timo Maran (mimicry and mimesis in the bio-semiosphere), Mark Vian (biotic integrity, ecosystemic archetypes, and the boundary of self), Morten Tønnessen (umwelt ethics), Tiberiu Mustata (the semiotic substance of homeopathy), Sune Frolund (teleology and the natural history of signification in Hans Jonas), Torsten Rütting (Jakob von Uexküll archive), and others.

The final session in Tallinn Zoo included an excursion guided by an Estonian zoosemiotician Aleksei Turovski, who described the zoo as a field of reestablishing semiotic boundaries.

The additional information about the event, and information about the past and coming meetings in biosemiotics is available at the web site of the Gatherings in Biosemiotics at <http://www.zbi.ee/~uexkull/biosemiotics/>. The Gatherings in Biosemiotics 3 will take place in Copenhagen, in summer 2003.

Kalevi Kull, University of Tartu, Estonia

Conference on Mathematical modelling of population dynamics

June 24-28, 2002 Bedlewo, Poland

This conference has been organized by the Institute of Mathematics, the Polish Academy of Sciences and the Institute of Mathematics of the University of Silesia, all within the EU 5th framework program "*Mathematical Modelling and Analysis of Cellular Populations*" coordinated by the Stefan Banach International Mathematical Centre.

By the organisers own words "the conference focused on mathematical modelling and model analysis of popula-

tions at various levels, including cells, genes, biomolecules and of population dynamics in evolution, ecology, epidemiology and infectious diseases, physiology and immunology and cancer growth“

First a short description of the conference site. The meeting was located at the Mathematical Conference Centre, a palace complex in Bedlewo, which is a property of the Institute of Mathematics of the Polish Academy of Sciences. The palace was built in the 19th century by a famous aristocratic Polish family in a neo-gothic style, and is surrounded by a 9 hectare park in which extended walks can be made. Without doubt this research centre has nearly all attributes which will surely make it one of the important sites for mathematical discussion and research in Europe. There are, due to its short age, still some ingredients missing, like a library or a high-speed internet connection, but its potential is enormous and the new guest houses, the lecture rooms and of course the castle itself are more than impressive.

The organisers managed to assemble many important researchers working inside population dynamics, like M. Gyllenberg, J. Hofbauer, M. Ianelli, G. Webb, K.P. Hadeler, U. an der Heiden, P. Auger, H. Thieme, P. Maini, M. Mackey, A. de Roos, O. Arino, M. Kimmel, T. Kostova-Vassilevska, M. Langlais, B. Kooi, Z. Taib, just to mention a few names. It was a week full of talks all pointing out different aspects of population dynamics, especially those that can be applied to cellular populations. By this concentration of talks it was easily possible to gain insight about the current state-of-the-art of the subject, reaching from theoretical to more applied approaches. The application, “cellular populations” is of immense importance, and the flood of data now available by sequencing techniques and microarray data (just to mention these two techniques) will surely have a major impact also on the further development of cellular population dynamics. It has been obvious at Bedlewo that this active field of research must open to some of these new challenges, but also that many current theories and approaches have attained a grade of maturity that will allow for many new insights in the next years.

In the end I would like to express my thanks to the organisers and the personnel managing the Bedlewo Mathematical Conference Centre. They have created a stimulating environment, and I wish them further success with the centre!

Markus Kirkilionis, University of Warwick

The Turing Day: Commemorating the Anniversary of Alan Mathison Turing’s 90th Birthday

June 28, 2002, Swiss Federal Institute of Technology, Lausanne, Switzerland

Alan Mathison Turing, born in London on June 23rd, 1912, is widely considered one of the most creative thinkers of the 20th century. Not only is he one of the great pioneers of computer science, laying much of the theoretical groundwork for modern computing, but his wide interests, from computing and the mind to information science and biology, span many of the emerging themes of the postmodern society. His concept of the *Universal Turing Machine* was revolutionary for a time

when most computers were designed for a specific purpose. During the World War II, Turing worked as chief cryptanalyst at Bletchley Park, where he succeeded in cracking the code of the German *Enigma* cipher machine. Turing spent the last few years of his life working on computer simulations of plant growth. He developed a morphogenetic theory for biological pattern formation and introduced a central concept of mathematical biology with his *Turing Instability*. Alan Turing died on June 7th, 1954, of cyanide poisoning.

The Turing Day (<http://www.epfl.ch/turingday>), held on June 28, 2002 at the Swiss Federal Institute of Technology (EPFL) in Lausanne, was intended to commemorate the anniversary of Alan Mathison Turing’s 90th birthday and to revisit his many contributions to computer science, biology, philosophy, and cryptography. The workshop consisted in a series of invited talks given by internationally renowned experts in the field.

Undoubtedly, the central question for Turing was, and always remained, whether machines can do as much as minds. After World War II Turing paved the way to what would later become known as *Artificial Intelligence (AI)*. Christof Teuscher (Swiss Federal Institute of Technology, Lausanne, CH) focused in his talk on the almost forgotten connectionist ideas that Turing had developed in the 1948 “Intelligent Machinery” NPL report, that was published in 1968, 14 years after his death. Teuscher emphasized that Turing not only pioneered AI, connectionist models, and learning machines but that he also proposed to apply “genetical or evolutionary search” to train his connectionist networks, a technique which is widely used today.

Douglas R. Hofstadter (Indiana University, Bloomington, IN, University of Bologna, I) revived his famous strange loops and extended their application to the central dogma of biology (from DNA to RNA to proteins) where a spiral of complexity emerges.

In his very lively talk “Watching the daisies grow: Turing and Fibonacci phyllotaxis”, Jonathan Swinton (Proteom Ltd, UK) introduced Turing’s seminal work on mathematical biology. Turing was mainly interested in biological pattern formation, in particular, one of the problems he was trying to solve was Fibonacci phyllotaxis. Fibonacci phyllotaxis deals with the appearance of Fibonacci numbers in the structures of plants, e.g., the floret arrangement of the sunflower. Turing used what is now known as *Turing Instability*—introduced in his celebrated paper “The Chemical Basis of Morphogenesis”—to explain Fibonacci phyllotaxis. According to Turing’s hypothesis, chemicals, called *morphogens*, generate organs when present in sufficient density using a reaction-diffusion mechanism. “It is suggested that a system of chemical substances, called morphogens, reacting together and diffusing through a tissue, is adequate to account for the main phenomena of morphogenesis” (Turing, 1951).

The *Turing Test* proposed by Turing in his famous 1950 “Mind” paper is certainly still a very disputed concept. B. Jack Copeland (University of Canterbury, NZ) argued that Turing explicitly did not want to give a definition of intelligence but preferred to propose a test. The Turing

Test is supposed to provide a sufficient, though not absolutely necessary criterion for intelligence.

Martin Davis' (Prof. Emeritus, New York University, NY; University of California, Berkley, CA) talk "Beyond the Church-Turing Consensus" made clear that any physically realizable process—including the Turing machine with random elements and the quantum computer—computes in the domain of the Turing machine. According to Davis, no meaningful and serious research is going on around hypercomputers and Turing had nothing in mind himself. All he said in his 1939 doctoral thesis (Turing 1939) was that "oracles" compute uncomputable functions and that they cannot be machines. In conclusion, the strong version of the Church-Turing thesis—stating that no realizable physical device can be more powerful than a Turing machine—seems still valid and the much disputed question whether non-Turing computation is relevant to human-like artificial intelligence remains unsolved.

Turing's famous biographer Andrew Hodges (Wadham College, University of Oxford, UK) concluded the day with the hypothetical question "What would Alan Turing have done after 1954?" He draw the attention on Robin Gandy, a very close friend of Turing, who wrote a personal letter to Newman (Gandy 1954) in which he described what he thought would have been Turing's plans for the near future. Gandy mentioned eight points, and—interestingly enough—only one of them was about computing. In that point he refers to the 1948 "Intelligent Machinery" paper: "I always hoped that he would return one day to the practical problems of making a machine learn."

The Turing Day has shown that a number of researches lead or inspired by Turing continue to feed passionate scientific debates and that a number of questions remain unsolved. The day was a huge success: more than 200 people from all over the world assisted. In 2003, Springer-Verlag will publish a commemorative anthology in honor of Alan Turing. For more information see: <http://www.teuscher-research.com/festschrift>

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The 5th ESMTB Conference on Mathematical & Computing in Biology and Medicine (ECMTB2002)

July 2-6, 2002, Milano, Italy

The 5th tri-annual conference of ESMTB was held in Milano during July 2002. As in previous editions, it attracted most of the leading scientists in the field. The statistics of participants shows that over 380 were from the EU system, 140 of them being young researchers; 27 from USA, 8 from Japan, 10 from the New Independent States (NIS), etc., for a total of 440.

As in all previous editions, strong attention has been paid to the scientific community at large, by including

delegates of the major scientific societies from outside Europe (e.g. SMB, Japan SMB) in the International Scientific Committee, and inviting speakers and minisymposia organizers from all over the world.

The conference included 17 invited lectures, 27 minisymposia (either invited or proposed), 156 contributed papers, 51 posters organized in a cylindrical structure along the following topics:

Biotechnology and Bioengineering
Bioinformatics and Computational Biology
Biomedical Imaging
Cardiovascular System
Cell Signalling and Cellular Organisation
Ecology
Environmental Sciences
Evolution
Immunology
Infectious Diseases
Individual Based Models
Regulatory Gene Networks
Shape and patterns
Stochastic modeling
Tumor Growth and therapy

The conference has shown a significant shift of attention of the scientific community towards the development of efficient algorithms for complex computations and visualisation, notably for mathematical models in molecular biology and genetics; fast developments in areas such as biotechnology (e.g. genome projects, tissue engineering) continue to add new focal points of activity to the field.

An international scientific committee did the choice of the invited lectures and invited minisymposia in order to expose the scientific community and in particular young researchers to these recent developments.

Some mini-symposia were specifically organised inviting experts from different fields (e.g. a biologist, a biophysicist, a mathematician, and so on) to talk about a particular topic or experts using different mathematical tools to describe a particular phenomenon. From the training point of view this was a wonderful opportunity of cross-fertilisation.

In the original project it was felt necessary to involve researchers in the field of engineering in order to fill the gap with the final application. 14 engineers came.

Special attention has been paid to the young researchers. Indeed, the successful development of research activities in the field of mathematical and theoretical biology and medicine requires a synergy of research efforts and knowledge of mathematics, biology, medicine, computer science, and physics. In addition, it requires the development of different phases referring to the modelling process: phenomenological observation, mathematical modelling, mathematical methods, simulation, prediction, experiments, model validation and refinement. The development of all this requires an interdisciplinary work. The Conference gave the young researchers the

possibility of looking into this kaleidoscope and understanding the different features of this research field.

Almost one third of the participants were young researchers and more than 50 researchers came from Eastern European countries.

The participation of young researchers can be schematized as follows:

about 150 young researchers,

59 gave an oral/poster presentation,

67 of the young researcher present were co-authors of an oral presentation or a poster.

The large participation of young researcher has been favoured by the generous financial support offered by the European Union; in fact 68 have been fully supported including registration fee, accommodation, and social events. A number of scientists from Eastern Europe has also been supported by the local organizers.

The field of theoretical and mathematical biology and medicine has kept profound connections to many current problems of great relevance to society. Insights and predictions from mathematical modelling are used increasingly in decision support in medicine, environmental and nature management, climate problems, agriculture and management of natural resources.

