Mathematical Biology Newsletter

Society for Mathematical Biology Volume 4, Number 3 February, 1991

SMB Election Results

Alan Perelson is President-Elect of the Society for Mathematical Biology. **James Keener** and **Donald Ludwig** will serve on the Board starting at the summer meeting and will serve until the summer of 1994. **Joan Aron** and **Bard Ermentrout** will start service on the Board immediately and will serve until 1993.

The Nominating Committee consisted of L. Edelstein-Keshet (Chairperson), S. Kauffman, N. Kopell, C. Macken, and M. Savageau.

Annual Meeting

The 1990 Annual Meeting of the Society was held in Chicago during the week of July 16-20 in conjunction with the Annual Meeting of the Society for Industrial and Applied Mathematics (SIAM). The scientific component of the meeting comprised several minisymposia and two contributed paper sessions (see Math. Bio. Newsletter, Vol. 4, No. 2). The contributed paper sessions, with eighteen talks in total, were notable for the substantial attendance they attracted and for the vigorous discussion they generated. These sessions were organized by Torcom Chorbajian, and hopefully will be an integral component of all future meetings.

The main topics discussed during the Board and Business Meetings were the Treasurer's report, the status of the *Bulletin*, election procedures, and the site and nature of the next annual meeting. Torcom Chorbajian, the Treasurer, reported that total assets were now $68,500, with the precise amount depending on the timing of payments from Pergamon Press. Somewhat more than half of this ($35,000) belongs to the Landahl Scholarship Fund, used to support student travel to SMB sponsored meetings. The cost of producing the *Bulletin* has gone up, largely because of a 20% increase in size. It was decided to hold costs to the membership the same for one year, and to use the Society General Fund to subsidize this.

To put the election schedule in order, eight candidates were nominated for four board positions (see election results above). Possible procedural flaws in the present Bylaws were discussed. Election on the basis of the present Bylaws appears to require a plurality of votes. This can give rise to problems if more than two candidates are nominated for each office. Also there is no provision for nominations from the membership. Addressing these issues would involve amendment of the Bylaws and therefore a vote of the entire membership.

The main issue connected with meetings is whether they should be stand-alone or held in conjunction with other societies. The argument for cooperative meetings with other societies was that they enhance the professional stature of mathematical biology; the argument for a stand-alone meeting is that it could be intellectually more vigorous and open. Possibilities considered included a stand-alone meeting in Santa Fe or Washington, or cooperative meetings with FASEB, AIBS, SIAM, or AAAS. The Board authorized Stuart Kauffman, the Society President, to explore the feasibility of a three-day meeting, with two days of plenary and contributed sessions and a one-day workshop, and authorized a $6000 allocation to support such a meeting.

Professor Kauffman communicated the results of the Board discussions and commented on the general state of the Society at the Business Meeting. He noted that Torcom Chorbajian had developed the directory of current members, and that starting with Simon Levin's presidency membership had grown from approximately 200 to approximately 400 at the present time, with about 100 new members during the past year.

M. Conrad, Secretary

President's Message

Several events of the recent past and planned for next August are of moment to the members of the Society. These include the formation of a European Society for Theoretical Biology initiated at the meeting in l'Alp d'Huez in January 1991, growing interest in forming a Society for Computational Molecular Biology here in the United States, and a stand-alone SMB meeting planned for August 18-21, 1991 in Santa Fe.

Theoretical biology is fast maturing. This maturation is reflected not only in the increased membership in SMB, but in the growing enthusiasm to form professional organizations in Europe, the United States, and elsewhere. As our field matures, it is important to assure flexible, effective, coordinated internal communication within the field and interaction with neighboring intellectual areas, and other interested groups. At the Mathematical Biology and Medicine Meeting in l'Alp d'Huez, France, with representatives of all major European nations, this growing confidence, coupled with a profound sense of European identity, led to the initial steps in the formation of a European Society of Theoretical Biology. Its President is Dr. Jim Murray, whose tenure lasts until the next meeting at which the Society shall be officially formed, and official elections held by its formal membership.

Formation of this Society raises urgently the question of the relationship between the European Society and SMB. My own strong view, expressed at that meeting, and reiterated here, is that we welcome the sense of European identity underlying the formation of a separate European society. On the other hand, SMB in its current form is an international organization. I proposed at the l'Alp d'Huez meeting that the SMB consider reformulating itself as a Society for Theoretical Biology: American Division, while the European Society constitute itself the sister Society for Theoretical Biology: European Division. This suggestion has been warmly accepted as a useful basis for discussion by the European Society, with assurance that I may so represent their views to the membership of SMB. Considering this proposal will require detailed thought, discussion and approval of the SMB membership. In particular, one model would afford automatic membership, perhaps with a minimal annual dues, to members of each society in the other society. The *Bulletin of Mathematical Biology* is the official organ of SMB. The European Society may or may not wish to make use of the *Bulletin*, and its members may or may not wish to receive it. This, I believe, would have to be left flexible. On this model, as societies spring up in Latin America, or Asia, new divisions would be created, yet would require only a minimal supraordinate international organization. Coordination might be achieved by a committee formed of the presidents of the respective divisions.

Other alternatives include the continued activity of SMB as an international organization. The clear disadvantage is that SMB might then function in competition with the European Society. The potential advantage might be the emergence of different intellectual agendas, represented in the same geographical area. We will have to understand our own views on this. I will discuss an initial format for these considerations below.

Recent work in knot theory and molecular biology, in addition to the computational needs of the Human Genome Project, are powering an interest in a Society for Computational Biology. I believe the interests in computational biology largely overlap those of theoretical biology. It is important, therefore, to foster early discussions between those with focal interest more in one or the other areas, to see whether it may be better to house all such activities in a broadened Society for Theoretical Biology. I have initiated discussions with Sylvia Spangler, one of the people interested in forming a Society for Computational Biology. These efforts should continue, and receive the attention of the membership.

SMB has traditionally met in conjunction with other societies. I believe it is time that we tried our collective minds at our own meeting. We have a lot to say to one another. This possibility was discussed at the last meeting, and I have been formally authorized to organize such a meeting in Santa Fe, and expend up to $6000.00 of SMB funds. The meeting is planned for Sunday, August 18 until Wednesday, August 21, at the Hotel Santa Fe. Rooms have been reserved beginning on Saturday, August 17. We can cancel without financial loss up to three months prior to the meeting. This sets the corresponding date of May 16, 1991, as the final date for registration which can confirm the following rates: On August 17, $95.00 for a single room, $115 for a double. Ten rooms have been reserved. Thereafter, rates are $80.00 a day for a single and $100 for a double. Fifty rooms have been reserved for the nights of August 18 to 20th, and twenty-five rooms for the night of August 21. Indian Market Week ends August 17th in Santa Fe. Rooms will be held on a first-come first-serve basis. If those become filled or unavailable, it will be advantageous to know if you are coming as soon as possible. August is high season, and beautiful, in Santa Fe.

The meeting is being organized by myself, Simon Levin, Alan Perelson, Jack Cowan and Nancy Kopell. The general format envisions a two-and-a-half-day meeting, starting with an informal gathering on Sunday evening, three formal organized sessions with invited papers over a day-and-a-half and two formal sessions, over a day, with contributions submitted by members of SMB at large. In addition, a poster session will be organized. The organizing committee at present intends to focus on "network" properties arising in models of genetic, immunological, neural, and ecological systems. The $6000.00 will be expended first, to cover costs of invited speakers, and then