A Round Table was organized on “Hot topics in Biology and Medicine. A call for mathematical and theoretical biologists”. Delegates from both mathematical and biomedical were invited to a confrontation of their opinions about the most relevant problems the scientific community is challenged to solve regarding improving human health and better control of environmental quality. The participation was very high both in number and in interest and stimulated a vivid discussion, confirming the genuine interest of our community to attack real and relevant for the bioscientist by reducing the time-lag between development of mathematical methods and their use in problem solving.

The book of abstract has been made available at the web at the following address:

<http://www.mat.unimi.it/~ecmtb>.

Based on the very positive reaction of a specific questionnaire to all speakers, proceedings of the conference will be published as a special issue of the editorial series of MIRIAM, the Milan Research Centre for Industrial and applied Mathematics that coordinated the organization of the conference.

It may be interesting to record that all sessions from the first to the very last day have been highly attended, notwithstanding various attractions and opportunities of social life in Milano.

All the above shows that the tri-annual conferences constitute one of the major events in the field of worldwide interest.

On behalf of the Organizing Committee:

Daniela Morale, Univ. Torino, Italy

Round Table Discussion: Hot Problems in Biology and Medicine

ECMTB, Milano, 3.6.02

Moderator: C. Tonelli (Milano)

Participants: E. Boncinelli (Trieste), A. D’Angelo (Pavia), H.C. Hege (Berlin), P. Jagers (Chalmers), R. Jeltsch (Zürich), A. Pugliese (Trento), A. Villa (Grenoble).

Statements:

E. Boncinelli: In the postgenomic area a huge amount of raw data is available. These can be dealt with only by informatics. There are many different genes in different cells and different tissues, which are themselves in different phases. Many regions of our genetic code do not code for proteins. We can deal with data from astronomy because we know some basic rules. How do we have to read the genetic data? Every gene “knows” where to be active, when to switch on, and when to switch off. A major goal is to understand the networks of gene regulation.

A. D’Angelo: Central problems of neuroscience are to understand the principles of the functioning of the nervous system, of brain behaviour and cognition. Signals are received, processed, transmitted to other neurons. Also ionic channels and receptors play a role. We need interplay between experiments, computational theories, and biophysical models to explain the emergence of oscillations and resonance in the cerebellum. We are interested in computational learning and time coding of networks. Genetic models and mathematical models are needed to understand how information is coded.

A. Villa: Most communication is carried out by spikes. Each neuron generates a number of spikes. So we are interested in time series and multivariate time series (information is checked over hours or even days). There is an enormous amount of data, which needs computers, computer scientists and mathematicians who decide how to deal with the analysis of these data, and how to modify this information. One question of interest is if string theory is related to the spatial and temporal code. In neurology patients with electrodes in the brain can be subjected to impulses, this might treat e.g. Parkinson, but cannot cure it. A future goal is surgical treatment.

H.C. Hege: We are looking at 3D images for virtual patients and reconstruction of the patient model. We aim for automatic accurate real time segmentation, for adaptive imaging, shape comparison, averaging, quantification of variations, and an automated detection of correspondence between geometrical shapes.

P. Jagers: We are interested in branching processes and comparative genomics. How is the relation between mathematics and biology? Is there an unreasonable effectiveness of mathematics in the natural sciences or an unreasonable lack of effectiveness of mathematics in the natural science? Mathematics is the language of physics. In biology mathematics is considered to be helpful aside. (Comment from the audience: But it is the language of biology!)

An own language for biology has to be developed since the building stones for life have been discovered. Basic

rules should apply to them. It is an urgent need to engage mathematicians into this research.

A. Pugliese: To understand the dynamics of populations in ecology it is important to understand the effects of different scales, not necessarily to understand the whole genome. In ecology there is an enormous complexity one has to deal with. A number of different scales in space, and many different species are involved, like for instance the ecology of pathogens and parasites. Questions are for example: What is the relation between diversity and stability? What happens if one introduces alien species into a population? In this situation data are sparse, and only short time series are available. Here methods for robust predictions are needed.

R. Jeltsch: Large scale simulations as needed e.g. in models for surgery planning easily contain $10^7 - 10^8$ equations. These deal for example with the interaction of implants in the body, drug transport, and tissue growth. Modelling the plan for an operation of a facial disfiguration has to deal with questions like what is a surface or, how does the modelling of tissues depend on the properties of a person (on age, for instance). For the implantation of a heart bypass models should become good enough to plan operations, e.g. to answer questions like where should the bypass be done. Models should simulate the cardiac electrical activity well enough so that heart surgeons could be trained on them.

Should we ask for more mathematical training of biologists? Should we ask for more biological training of some mathematicians? Should we make this a hot topic?

General Discussion with the audience:

Are problems in biology more of a quantitative nature or more of a conceptual one?

New methods for the data are needed, but really new methods. These should extract what is relevant in the huge amount of data.

What we need is not only data-mining but concepts. Very often outdated mathematical concepts are used in biology. We have to ask what the fundamental laws of biology are. Then we have to develop suitable models and can perform model driven statistics.

A good biologist is able to sort out important features also experimentally.

Mathematics has to be “biologized”. There are principles for biological interaction, say, and the power of mathematics is challenged to detect such essential principles, and in that way Mathematics may try to copy Nature, which extracts its essential components of life by evolution and thus makes life simpler.

Nature does not make things simple; look, for instance, at the 3-body problem. It is not good that less and less mathematics is taught to scientists.

However, take as an example the recent findings about regulation of the cell cycle, for which the Nobel Prize was granted to Paul Nurse last year. The essentials of corresponding mathematical models are 2 or 3 simple negative feedback loops, and some positive feedback

loops. For a theoretical understanding mainly reduction to some essential mechanisms was the crucial thing.

We may need a new “Copernican” revolution: complexity might just be a consequence of a “Ptolemaic” mathematical modelling of biological systems.

Start bottom up in complex biological systems, since it is hard to guess mechanisms. First one has to pass through the complexity of the lower levels.

Report by A. Stevens, Max-Planck-Institute for Mathematics in the Sciences, Leipzig, Germany.

3rd ESMTB Biomathematics Euro Summer School “Dynamical Systems in Physiology and Medicine”

Urbino, 8th-19th July 2002

Programme

Periodic haematological diseases and leukemia (10 units, Jacques Belair, Joseph Mahaffy); modelling and cellular automata in the study of cardiac arrhythmias and ventricular fibrillation (8 units, Alain Bardou, Pierre Auger); modelling Aspects of Airflow and Gas exchange (8 units, George I. Cremona, Oliver Jensen); models for the Glucose-Insulin system (12 units, Andrea De Gaetano, Andrea Mari, Jeppe Sturis); neuronal modelling (10 units, K. Pakdaman, A. Longtin); delay differential equations (14 units, Edoardo Beretta, Mostafa Adimy, Uwe an der Heiden, Ovide Arino, Shigui Ruan, Yasuhiro Takeuchi); numerical methods (10 units, Rodolfo Bermejo, Luis Abia, Oscar Angulo); workshop “Medical applications of mathematical models of the Glucose/Insulin System”.

The themes covered in the school included blood precursor cell proliferation, diseases thereof and models of the oscillating behaviour of some such diseases (Belair, Mahaffy); physiology of neurons, the Hodgkin-Huxley model, the Fitzhugh-Nagumo model (Bardou, Pakdaman, Longtin); physics of viscous fluid flow as applied to models of air and blood flow in the lungs (Jensen), Nitric Oxide physiology and modelling of its release and uptake from the respiratory tree wall (Cremona), the glucose/insulin metabolic control system in vivo (Mari, De Gaetano), physiology of the oscillatory release of insulin (Sturis).

The methods covered included modelling with cellular automata (Auger); encoding by means of generating spike bursts and altering the frequency of firing of neurons (Pakdaman, Longtin); an entire course on the linear and nonlinear theory of delay differential equations, including geometrical topics and methods for detecting stability switches (Beretta, Arino, Adimy, an der Heiden, Ruan, Takeuchi); numerical methods for the integration of ordinary, partial and delayed differential equations (Abia, Angulo, Bermejo).

The courses consisted of 75 formal didactic units and 2 invited talks (40’ each including discussion), a 4 hr-workshop on the medical applications of mathematical modelling of the glucose/insulin system, 16 presentations by participants (20’ each plus discussion), fitting into the foreseen 86-unit schedule (8 or 9 units a day over two 5-days weeks plus 4 units on the intervening

Saturday morning). Teamwork was conducted during the intermissions and after dinner in the evening. Key concepts for the teaching environment were: short lectures with enough breathing space in between; large overall number of teaching units (on the average 8 per day); high instructor to attendee ratio (23 to 54) with instructors being available and talking with the participants in all working and social occasions (favoured by the cohabitation of all participants in a single venue and by the communal lifestyle); specific presentation opportunities for younger researchers in front of instructor panels.

At the end of the school, anonymous participant evaluations were collected: the overwhelming majority showed to appreciate the relaxed, friendly atmosphere and the dense teaching program. Most made interesting and/or useful acquaintances for their future activity and were very happy to have attended.

More information and the school photos are on www.biomatematica.it/urbino2002.

Report by: *Andrea De Gaetano, Biomath Lab, CNR IASI, Rome.*

Short Report on the 3rd International Conference on Mathematical Biology

Guilin (P.R. of China), 15-18 August 2002

The conference took place at the Guangxi Normal University of Guilin. It was one of the Satellite Conferences of the International Congress of Mathematicians at Beijing.

There were approx. 275 participants, 230 of them from China. Lansun Chen (Chinese Academy of Sciences, Beijing) and Karl Sigmund (University of Vienna) were the chairmen of the scientific committee. The conference was organized in plenary and up to 5 parallel sessions. The variety of topics was very large, ranging from mathematical investigations of ODE models of local population dynamics (bifurcation and catastrophe theory) and PDE models of standing and travelling population waves to metapopulation dynamics, noise, spatio-temporally discrete as well as hybrid models.

The proceedings will be published next year in *Discrete and Continuous Dynamical Systems, Series B*.

Webpage of the conference

http://www.icm2002.org.cn/satellite/satel_4.htm

Contact: Horst Malchow, University of Osnabrück
(malchow@uos.de)

III Summer School and Scientific Workshop -- Focus on Signalling and Cellular Interactions

September 2-6, 2002, Propriano (Corse, France)

The III summer school and workshop organized by the EU Research Training Network "Using mathematical modelling and computer simulation to improve cancer therapy", held in the beautiful natural setting of Propriano, was devoted to the analysis and modelling of signalling and cellular interactions in physiologic and pathologic conditions.

This year's school continued a tradition of interdisciplinary fertilization, by presenting a series of lectures by biologists, physicists and mathematicians, who tried to build up a common ground and a common language to get a grasp on some of the complexity of interactions at the cellular and sub-cellular level.

The structure of the school and workshop was planned to allow young researchers coming from different areas of science to get a flavour of problems and methods arising in this growing field of research. Participants were young as well as experienced scientists coming from Italy, France, Germany, Greece, Macedonia, Poland, Portugal, Spain, United Kingdom, United States, and they gave life to a truly international encounter.

Modelling of living systems requires a full-fledged set of mathematical methods, like dynamical system theory, diffusion-reaction equations, cellular automata, Langevin and Montecarlo simulations, and advanced statistical tools for data acquisition and interpretation. Several lectures were devoted to the exposition of these methods, some being more pedagogical, others held by young researchers (in the afternoon workshop) focused on research topics of current interest.

Regarding the biological part, we attended general lectures on cell biology, followed by seminars on specific "hot" topics, like differentiation, adhesion, and motility. A series of lectures was devoted to the exposition and discussion of advanced tools of statistical analysis to the study of gene expression schemes and protein networks, the so called 'transcriptome' and 'proteome' which represent one of the most exciting frontiers in the advancement of our understanding of the living and in the interaction between biology and other sciences, in particular mathematics, statistics, physics and informatics.

Many detailed information, like the scientific programme and the list of participants of the school can be retrieved on the web page

<http://calvino.polito.it/~biomat/>

Report by: *Andrea Gamba, Dipartimento di Matematica, Politecnico di Torino*

Group Presentations

Department of Theoretical Biology, Institute of Entomology

Ceske Budejovice, Czech Republic

The Department of Theoretical Biology was formally established in 1996 as one of several departments of the Institute of Entomology of the Academy of Sciences of the Czech Republic.

The Institute is located in the town of Ceske Budejovice (Budweis) in Southern Bohemia, 160 km south of Prague, on a campus shared with five other Academy Institutes (Hydrobiology, Landscape Ecology, Molecular Biology of Plants, Parasitology, and Soil Biology) and the University of South Bohemia. The Department focuses its research mainly on theoretical behavioral and population ecology and it fosters collaboration between theoreticians and experimenters.

Main Research Areas are:

Theoretical population ecology: This research focuses on mathematical modelling of population dynamics. Classical models of population dynamics neglect some important aspects of animal behaviour such as changes of prey behaviour under predation hazard, adaptive habitat choice, optimal foraging, sexual reproduction and cooperative behaviour that can have strong influence on population dynamics including its stability and persistence. We study models of population dynamics that include such realistic behavioural aspects. Understanding the effects of adaptive behaviour on population dynamics and on the structure of food webs is important in the search for mechanisms that maintain ecosystem structure and biodiversity in general.

Theoretical behavioural ecology: This research focuses on modeling various adaptive behavioural strategies. These include, e.g., optimal foraging theory, ideal free distribution, some trade-offs in host-parasitoid interactions etc. The aim of this work is to define and find evolutionarily stable strategies and to show their ecological implications. The predictions of these models are used as null hypotheses for experimental tests on optimal foraging. Moreover, the resulting strategies are used to study consequences of such adaptive behaviour on population dynamics. In the framework of sexual reproduction, we study how various mating strategies and dispersal of individuals affect survival/extinction of populations, and the interplay between habitat structure and optimal reproductive behaviour.

Methodological aspects of mathematical modeling: Solution of biological problems often requires development of adequate mathematical methodologies which are based either on the traditional functional approach or on the individual-based approach. The areas for which we develop adequate mathematical descriptions include, among others, models of food webs, various ways of sexual reproduction, models of fluctuating environments, morphogenesis, olfaction, and viability theory. Examples

of such methodological approaches include differential inclusions, differential equations (possibly with discontinuous right-hand sides), difference equations, partial differential equations and spatially explicit, rule-based individual simulations.

Current staff consists of three researchers, one postdoc, one PhD student and one emeritus. The Department offers three courses at the Faculty of Biological Sciences (Theoretical Population Ecology, Evolutionary Game Theory, Theoretical Behavioral Ecology).

For more details and updates, see

<http://www.entu.cas.cz/dtb>

Contact: Vlastimil Krivan (krivan@entu.cas.cz)

The new department "Methods of Innovative Computing"

University of Technology, Dresden

The department was established in October 2001 and belongs to the "Center for High Performance Computing" (ZHR, www.tu-dresden.de/zhr, director: Prof. W. E. Nagel), a central scientific facility at the Dresden University of Technology. The well-equipped ZHR together with the excellent scientific landscape in Dresden (Technical University, three Max Planck Institutes!) provide excellent working and research opportunities.

The head of the new department is Andreas Deutsch, who studied mathematics and biology at the University of Mainz, received his PhD in biology from the University of Bremen, and his habilitation in theoretical biology from the University of Bonn.

The department's activities are:

- (A) original research in biomathematics and theoretical biology,
- (B) initiation and organization of research networks,
- (C) maintenance and development of the competence network MTBio (Modelling and Theory in the Biosciences),
- (D) consulting of external users of the ZHR computing facilities.

(A) Original research:

In the focus of our research are "cellular systems". Biological cells have developed a multitude of interaction possibilities whose cooperative interplay guarantees the development of organismic forms. Disorders in cell interaction can lead to disease situations and malignant pattern formation (e.g. tumour growth) if the immune system is not able to counteract the disturbances. It is therefore of crucial importance to understand the principles of collective phenomena in interacting cell systems.

In our quickly growing research group, mathematical models and simulation tools are developed for the analysis of cooperative phenomena in interacting cell systems. Modelling efforts typically rest upon data from in vitro experiments (predominantly microorganisms and cell

cultures) and clinical patients. Important insights into the function and regulation of cellular systems can be gained from this highly interdisciplinary approach which is based on the connection of cellular data with appropriately constructed mathematical models.

We have recently entered a further research field which focuses on the exploitation of ideas taken from self-organizing biological systems (particularly the immune system) for solving problems (e.g. search for information) in dynamic technical networks.

Research cooperations exist in particular with Charité University Hospital, Berlin, Max Planck Institute for the Physics of Complex Systems, Dresden, Max Planck Institute for Molecular Cell Biology and Genetics, Dresden, Department Theoretical Biology at University of Bonn, University Clinic Bonn, University Erlangen-Nürnberg, University Magdeburg and University Warsaw.

Selected recent publications:

1. U. Börner, A. Deutsch and M. Bär: Rippling patterns in aggregates of myxobacteria arise from cell-cell collisions. *Phys. Rev. Lett.* 89: 078101, 2002
2. S. Dormann and A. Deutsch: Modeling of avascular tumor growth with a hybrid cellular automaton. *In Silico Biology* 2: 1-14, 2002
3. A. Deutsch and S. Dormann: Principles and mathematical modeling of biological pattern formation. *Mat. Stos.* 3, 2002, to appear
4. J. Moreira and A. Deutsch: Cellular automaton models of tumour development - a critical review. *Adv. in Complex Systems (ACS)* 5(2), 2002, to appear
5. A. Deutsch and S. Dormann: Cellular automaton modeling of biological pattern formation. Birkhäuser, New York, 2002, to appear
6. A. Deutsch, M. Falcke, J. Howard and W. Zimmermann (eds.): *Function and regulation of cellular systems: experiments and models.* Birkhäuser, Basel, 2002, to appear

(B) Research networks:

Andreas Deutsch is active member of the EU-RTN network "Using mathematical modelling and simulation to improve cancer therapy" (<http://calvino.polito.it/~biomat/>) and of the new EU-RTD network "Biology-inspired techniques for self-organization in dynamic networks" (starting this year). Further research networks at the national and European level are planned, which are all directed towards the improvement of research conditions in the field of biomathematics and theoretical biology.

(C) MTBio network (www.mtbio.de)

Andreas Deutsch coordinates the competence- and communication network MTBio. The Network MTBio (founded 2000, currently ca. 380 members worldwide) is an initiative of researchers primarily from German Universities and research institutes specialized in biomathematics, biophysics and bioinformatics. Main MTBio objective is to catalyse interdisciplinary communication and to initiate interdisciplinary research activities.

The MTBio network organizes workshops directed on biological key issues. The first international MTBio workshop "Function and regulation of cellular systems: experiments and models" took place in 2001 (scientific coordinators: A. Deutsch, M. Falcke, J. Howard, W. Zimmermann). The next international MTBio workshop will probably focus on developmental biology and evolution. Further MTBio activities shall improve university education in the field "Modelling and Theory in the Biosciences". Therefore, an initiative for a MTBio curriculum has been started.

(D) Consulting:

The Center for High Performance Computing (ZHR) offers its powerful computing facilities particularly for the solution of pretentious computing problems in the biosciences. Currently, there are four parallel computers with totally ca. 270 processors available. If you are interested to use these facilities you can take advantage of intensive support by the ZHR. Please email all enquiries to the contact address given below.

Contact: Andreas Deutsch, Center for High Performance Computing, Dresden University of Technology, Zellescher Weg 12, Willersbau A-103, D-01069 Dresden, Tel.: 0351-463-31943, Fax: 0351-463-37773, email: deutsch@zhr.tu-dresden.de

Junior Research Group "Theoretical Immunology"

Institute for Theoretical Biology, Humboldt University, Berlin, Germany

The Junior Research Group "Theoretical Immunology" has been established at the Institute for Theoretical Biology (ITB) of the Humboldt University of Berlin in March 2002, with Dr. Michal Or-Guil as the group leader. The Volkswagen Foundation funds the group. Other than the name suggests to many, this is not a funding agency for car and traffic research, but a private research-funding foundation, its support being available for projects in all disciplines (<http://www.volkswagenstiftung.de>).

What is Theoretical Immunology? The immune system consists of a huge number of different types of cells that communicate by cell-cell contact and through the release of proteins. Moreover, various types of molecules are able to tag and destroy pathogens. This sums up to an extremely complex, distributed system, which has to accomplish tasks like detecting the presence of pathogens and toxins, deciding how to fight them most effectively, remembering how to best fight a pathogen in case it appears again, and evolving towards more specialized immune responses during the life time of its owner.

Often, it is difficult to discern from experimental data what are the mechanisms governing the immune system's behaviour. In vivo measurement of changes in the number of cells and molecules do not give away how this changes are controlled. Very detailed knowledge from in vitro experiments, however, does not always lead to an understanding of how and why the found phenomena fit in into a larger picture. Even if one could

measure everything in vivo, observing every cell and grasping what it is up to in a given situation, this could result in far too much information for improving our understanding.

Theoretical Immunology sets itself the task of bridging this gap by using mathematical models and statistical data analysis to infer mechanisms and laws otherwise difficult to discern out of the large amount of some data and lack of other. In the ideal case, theoretical models will be formulated in such a way that notions won by the theoretical approach can be, in the aftermath, falsified or verified by further experimental findings.

With the aim of improving general knowledge on the subject, an Autumn School about "Theoretical Immunology" has been organized together with Prof. Hammerstein (ITB). Renowned speakers will give lectures during the School, which will take place on October 14-16, 2002.

(http://itb.biologie.hu-berlin.de/events/autumnschool_2002.html)

Despite of its name, the group "Theoretical Immunology" is not only committed to mathematical modelling and data analysis, but enrolled in experimental research as well. It pursues an interdisciplinary approach, its member's background ranging from physics to medical biotechnology.

The group's interests presently concentrate in three fields:

(i) Uncovering Cell Selection Mechanisms. The dynamical behaviour of B cells in tissues where selection occurs is being investigated by means of computer simulations and data analysis, as well as experimentally in cooperation with the Deutsches Rheuma-Forschungszentrum. The focus is laid on investigation of the selection mechanism of B-cells in germinal centers.

(ii) Statistical Analysis of Protein Binding Data. The aim of this project is to develop methods of characterization of protein binding properties and definition of features of sets of antibodies by means of simulations and analysis of protein binding data. This project is pursued in coop-

eration with the Charité in Berlin and the IGC in Portugal.

(iii) Parasitic Interference in the Host Immune System. Some parasitic nematodes suppress an effective immune response of the host by releasing certain cytokines. Non-parasitic nematodes, supposedly evolutionary older, release partly the same cytokines. We work to unveil the immune suppression strategy of the parasite and the evolutionary paths leading from non-parasitic to parasitic behaviour. This work is being accomplished within the scope of a joint project of ITB and Department of Molecular Parasitology within a newly founded Collaborative Research Center (SFB).

The group is hosted by the ITB. This institute is integrated into the biology department and the medical school (Charité) of the Humboldt University of Berlin. Research groups at the ITB focus on Molecular and Cellular Evolution, the Evolution of Organismic Systems, and Computational Neurobiology, hosting a further junior research group in Neural Computation and in future yet another one on Recurrently Coupled Networks of Spiking Neurons. A Collaborative Research Center "Theoretical Biology: Robustness, Modularity and Evolutionary Design of Living Systems" was established on July 2002, promoting Berlin into a national center for theoretical biology.

The ITB feels itself especially committed to teaching, offering courses in theoretical biology for biology and biophysics students. Already early in their studies, students are exposed to unifying theoretical concepts and learn how to apply mathematical methods in research work. For more advanced students, a variety of specialization courses is offered - including a course in Theoretical Immunology (Höfer, Or-Guil).

Interested in a Ph.D. position in the Theoretical Immunology Group? Please contact Michal Or-Guil, m.orguil@biologie.hu-berlin.de.

Junior Research Group "Theoretical Immunology", Institute for Theoretical Biology, Humboldt-University Berlin, Invalidenstr. 43, 10115 Berlin, Tel.: +49-30-2093 9105

Recent Theses

Essays on optimal foraging and the Allee effect

David Boukal, *Department of Mathematics, Faculty of Nuclear Sciences and Physical Engineering, Czech Technical University, Prague, March 2002*

The thesis investigates selected problems that link individual behaviour and population dynamics in the context of optimal foraging and sexual reproduction. The first part of the thesis (Chapters 2-5) deals with optimal foraging phenomena. It studies several simple predator-prey food webs consisting of at most two patches (Chapters 2, 4 and 5) and briefly addresses the role of increased habi-

tat heterogeneity (Chapter 3). Optimal foraging theory predicts abrupt changes in consumer behaviour which lead to discontinuities in the functional response. Population-dynamical models with optimal foraging behaviour can thus be described by ordinary differential equations (ODEs) whose right-hand sides are set-valued along a set of smooth manifolds of codimension equal to or larger than one. The models rely on selected results from the theory of differential inclusions and on the notion of Filippov solutions. Qualitative methods based on the use of Lyapunov functions or results of matrix theory are implemented for global qualitative analysis. It is

shown that optimal foraging may have profound effects on the system and entirely change predictions of models which ignore these behavioural traits. For example, it seems that exploitative competition of optimal foragers has not been previously studied except one case covered by Krivan and Sirot (American Naturalist, in press). The surprisingly complex behaviour of the "pure" Lotka-Volterra model (with linear growth and bilinear interaction terms) of exploitative competition of two optimally foraging predators in a two-patch environment (Chapter 5) includes, among other phenomena, large-amplitude limit cycles and apparently chaotic behaviour.

The second part of the thesis (Chapters 6-8) deals with the Allee effect. It reviews and enhances basic methodology in deterministic modelling of ecological dynamics of sexually reproducing populations. Apart from the standard approach that relies on ODEs and ordinary difference equations, spatially explicit individual-based models (IBM) are also used. Obtained results suggest that the Allee effect is closely linked to spatial phenomena. Chapter 6 provides a thorough review of known single-species, mainly deterministic models and proposes basic criteria (extinction-survival scenarios, shape of extinction boundary in male-female state space) for their assessment. Chapter 7 addresses the role of various mate search strategies using a spatially explicit IBM; it also touches the phenomenon of environmental sex determination, exemplified by the temperature-dependent sex determination of reptiles. Finally, Chapter 8 studies the role of pair formation in the Allee effect and emphasizes the link between various mathematical descriptions of the underlying demographic processes and the resulting population dynamics.

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

Boukal D.S., Krivan V. (1999), Journal of Mathematical Biology 39, 493-517;

Berec L., Boukal D.S., Berec M. (2001), American Naturalist 157, 217-230;

Boukal D.S., Berec L. (in press), Journal of Theoretical Biology.

Predictive microbiology of complex bacterial/ food systems: Analysis and synthesis of new modeling approaches

Els Dens, Department of Food and Microbial Technology, Katholieke Universiteit Leuven, December 2001

In this work, we contribute to the development of predictive models for complex bacterial/food systems. More specifically, (i) interactions between microorganisms, (ii) the influence of a solid food matrix and (iii) fluctuating environmental conditions are addressed. Hereby, emphasis lies on the analysis and synthesis of new modelling approaches. Two major modeling methodologies are identified.

In the continuous approach using (*partial*) differential equations, the evolution of a population of microorganisms is described by a macroscopic population variable like, e.g., biomass concentration or cell number. Therefore, these models are also denoted as *population models*.

In the discrete, *rule based* modelling approach, the evolution of a population of microorganisms is described on a microscopic level, e.g., by the superposition of the behavior of individual cells which grow, move, divide, die, ..., interacting with each other. The behavior of the microscopic entities (e.g., the cells) is described by a number of *rules*.

Both approaches are evaluated. More specifically, partial differential equations (i.e., a population model) are used to describe two species microbial interaction in a solid environment, while the individual based modeling approach (i.e., a rule based approach) is employed to describe microbial lag behavior in dynamic temperature conditions.

As a conclusion, we can state that the rule based modeling approach is particularly well-suited to incorporate (and learn about) the underlying mechanistic principles of microbial growth under various environmental conditions. The incorporation of mechanistic knowledge into the models is important with respect to the validity region of the models. This is of major importance in the domain of predictive microbiology, in which *per definition*, predictions on microbial evolution in different environmental conditions are made.

A disadvantage of microscopic, rule based models is, however, that their simulation can be computationally intensive. Also, they are largely non-analytic, which results in the fact that a large number of simulations may be necessary to determine the global behavior of the model. Therefore, it is advisable to eventually bring them back to a macroscopic population type model. The knowledge obtained from the implementation of the microscopic model can thereby serve as a guideline in the model-building process. In this way, models incorporating more mechanistic knowledge can be constructed in order to be more generally valid.

Striking the metapopulation balance: Mathematical Models & Methods Meet Metapopulation Management

Rampal S. Etienne, Wageningen University, The Netherlands, March 2002

There are two buzz words in nature management: fragmentation and connectivity. Not only (rail) roads, but also agricultural, residential and industrial areas fragment previously connected (or even continuous) habitat. Common sense tells us that the answer to habitat fragmentation is defragmentation and hence much effort is put into building corridors, of which fauna crossings are just one example. Corridors are conduits connecting two pieces of habitat through an environment of hostile non-habitat. Needless to say, there are good reasons for building corridors. Yet, there are some valid arguments against connecting everything. The risk of spreading of infectious diseases through these corridors is one of the most prominent arguments. The spread of the effects of (natural) catastrophes such as fire is another. But even when dismissing such negative effects of connectivity, there may be other mitigating measures which are much more efficient (and less expensive) than building corridors. The question whether this is the case and how al-

ternatives should be compared stimulated the work for this thesis.

Metapopulation theory seems the appropriate tool to answer these questions. A metapopulations is a collection of (local) populations, each of which runs a considerable risk of extinction, but can also be recolonized by dispersers from other populations. Through a balance of local extinctions and recolonization, the metapopulations can persist for a very long time although the local populations cannot. Using a stochastic patch occupancy metapopulations model, I was able to formulate the following rules of thumb: to optimize metapopulation extinction time, decreasing the risk of local extinction is preferable over increasing colonization probability and this should generally be done in the least extinction-prone patches; if changing local extinction risk is impossible, then increasing the colonization probability between the two least extinction-prone patches is most preferable. When extinction and colonization are related to patch size and interpatch distance by mechanistic submodels of the corresponding processes, the last two of these rules transform into: the preferred strategies to optimize the metapopulation extinction time and the basic reproduction number are, firstly, increasing the size of the largest patch (which is least extinction-prone) and, secondly, decreasing the effective interpatch distance between the two largest patches. These rules are less strongly supported than the rules in terms of extinction and colonization probabilities. And if absolute (instead of relative) increases in patch size are considered, the smallest patch should be increased. The reason for this is that in the mechanistic submodel for local extinction a large patch requires a large increase in size to substantially alter its local extinction probability. Since it is not a priori clear whether increases in patch sizes must be compared on an absolute or a relative basis, final conclusions cannot be drawn. We still need a socio-politico-economic study taking into account e.g. the costs of habitat creation in relation to the size of the patch to which habitat is added. We also require additional work on the important biological question how ecoducts and the like change the effective interpatch distance; this is usually merely hidden in the parameters. Although the answers are not final, at least more light has been shed on the range of possible final conclusions and, more importantly, the conditions under which they are valid.

Two chapters of my thesis deal with the questions above. I also looked into the problem whether it is better to have a few large or many small habitat patches. Furthermore, I studied several extensions of the simplest metapopulation model, the Levins model, and the influence of time-lags on metapopulation extinction time. The last part of the thesis deals with applications of stochastic patch occupancy models to real metapopulation. One is concerned with predicting the impact of reinstating an old railway track on two amphibian species, the other introduces a Bayesian approach to parameter estimation which is applied to a tree frog metapopulation.

Parts of the thesis were co-authored by Hans Heesterbeek (University of Utrecht, The Netherlands), Kees Nagelkerke (University of Amsterdam), Lia Hemerik and Marjolein Lof (Wageningen University), Claire Vos

(Alterra, Wageningen, The Netherlands), Michiel Jansen and Cajo ter Braak (Biometris, Wageningen, The Netherlands).

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On Weed Competition and Population Dynamics: Considerations for crop rotations and organic farming

Shana K. Mertens, *Wageningen Universiteit, The Netherlands, October 2002*

Experiments, monitoring studies and modelling of weed population dynamics were carried out to investigate potential methods for reducing weed populations in farming systems where herbicides are not applied (organic farming). Six years of monitoring weed populations on five organic farms showed that farmers who took a long-term approach to weed management had lower weed populations. Farms with low weed densities also had a lower diversity of weed species. An experiment was carried out to investigate whether using the combination of a wide row spacing and aggressive weed control (mechanical hoeing) or a narrow row spacing and less aggressive weed control (harrowing) would decrease weed populations more. Using weed seed production as the criterion for comparing the row spacing/weed control combinations, it was concluded that a narrow row spacing with less aggressive control resulted in fewer weed seeds being produced. Because the experiment involved marking individual plants of the species *Polygonum convolvulus*, *Polygonum persicaria*, and *Stellaria media*, it was possible to investigate how individual plant biomass and survival are related to descriptors of the local environment. In this case the descriptors were distance to the nearest crop plant and the local row width. For all three species it was shown that the same form of predictor gave the best fit and included distance to the nearest crop plant and the crop row spacing where the plant is located. Survival in the wide spacing could be predicted using the distance to the nearest crop row, while in the other row spacings all plants had an equal chance of survival. Predictors of individual plant biomass and survival can be used in modelling the spatial dynamics of weed populations. Finally the effect of crop sequence on weed population dynamics was investigated. Using a periodic matrix model, it was shown that the order of crops in a crop rotation will affect the weed population growth rate and its sensitivity to changes in underlying parameter values. It is stressed that research on weed ecology and non-herbicide management would benefit from long-term experiments and monitoring studies and a closer integration of modelling of weed population dynamics and long-term data.

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Stability of Complex Food Webs: pyramids of biomass, interaction strengths and the weight of trophic loops

Anje-Margriet Neutel, *Dep. of Environmental Sciences, Utrecht University, The Netherlands, May 2001*

Chapter 1 shows that patterns of interaction strengths in Jacobian “community” matrices derived from observations on real food webs are much more stable than those with “randomised” interaction strengths. The “randomised” systems are systems that have the same complexity (in the sense of diversity, connectance and average interaction strength (May 1972)) as the observed systems, that even have the same structure of positive and negative interaction strengths and the same set of paired positive and negative values, but where the pairs of interaction strengths are randomly exchanged (Yodzis 1981). We obtained the patterns of interaction strengths by assuming that our (average) observations on population sizes represent equilibrium states, assuming Lotka-Volterra dynamics to translate these equilibria in Jacobian community matrices.

Chapter 2 explains the stabilising effect of the patterns of interaction strengths. It shows that the incorporation of a “biomass pyramid” in food-web models gives that the longer loops in the food webs have relatively many weak links. This results in systems with a low maximum loop “weight”. It is this low maximum loop weight that enhances stability through enhancing “diagonal dominance” in the community matrix.

Chapter 3 analyses the relation between a biomass pyramid and food-web stability in more detail, and shows that the stronger the biomass decrease over trophic levels, the more stable the resulting system. It shows why a high degree of complexity or omnivory does not lead to instability in food webs with “strong” biomass pyramids.

Chapter 4 argues that the considerable decrease in biomass over trophic levels commonly observed in ecosystems is brought about by trophic-level dependent body sizes and conversion efficiencies. Conversion efficiencies imply that energy is lost in converting food into new biomass at each step along the food chain, so that less and less energy is available along the food chain. It is argued however that it is not enough to assume the existence of conversion efficiencies, but that the commonly observed trend of increasing body sizes and conversion efficiencies along the food chain contributes importantly to a decrease in biomass over trophic levels.

Chapter 5 returns to field observations and shows that in primary vegetation successions, below-ground complexity and food-chain length increases with developmental age. The average strengths of the interactions does not decrease with increasing complexity. Stability is strongly enhanced by the particular distribution of the interaction strengths among the trophic loops. The maximum weight of loops of length three and longer is found to correspond with food-web stability. The slope of the biomass pyramid in the bacterial “chain” in the food webs turns out to be a good indicator of food-web stability. The results identify properties of the “energetic” organisation

of trophic communities that explain differences in stability of the communities.

Chapter 6 describes earlier work on the global stability of detritus-decomposer food chains. By finding a Lyapunov function, we show that detritus-decomposer food chains can be asymptotically stable without assuming intraspecific interaction of the decomposer. The chapter deals with an aspect of food-web complexity that has been given relatively little attention in studies on food-web stability, and the results are of new interest in the light of the results of the other chapters of the thesis.

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Analysis and synthesis of mathematical algorithms for optimization and control of complex (bio)chemical conversion processes

Ilse Smets, *Department of Chemical Engineering, Katholieke Universiteit Leuven, Belgium*

Since research over the last decades has proven the superiority (with respect to performance and robustness) of *model based* process design, optimization and control strategies over *heuristic, experience based* approaches, this work concentrates on the development of adequate mathematical models in the context of (bio)chemical conversion processes. More specifically, an acceptable balance between accuracy with respect to the description of the biological and physicochemical phenomena on the one hand and mathematical simplicity, in terms of the number of process states and model parameters, on the other hand, has to be established.

To maintain as much mechanistic knowledge as possible, this work starts from a primary, *first principles* balance type model, the complexity of which is reduced afterwards to a level appropriate for model based design, optimization and control. Different complexity levels are considered, exemplified with representative case studies.

Model complexity related to the number of states is studied in the context of simulation, control and risk assessment of biological wastewater treatment systems. A *multi-model* type linearized version of the well-established Activated Sludge Model no. 1 for the bio-transformation processes in a carbon and nitrogen removing activated sludge plant is developed, enabling fast but still highly reliable simulations.

Model complexity related to the reaction kinetics is addressed in the framework of modelling, optimization and control of cell metabolism in response to external factors. On the one hand, a generic model reduction strategy based on sensitivity function analysis is presented to reduce the number of kinetics parameters. On the other hand, a broadly applicable feedback stabilizing controller is designed for fed-batch production processes exhibiting inhibition kinetics.

Model complexity related to the number of independent variables is discussed in the domain of chemical tubular reactor processes in which space dependency has to be taken into account explicitly. For a steady-state plug flow reactor, optimal jacket fluid temperature profiles are analytically derived.

By combining basic concepts from 1.) system theory, 2.) process modelling, identification and control, and 3.) (bio)chemical engineering, for all complexity levels considered in this work, generic and widely applicable complexity reduction, optimization and control strategies are developed.

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New Journals and Books

Handbook of Dynamical Systems, Volume 2

B. Fiedler (Eds.), *Freie Universität Berlin*

Elsevier 2002, hardbound, 1100 pages ISBN: 0-444-50168-1

Further details and an order form can be found at

<http://www.math.fu-berlin.de/~Dynamik/HoDS3TA/OrderForm.pdf>

Description:

This handbook is volume II in a series collecting mathematical state-of-the-art surveys in the field of dynamical systems. Much of this field has developed from interactions with other areas of science, and this volume shows how concepts of dynamical systems further the understanding of mathematical issues that arise in applications. Although modeling issues are addressed, the central theme is the mathematically rigorous investigation of the resulting differential equations and their dynamic behavior. However, the authors and editors have made an effort to ensure readability on a non-technical level for mathematicians from other fields and for other scientists and engineers.

The eighteen surveys collected here do not aspire to encyclopedic completeness, but present selected paradigms. The surveys are grouped into those emphasizing finite-dimensional methods, numerics, topological methods, and partial differential equations. Application areas include the dynamics of neural networks, fluid flows, nonlinear optics, and many others. While the survey articles can be read independently, they deeply share recurrent themes from dynamical systems. Attractors, bifurcations, center manifolds, dimension reduction, ergodicity, homoclinicity, hyperbolicity, invariant and inertial manifolds, normal forms, recurrence, shift dynamics, stability, to name just a few, are ubiquitous dynamical concepts throughout the articles.

Audience: Departments of physics, chemistry, engineering, biology, mathematics and applied mathematics.

Contents:

A. Finite-Dimensional Methods: 1. Mechanisms of phase-locking and frequency control in pairs of coupled neural oscillators (N. Kopell, G.B. Ermentrout). 2. Invariant manifolds and Lagrangian dynamics in the ocean and atmosphere (C. Jones, S. Winkler). 3. Geometric singular perturbation analysis of neuronal dynamics (J.E. Rubin, D. Terman).

B. Numerics 4. Numerical continuation, and computation of normal forms (W.-J. Beyn, A. Champneys, E. Doedel, W. Govaerts, Y.A. Kuznetsov, B. Sandstede). 5. Set oriented numerical methods for dynamical systems (M. Dellnitz, O. Junge). 6. Numerics and exponential smallness (V. Gelfreich). 7. Shadowability of chaotic dynamical systems (C. Grebogi, L. Poon, T. Sauer, J.A. Yorke, D. Auerbach). 8. Numerical analysis of dynamical systems (J. Guckenheimer).

C. Topological Methods 9. Conley index (K. Mischaikow, M. Mrozek). 10. Functional differential equations (R.D. Nussbaum).

D. Partial Differential Equations 11. Navier-Stokes equations and dynamical systems (C. Bardos, B. Nicolaenko). 12. The nonlinear Schrödinger equation as both a PDE and a dynamical system (D. Cai, D.W. McLaughlin, K.T.R. McLaughlin). 13. Pattern formation in gradient systems (P.C. Fife). 14. Blow-up in nonlinear heat equations from the dynamical systems point of view (M. Fila, H. Matano). 15. The Ginzburg-Landau equation in its role as a modulation equation (A. Mielke). 16. Parabolic equations: asymptotic behavior and dynamics on invariant manifolds (P. Poláčik). 17. Global attractors in partial differential equations (G. Raugel). 18. Stability of travelling waves (B. Sandstede).

Reading Hoffmeyer, Rethinking Biology

Claus Emmeche, Kalevi Kull, Frederik Stjernfelt

Tartu University Press, 2002, ISBN 9985-56-632-7, 79 pp., USD 8.00.

This book is about biosemiotics — a paradigm for both biological and semiotic thinking — as approached by Tartu-Copenhagen group in the field. Intended as a *Festschrift* for a Danish biosemiotician Jesper Hoffmeyer, this book provides also a brief introduction to semiotic biology. The approach embraces all processes that take place in animate nature at whatever level, from single cell to ecosystem, as concerned with the sign aspects of the process of life itself. It is a scientific study of signs and semiosis in living systems, or synonymically, a study of living systems as sign systems. In the chapter *A biosemiotic building: 13 theses*, the authors formulate the biosemiotic approach in the form of 13 statements. Includes a glossary of terms and list of Hoffmeyer's publications.

Adaptive Dynamics of Infectious Diseases: in pursuit of virulence management

U. Dieckmann, *IIASA*, **J.A.J. Metz**, *University of Leiden*, **M.W. Sabelis**, *University of Amsterdam*, **K. Sigmund**, *University of Vienna*, (Eds.)

Cambridge University Press, 2002, xviii + 532p., ISBN 0-521-78165-5, hardback £ 50

There was a time period, almost half a decade ago, in which man considered infectious diseases problems that were well on the way of being overcome. Since then, and particularly in recent decades, this belief has proved, both for humans and animals (wild and farmed), a false one. Important existing agents have gained potency and managed to make a comeback despite control measures (e.g. malaria), finding ways to resist current drugs and treatments (many bacteria), or proved much more persistent than originally thought (notably viruses). In addition, many "new" infectious agents have emerged (for example making the jump to new species of host, including humans; think of HIV and diseases caused by prions). Agents also appear in geographic locations where they were not present before (e.g. due to increased travel and commerce) or in environments to which they were previously not adapted (e.g. due to global warming). Infectious diseases are once again a major (and increasing) threat for human, animal and plant populations. The study of the genetics, pathology, epidemiology, prevention, cure and control has become a large scientific multidisciplinary undertaking. Of particular interest for increasing our understanding of the past, present and future spread and potency of infectious agents, is the link between genetics, epidemiology and evolution. The evolution and possible management of virulence is an important topic in understanding why agents are posing an increased threat and how virulence and changes in virulence interact with control measures, factors relating to the host and (changes in) the environment. That, and particularly the contributions that theoretical considerations and mathematical modeling can make, is the subject matter of the book edited by Dieckmann, Metz, Sabelis and Sigmund.

This is the second volume in the new series on Adaptive Dynamics, presented by Cambridge University Press and the International Institute for Applied Systems Analysis (IIASA) in Laxenburg, Austria. The first book was called *The Geometry of Ecological Interactions: simplifying spatial complexity*, edited by Ulf Dieckmann, Richard Law and Hans (J.A.J.) Metz (for a review see issue nr. 3 of these Communications). The fruitful principle by which the new book came about is much the same as for the first volume. The Adaptive Dynamics Network of IIASA organized a series of meetings, inviting many of the world's experts on the topic of virulence and its evolution. The experts are asked to write an overview of their area of expertise and then the editors set out to create a coherent, carefully structured text (with commendable uniform notation for all chapters), that is both an overview of the state-of-the-art and a detailed introduction to the field. As in the first volume of the series, the effort that the editors have clearly put into this book (chapters in harmony with each other, an integrated

whole, important concepts and techniques are explained in boxes throughout), more than pays off.

The 30+ chapters are divided into seven parts: Setting the stage Host population structure; Within-host interactions; Pathogen-host coevolution; Multilevel selection; Vaccines and drugs; Perspectives for virulence management. These aspects are all treated for a wide range of hosts (humans, wild life species, insects, farmed animals, plants) and a wide range of pathogens. A thorough index and a very extensive reference section complete the book. Listing these part-titles alone certainly does no justice to the book. There are so many interesting, well-written and valuable chapters here, by so many recognized experts that a complete listing would be called for. I therefore urge the reader to view the full list on the IIASA web-site: www.iiasa.ac.at/Admin/INF/recent-pubs/adn/diseases.html

This volume is not to be missed by anyone interested in the evolution of virulence, theoretical epidemiology, and the management of infectious diseases. It is, in addition, an ideal introduction for advanced students (and professional scientists) wishing to learn mathematical modeling for evolutionary questions in general and for infectious diseases in particular.

Hans Heesterbeek, University of Utrecht

Biological Evolution and Statistical Physics

Lässig, M., *Universität zu Köln*, **Valleriani, A.**, *Max-Planck-Institute for Colloids and Interfaces* (Eds.)

Springer-Verlag, 2002. XI + 337 pp. Hardcover, ISBN 3-540-43188-8, EUR 72,95

"This set of lecture notes gives an account of an aspect of the living world that can be called biological information. The book aims to present both a pedagogical and state-of-the art roadmap of this rapidly evolving area and deals with the range of the field, from information that is encoded in the molecular genetic code to the description of large-scale evolution of complex species networks.

From the contents: Statistical Significance and Extremal Ensemble of Gapped Local Hybrid Alignment.- On the Design of Optimization Criteria for Multiple Sequence Alignment.- Red Queen Dynamics and the Evolution of Translational Redundancy.- A Testable Genotype-Phenotype Map: Modeling Evolution of RNA Molecules.- Evolutionary Perspectives on Protein Structure, Stability, and Functionality.- The Statistical Approach to Molecular Phylogeny: Evidence for a Nonhyperthermophilic Common Ancestor.- Principles of Cophylogenetic Maps.- Accounting for Phylogenetic Uncertainty in Comparative Studies of Evolution and Adaptation.- The "Shape" of Phylogenies Under Simple Random Speciation Models.- Fitness Landscapes.- Tempo and Mode in Quasispecies Evolution.- Multilevel Processes in Evolution and Development.- Evolutionary Strategies for Solving Optimization Problems.- Review of Biological Ageing on the Computer.- Spatio-Temporal Modes of Speciation."

Self-Organization in Biological Systems

Scott Camazine, *Pennsylvania State University*, **Jean-Louis Deneubourg**, *Université Libre de Bruxelles*,

Nigel R. Franks, *University of Bristol*, **James Sneyd**, *Massey University*, **Guy Theraulaz**, *Paul Sabatier University* and **Eric Bonabeau**, *EuroBios*

Princeton University Press, 2001, 535p., \$65.00 / £45.00, ISBN: 0-691-01211-3

“The synchronized flashing of fireflies at night. The spiralling patterns of an aggregating slime mold. The anastomosing network of army-ant trails. The coordinated movements of a school of fish. Researchers are finding in such patterns--phenomena that have fascinated naturalists for centuries--a fertile new approach to understanding biological systems: the study of self-organization. This book, a primer on self-organization in biological systems for students and other enthusiasts, introduces readers to the basic concepts and tools for studying self-organization and then examines numerous examples of self-organization in the natural world. Self-organization refers to diverse pattern formation processes in the physical and biological world, from sand grains assembling into rippled dunes to cells combining to create highly structured tissues to individual insects working to create sophisticated societies. What these diverse systems hold in common is the proximate means by which they acquire order and structure. In self-organizing systems, pattern at the global level emerges solely from interactions among lower-level components. Remarkably, even very complex structures result from the iteration of surprisingly simple behaviors performed by individuals relying on only local information. This striking conclusion suggests important lines of inquiry: To what degree is environmental rather than individual complexity responsible for group complexity? To what extent have widely differing organisms adopted similar, convergent strategies of pattern formation? How, specifically, has natural selection determined the rules governing interactions within biological systems? This book is an introduction to self-organization and complexity in biology--a field of study at the forefront of life sciences research.”

The Functional Consequences of Biodiversity: Empirical Progress and Theoretical Extensions

Ann P. Kinzig, *Aizona State University*, **Stephen Pacala**, *Princeton University*, and **G. David Tilman**, *University of Minnesota*

Princeton University Press, 2002, 392p., ISBN: 0-691-08822-5, paper: \$29.95 / £19.95, ISBN: 0-691-08821-7, Cloth, \$75.00 / £52.00

“Does biodiversity influence how ecosystems function? Might diversity loss affect the ability of ecosystems to deliver services of benefit to humankind? Ecosystems provide food, fuel, fiber, and drinkable water, regulate local and regional climate, and recycle needed nutrients, among other things. An ecosystem's ability to sustain functioning may depend on the number of species residing in the ecosystem--its biological diversity--but this has been a controversial hypothesis. There are many unanswered questions about how and why changes in biodiversity could alter ecosystem functioning. This volume synthesizes empirical studies on the relationship between biodiversity and ecosystem functioning and extends that

knowledge using a novel and coordinated set of models and theoretical approaches.

These experimental and theoretical analyses demonstrate that functioning usually increases with biodiversity, but also reveals when and under what circumstances other relationships between biodiversity and ecosystem functioning might occur. It also accounts for apparent changes in diversity-functioning relationships that emerge over time in disturbed ecosystems, thereby addressing a major controversy in the field. The volume concludes with a blueprint for moving beyond small-scale studies to regional ones. In addition to the editors, the contributors are Juan Armesto, Claudia Neuhauser, Andy Hector, Clarence Lehman, Peter Kareiva, Sharon Lawler, Peter Chesson, Teri Balsler, Mary K. Firestone, Robert Holt, Michel Loreau, Johannes Knops, David Wedin, Peter Reich, Shahid Naeem, Bernhard Schmid, Jasmin Joshi, and Felix Schläpfer.”

Computational Cell Biology

Fall, C.P., *University of New York*, **Marland, E.S.**, *Appalachian State University*, **Wagner, J.M.**, *University of Connecticut Health Center*, **Tyson, J.J.**, *Virginia Polytechnic Institute & State University* (Eds.)

Springer-Verlag, 2002. XX + 468 p., Hardcover, ISBN 0-387-95369-8, EUR 64,95.

“This textbook provides an introduction to dynamic modelling in molecular cell biology, taking a computational and intuitive approach. Selected biological examples are used to motivate concepts and techniques used in computational cell biology through a progression of increasingly more complex cellular functions modelled with increasingly complex mathematical and computational techniques. Detailed illustrations, examples, and exercises are included throughout the text. Appendices containing mathematical and computational techniques are provided as a reference tool.

Contents: Preface; Dynamic Phenomena in Cells; Voltage Gated Ionic Currents; Transporters and Pumps; Reduction of Scale; Whole Cell Models; Intercellular Communication; Spatial Modeling; Modeling Intracellular Calcium Waves and Sparks; Biochemical Oscillations; Cell Cycle Controls; Modeling the Stochastic Gating of Ion Channels; Molecular Motors: Theory; Molecular Motors: Examples; Appendices.”

Mathematical Biology

Murray, J.D., *University of Washington, Seattle*

Springer-Verlag, 3rd ed. 2002. XXIII + 551 p., Hardcover, ISBN 0-387-95223-3, EUR 44,95.

“It has been over a decade since the release of the now classic original edition of Murray's *Mathematical Biology*. Since then mathematical biology has grown at an astonishing rate and is well established as a distinct discipline. Mathematical modelling is now being applied in every major discipline in the biomedical sciences. Though the field has become increasingly large and specialized, this book remains important as a text that introduces some of the exciting problems that arise in biology and gives some indication of the wide spectrum of questions that modelling can address. Due to the tremendous

development in the field this book is being published in two volumes. This first volume is an introduction to the field, the mathematics mainly involves ordinary differential equations that are suitable for undergraduate and graduate courses at different levels. For this new edition Murray is covering certain items in depth, giving new applications such as modelling marital interactions and temperature dependence sex determination.

Contents: Continuous Population Models for Single Species.- Discrete Population Models for a Single Species.- Models for Interacting Populations.- Temperature-Dependent Sex Determination (TSD): Crocodilian Survivorship.- Modelling the Dynamics of Marital Interaction: Divorce Prediction and Marriage Repair.- Reaction Kinetics.- Biological Oscillators and Switches.- BZ Oscillating Reactions.- Perturbed and Coupled Oscillators and Black Holes.- Dynamics of Infectious Diseases: Epidemic Models and AIDS.- Reaction Diffusion, Chemotaxis, and Non-local Mechanisms.- Oscillator Generated Wave Phenomena and Central Pattern Generators.- Biological Waves: Single Species Models.- Use and Abuse of Fractals.”

Neuroscience: A Mathematical Primer

Scott, A., *University of Arizona*

Springer-Verlag, 2002. XX + 352 p., Hardcover, ISBN 0-387-95403-1, EUR 109,00

“This is an introductory text of mathematical neuroscience intended for anyone who wants to appreciate the role that mathematics and mathematical modelling and analysis can do to aid an understanding of how the brain works and the nature of the mind. For this purpose, the book is designed as a text with problems at the end of each chapter. It is expected that this text will be interesting for mathematics faculty teaching in neuroscience programs. It also aims to serve as a general introduction to neuro-mathematics in neuroscience programs at both undergraduate and graduate levels. Mathematical formulations in neuroscience are of five sorts: (i) Exact descriptions of well understood dynamic processes, like the Hodgkin-Huxley theory of the nerve impulse. (ii) Metaphorical descriptions of more complex phenomena, like the stationary states of a Hopfield model. (iii) Information theory for dealing with the storage and transmission of data. (iv) Logical calculus (Boolean algebra) for the analysis of information processing systems. (v) Number theory for counting large numbers of possibilities. (vi) Statistical tools for organizing and evaluating data.

Contents: A Short History of Neuroscience.- Structure of a Neuron.- Nerve Membranes.- The Hodgkin-Huxley (H-H) Axon.- Leading Edge Models.- Recovery Models.- Myelinated Nerves.- Ephatic Interactions Among Neurons.- Neural Modeling.- Constructive Brain Theories.- Neuronal Assemblies.- The Hierarchical Nature of Brain Dynamics.”

Computational Methods for Macromolecules: Challenges and Applications

Schlick, T., *New York University*, **Gan, H.H.**, *New York University* (Eds.)

Springer-Verlag, 2002. IX + 504 p., Softcover, ISBN 3-540-43756-8. EUR 79,95.

“This special volume collects invited articles by participants of the Third International Workshop on Methods for Macromolecular Modeling, Courant Institute of Mathematical Sciences, Oct. 12-14, 2000. Developers of methods for biomolecular simulations review advances in Monte Carlo and molecular dynamics methods, free energy computational methods, fast electrostatics (particle-mesh Ewald and fast multipole methods), mathematics, and molecular neurobiology, nucleic acid simulations, enzyme reactions, and other essential applications in biomolecular simulations. A Perspectives article by the editors assesses the directions and impact of macromolecular modeling research, including genomics and proteomics.”

Molecular Modeling and Simulation

Tamar Schlick, *New York University*

Springer-Verlag, 2002, 656 pages, hardcover, ISBN: 0-387-95404-X, \$79.95

“This book evolved from an interdisciplinary graduate course entitled Molecular Modeling developed at New York University. Its primary goal is to stimulate excitement for molecular modelling research while introducing readers to the wide range of biomolecular problems being solved by computational techniques and to those computational tools. The book is intended for beginning graduate students in medical schools and scientific fields such as biology, chemistry, physics, mathematics, and computer science.

The book surveys three broad areas: biomolecular structure and modelling: current problems and state of computations; molecular mechanics: force field origin, composition, and evaluation techniques; and simulation methods: geometry optimization, Monte Carlo, and molecular dynamics approaches. Appendices featuring homework assignments, reading lists, and other information useful for teaching molecular modelling complement the material in the main text. Extensive use of world wide web resources is encouraged, and additional course and text information may be found on a supplementary website.”

An Introduction to Mathematical Modeling in Physiology, Cell Biology, and Immunology

James Sneyd, *Massey University*

American Mathematical Society, December 2002, 192 p., hardcover, ISBN: 0-8218-2816-9, \$49.

“In many respects, biology is the new frontier for applied mathematicians. This book demonstrates the important role mathematics plays in the study of some biological problems. It introduces mathematicians to the biological sciences and provides enough mathematics for bioscientists to appreciate the utility of the modelling approach. The book presents a number of diverse topics,

such as neurophysiology, cell biology, immunology, and human genetics. It examines how research is done, what mathematics is used, what the outstanding questions are, and how to enter the field. Also given is a brief historical survey of each topic, putting current research into perspective.

Contents: D. Terman -- Dynamics of singularly perturbed neuronal networks; D. Tranchina -- Mathematics in visual neuroscience: The retina; J. P. Keener -- Arrhythmias by dimension; J. Sneyd -- Calcium excitability; K. Lange and B. Redelings -- Disease gene dynamics in a population isolate; A. S. Perelson and P. W. Nelson -- Modeling viral infections; Index."

Chaos in Ecology

J.M. Cushing, Robert F. Costantino, Brian Dennis, Robert Desharnais, Shandelle Marie Henson

Academic press, September 2002, ISBN 0121988767, \$65

"It is impossible to predict the exact behaviour of all biological systems and how these same systems are exemplified by patterns of complexity and regularity. Decades of research in ecology have documented how these sorts of patterns are the consequences of deceptively simple rules that determine the nature of the patterns created. Chaos in Ecology aims to explain how simple beginnings result in complicated results.

Contents: Introduction. Models. Bifurcations. Chaos. Patterns in Chaos. What We Learned. Bibliography. Appendix."

The Application of Mathematics to the Sciences of Nature Critical Moments and Aspects

Claudio Pellegrini, University of California, Paola Cerrai, University of Pisa, Paolo Freguglia, Università de L'Aquila (eds.)

Kluwer Academic/Plenum Publishers, Hardbound, ISBN 0-306-46694-5, 2002, 300 pp., EUR 161.00 / USD 125.00 / GBP 87.50

"Contents: Preface. Physics. Quantum Probability and the Interpretation of Quantum Mechanics: A Crucial Experiment; L. Accardi, M. Regoli. An Optical Geometric Model of the Betatron Motion; A. Bazzani, P. Freguglia. Some Remarks on the Theory of Relativity and the Naïve Realism; V. Benci. Pattern Induced by Parameter Modulation in Spatiotemporal Chaos; L. Fronzoni. Chaos and Orbit Complexity; S. Galatolo. On the Riemann-Mangoldt Constant; D. Merlini, L. Rusconi. Long-Term Stability in Circular Accelerators; W. Scandale. Mathematical Models in Beam Dynamics; G. Turchetti. Biology. An Axiomatic Approach to Some Biological Themes; M. Forti, et al. A Proposal for an Axiomatic Theory of the Evolutionary Darwinian Ideas; P. Freguglia. Fractal Complexity of Membrane Structures in Normal and Neoplastic Cells; G.A. Losa. The Arc, an Unexpected and Still Not Explained Element of the Tracks of Creeping Ciliates; N. Ricci, et al. Natural Population and Community Structure and Dynamics: The 'Supply-Side Ecology', Theory and the Field Data; G. Santangelo. History of Science. The History of Theoretical Population Ecology. Which Role for Mathematical Modeling? L.

Andreozzi. The Mathematics Implied in the Laws of Nature and Realism, or the Role of Functions Around 1750; J. Dhombres. Geometry, the Calculus and the Use of Limits in Newton's Principia; N. Guicciardini. The Two Faces of Mathematical Modeling: Objectivism vs. Subjectivism, Simplicity vs. Complexity; G. Israel. The Search for the Mathematization of the Social Disciplines; S. Menteiro. Mathematization of the Science of Motion and the Birth of Analytical Mechanics. A Historical Note; M. Panza. Models, Analogies, and Statistical Reason, 1760-1900; T. Porter. Is Music Relevant for the History of Science; T. Tonietti."

Differential Equations and Mathematical Biology

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

Chapman & Hall/CRC, March 2003, 556 p., ISBN 1584882964, \$79.95.

"The conjoining of mathematics and biology has brought about significant advances in both areas, with mathematics providing a tool for modelling and understanding biological phenomena and biology stimulating developments in the theory of nonlinear differential equations. The continued application of mathematics to biology holds great promise and in fact may be the applied mathematics of the 21st century. Differential Equations and Mathematical Biology provides a detailed treatment of both ordinary and partial differential equations, techniques for their solution, and their use in a variety of biological applications. The presentation includes the fundamental techniques of nonlinear differential equations, bifurcation theory, and the impact of chaos on discrete time biological modelling. The authors also cover numerical techniques and address a range of applications, including heart physiology, nerve pulse transmission, chemical reactions, tumour growth, and epidemics."

Modelling Differential Equations in Biology

Clifford Henry Taubes, Harvard University

Prentice Hall, 2001, 479p., ISBN 0-13-017325-8, \$89.33.

"Designed for students who understand the simple basics of calculus, this text focuses on the differential equations and related subjects that are commonly used today by working life scientists. It emphasizes both the mathematics and how the mathematics is employed in order to introduce some potentially useful tools and modes of thought to future experimental biologists."

Mathematical Models of Crop Growth and Yield

Allen R. Overman, University of Florida, Gainesville, Richard V. Scholtz

Marcel Dekker, 2002, 344p., ISBN 0-8247-0825-3, \$150.

"This book describes the application of viable mathematical models in data analysis to increase crop growth and yields—highlighting effective, analytical functions that have been found useful for the comparison of alternative management techniques to *maximize water and*

nutrient resources. Features solutions to various differential equations and considers different characteristics of the functions related to the phenomenological growth model.

Contents: Introduction, Seasonal Response Models, Growth Response Models, Mathematical Characteristics of Models, Pasture Systems, Nonlinear Regression for Mathematical Models; Index."

The Unified Neutral Theory of Biodiversity and Biogeography

Stephen P. Hubbell, *Smithsonian Tropical Research Institute*

Princeton University Press, 2001, 448p., ISBN: 0-691-02128-7, Paper, \$35.00 / £24.95

"In this book, Stephen Hubbell develops a formal mathematical theory that aims to unify biogeography (the study of the geographic distribution of species) and biodiversity (the study of species richness and relative species abundance). When a speciation process is incorporated into Robert H. MacArthur and Edward O. Wilson's now classical theory of island biogeography, the generalized theory predicts the existence of a universal, dimensionless biodiversity number. In the theory, this fundamental biodiversity number, together with the migration or dispersal rate, completely determines the steady-state distribution of species richness and relative species abundance on local to large geographic spatial scales and short-term to evolutionary time scales. Although neutral, Hubbell's theory is nevertheless able to generate many quantitative predictions about biodiversity and biogeography.

Contents: MacArthur and Wilson's Radical Theory; On Current Theories of Relative Species Abundance; Dynamical Models of the Relative Abundance of Species; Local Community Dynamics under Ecological Drift, Metacommunity Dynamics and the Unified Theory, The Unified Theory and Dynamical Species-Area Relationships, Metapopulations and Biodiversity on the Metacommunity Landscape, Speciation, Phylogeny, and the Evolution of Metacommunity Biodiversity, Sampling, Parameter Estimation, and the Generality of the Unified Theory, Reconciling Dispersal-Assembly and Niche-Assembly Theories."

Biophysics

Roland Glaser, *Humboldt-University*

Springer-Verlag, 2001, 361p., ISBN 3-540-67088-2 Hardcover, EUR 45,95.

"The message of this book is that biophysics is the science of physical principles underlying the "phenomenon life" on all levels of organization. Rather than teaching "physics for biologists" or "physical methods applied to biology", it regards its subject as a defined discipline with its own network of ideas and approaches. The book starts by explaining molecular structures of biological systems, various kinds of atomic, molecular and ionic interactions, movements, energy transfer, self organization of supramolecular structures and dynamic properties of biological membranes. It then goes on to introduce the

biological organism as a non-equilibrium system, before treating thermodynamic concepts of osmotic and electrolyte equilibria as well as currents and potential profiles. It continues with topics of environmental biophysics and such medical aspects as the influence of electromagnetic fields or radiation on living systems and the biophysics of hearing and noise protection. The book concludes with a discussion of system analyses, including models of neural processes as well as of ecological interactions, growth, differentiation and evolution."

Biological Thermodynamics

Donald T. Haynie, *Louisiana Tech University*

Cambridge University Press, 2001, 396 p., ISBN: 0521795494, paperback, £22.95

"Biological Thermodynamics provides an introduction to the study of energy transformations for students of the biological sciences. The emphasis is on understanding basic concepts and developing problem-solving skills throughout the text, but mathematical complexity is kept to a minimum. Each chapter comprises numerous examples taken from different areas of biochemistry, as well as extensive exercises to aid understanding. Topics covered include energy and its transformation, the First Law of Thermodynamics, the Second Law of Thermodynamics, Gibbs Free Energy, statistical thermodynamics, binding equilibria and reaction kinetics, concluding with a survey of the most exciting areas of biological thermodynamics today, particularly the origin of life on h."

Datenanalyse in der Biologie

M. T. Hütt, *Technische Universität Darmstadt*

Springer, 2001, 312 p, ISBN 3-540-42311-7

"Datenanalyse geht heute weit über einfache Mittelwerte, Varianzen und Signifikanztests hinaus. Ein großer Teil der experimentellen Untersuchungen erfordert mittlerweile die Verwendung von neueren Methoden der Datenanalyse oder sogar den Entwurf einer speziellen Analysestrategie, z.B. die Interpretation von DNA-Sequenzen, von Musterbildungsprozessen und der Dynamik von Ionenkanälen. Der mathematische Aufwand hinter diesen Methoden ist recht hoch, so dass ihr Erlernen aus den bestehenden Lehrbüchern und Veröffentlichungen sich als äußerst schwierig erweist. Diese Kluft schließt das vorliegende Buch. Besonders bemerkenswerte und elegante Analysestrategien aus der Forschungsliteratur der letzten zehn Jahre werden beispielhaft besprochen. Drei wesentlichen Techniken der fortgeschrittenen Datenanalyse sind ausführliche Einzelkapitel gewidmet: nichtlineare Zeitreihenanalyse, Methoden der fraktalen Geometrie, Analyse von Daten mit raumzeitlicher Dynamik.

Inhalt: Mathematische Grundlagen. Grundbegriffe der nichtlinearen Dynamik. Zelluläre Automaten. Elemente der nichtlinearen Zeitreihenanalyse. Analyse raumzeitlicher Strukturen. Selbstähnlichkeit und fraktale Geometrie. Methoden aus der Informationstheorie. Software-Pakete und Internet-Datenbanken. Weiführende Literatur. Übungsaufgaben.

Forthcoming Events

Department of Theoretical Biology, Institute of Entomology Autumn School: Theoretical Immunology *Berlin, Germany, October 14-16, 2002*

The immune system protects us from potentially infectious agents and our own malignant cells. It is made up of a variety of organs, cells, and molecules distributed throughout the body. Cell-cell, cell-molecule and molecule-molecule interactions are crucial for the functioning of the immune response, resulting in a highly complex dynamical system. The task of theoretical immunology is to unveil principles and mechanisms by which the immune system works, and why it can sometimes be defeated, using mathematical modeling and data analysis as its main tools. The lecture series will start with an introduction to the cells and molecules in the immune system and its basic biological features, leading then into the most up-to-date examples of the theory of modeling immunological problems.

Lecturers are Alan Perelson, (Los Alamos National Laboratory), Rob de Boer, (University of Utrecht), Lee Segel (The Weizmann Institute of Science)

For registration, send an e-mail with your name and address to Dr. Michal Or-Guil (m.orguil@biologie.hu-berlin.de) before October 1. The registration fee is 25 Euro and for students 13 Euro.

Information:

http://itb.biologie.hu-berlin.de/events/autumnschool_2002.html

4th Asia-Pacific Conference on Simulated Evolution And Learning (SEAL'02)

9th International Conference on Neural Information Processing (ICONIP'02)

International Conference on Fuzzy Systems and Knowledge Discovery (FSKD'02)

November 18 - 22, 2002, Orchid Country Club, Singapore

SEAL'02, ICONIP'02, and FSKD'02 will be jointly held in Orchid Country Club, Singapore from November 18 to 22, 2002. The conferences will not only feature the most up-to-date research results in evolutionary computation, neural information processing, fuzzy systems, and knowledge discovery, but also promote cross-fertilization over these exciting and yet closely-related areas.

Topics of Interest

SEAL'02:

Theory: Co-evolution, Coding methods, Collective behavior. *Methodology:* Evolution strategies, Genetic algorithms, Genetic programming, Molecular and quantum computing, Evolvable hardware, Multi-objective optimization, Ant colony, Artificial ecology. *Evolutionary learning:* Artificial life, Bayesian evolutionary algorithms. *Hybrid Systems:* Evolutionary neuro-fuzzy sys-

tems, Soft computing. *Applications:* Scheduling, Operations research, Design, etc

ICONIP'02:

Artificial neural models: Learning algorithms, Neural modeling and architectures, Neurodynamics. *Natural neural systems:* Neuroscience, Neurobiology, Neurophysiology, Brain imaging, Learning and memory. *Cognitive science:* Perception, emotion, and cognition, Selective attention, Vision and auditory models. *Hardware implementation:* Artificial retina & cochlear chips. *Hybrid systems:* Neuro-fuzzy systems, Evolutionary neural nets, etc. *Applications:* Bioinformatics, Finance, Manufacturing, etc.

FSKD'02:

Theory and foundations: Fuzzy theory and models, Uncertainty management, Statistical & probabilistic data mining, Computing with words, Rough sets, Intelligent agents. *Methods and algorithms:* Classification, Clustering, Information retrieval & fusion, Data warehousing & OLAP, Fuzzy hardware, Visualization, Decision trees, Data preprocessing. *Hybrid systems:* Evolutionary neuro-fuzzy systems, Soft computing. *Applications:* Control, Optimization, Natural language processing, Forecasting, Human-computer interaction, etc.

web page.

Keynote Speakers

Shun-ichi Amari, RIKEN Brain Science Institute, Japan

David Fogel, Natural Selection, Inc., USA

Mitsuo Kawato, ATR, Japan

Xin Yao, The University of Birmingham, UK

Lotfi A. Zadeh, University of California, USA

Information:

Home Page: <http://www.ntu.edu.sg/home/nef>

Mirror Page: <http://www.cic.unb.br/~weingang/nef>

Mathematical and Numerical Methods for Modeling in the Life Sciences

November 28 - 29, 2002, University of Gent, Belgium

"Mathematical and Numerical methods for modelling in the life sciences" is organized by the Flemish Research Community "Advanced numerical methods for mathematical modelling" at the University of Gent, Belgium. Organizers are E. Dick (Fluid Mechanics Laboratory, University of Gent), W. Govaerts (Applied Mathematics and Computer Science, University of Gent) and D. Roose (Computer Science Department, University of Leuven, Belgium).

More complete information and details on participation and registration can be found at

<http://allserv.rug.ac.be/~ajdhooge/workshop.html>

Alcala 2nd International Conference on Mathematical Ecology

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

Mathematical Ecology originated in the work of Vito Volterra, although some would date its origins even earlier with Fibonacci's counts. Nowadays it has developed into a vast segment of ecology and has considerably broadened its scope, using mathematical techniques as varied as fractals or stochastic differential equations. It has also evolved towards computer implementation, which is now growing as a separate body but which we believe should still attract the interest of mathematicians. The conference will feature recent advances in mathematical ecology, using new but also classical approaches, in a variety of topics including (but not limited to) the following: population ecology, behavioral ecology, ecotoxicology, evolutionary dynamics, management of living resources, population grouping, spatial aspects of ecology, stochastic models in ecology, individual based models, multiple scaling, etc.. Proposals for organizing sessions on these topics or other related ones are encouraged.

The 2nd AICME is a follow-up of the 1st one, which was held in September 1998 in Alcalá de Henares; attended by more than 200 participants, it gave rise to special issues in four journals: Ecological Modelling, Nonlinear Analysis R.W.A., Mathematical Biosciences and Natural Resource Modeling

(http://www2.uah.es/matema/Aicme/inst_proceedings.htm)

Scientific committee: R. Arditi (U. Paris-Sud XI, France), P. Auger (U. Claude Bernard Lyon 1, France), J. Brindley (U. Leeds, UK), A. Calsina (U. Girona, Spain), H. Caswell (Woods Hole Oceanographic Institution, USA), J. Cushing (U. Arizona, USA), A. de Roos (U. Amsterdam, The Netherlands), P. Fergola (U. Naples, Italy), J.L. Gouzé (INRIA, France), T. Hallam (U. Tennessee, USA), A. Hastings (U. California, USA), M.L. Hbid (U. Marrakech, Morocco), H. Heesterbeek (U. Utrecht, The Netherlands), S.E. Jorgensen (U. Copenhagen, Denmark), V. Kaitala (U. Jyväskylä, Finland), S.A.L.M. Kooijman (Free U. Amsterdam, The Netherlands), T. Kostova (Lawrence Livermore National Laboratory, USA), V. Krivan (Institute of Entomology, Czech Republic), S. Levin (Princeton U., USA), H. Malchow (U. Osnabrück, Germany), F. Milner (Purdue U., USA), C. Mullon (I.R.D., France), M. Pascual (U. Michigan, USA), S. Rinaldi (Politecnico di Milano, Italy), H. Smith (U. Arizona, USA), A. Stevens (Max-Planck Institute, Leipzig, Germany), L. Stone (U. Tel Aviv, Israel), S. Tuljapurkar (Stanford U., USA).

Organizing committee: O. Angulo (U. Valladolid, Spain), O. Arino (I.R.D., France), A. Blasco (U. Alcalá, Spain), R. Bravo de la Parra (U. Alcalá, Spain), S. Charles (U. Claude Bernard Lyon 1, France), Pablo Gómez (U. Politécnica de Madrid, Spain), M.L. Hbid (U. Marrakech, Morocco), J.C. Poggiale (Marseille Oceanographic Center, France), E. Sánchez (U. Politécnica de Madrid, Spain), L. Sanz (U. Politécnica de Madrid, Spain), M.A. Zavala (U. de Alcalá, Spain).

Deadline for Session Proposals: December 1, 2002

Deadline for Abstracts: May 1, 2003

All information and more details can be found on the www-server:

<http://www2.uah.es/matema/Aicme/aicme.htm>

Equadiff: International Conference on Differential Equations

July, 22 – 26, 2003, Hasselt, Belgium

Organizing committee (Belgo-Dutch): F. Dumortier (Chairman, Diepenbeek), H. Broer (Groningen), J. Mawhin (Louvain-la-Neuve), A. Vanderbauwhede (Gent), S. Verduyn Lunel (Leiden).

All information, including the possibility for electronic registration will be made available on the web:

<http://www.equadiff.be>

Forthcoming Events in Short

Workshop on Ontology for Biology

Heidelberg, Germany, November 7-8, 2002

http://projects.villa-bosch.de/sdbv/people/luca_bernardi/bioontology/index.html

Plant Species-Level Systematics: Patterns, Processes and New Applications

Leiden, The Netherlands, November 13-15, 2002

<http://www.nationaalherbarium.nl/symposium2002/>

Congreso latinoamericano de biomatemática - xi alab vi elaem

Guanajuato, México, November 25-28, 2002

For further information send email to:

a1ab92002@yahoo.com

Understanding the Genome: Scientific Progress and Microarray Technology

Genoa, Italy, November 29 - December 1, 2002

<http://www.sispge.com/microarrays2002/>

Artificial Life VIII

December 9 - 13, 2002, UNSW, Sydney, Australia

<http://parallel.hpc.unsw.edu.au/complex/alife8/>

3rd International Conference on Systems Biology - The Logic of Life

Stockholm, Sweden, December 13-15, 2002

<http://www.ki.se/icsb2002/>

3rd WSEAS International Conference on Mathematics and Computers in Biology and Chemistry

Puerto De La Cruz, Tenerife, Canary Islands, Spain, Dec.19-21, 2002.

<http://www.wseas.org/conferences/2002/tenerife/mcbb/>

PSB 2003 - Pacific Symposium on Biocomputing

Kaua'i, Hawaii, January 3-7, 2003

<http://psb.stanford.edu/>

Course in Informatics for Biology 2003

Paris, France, January 6 - April 25, 2003

<http://www.pasteur.fr/formation/infobio/infobio-en.html>

4th Geoffrey J. Butler Memorial Conference: differential equations and mathematical biology

University of Alberta, Edmonton, Alberta, Canada, June 17 - 21 (Tuesday - Saturday), 2003.

<http://conley.math.ualberta.ca/butler.html>

IPCAT 2003

Lausanne, Switzerland, September 8-11, 2003

<http://lslwww.epfl.ch/ipcat2003/>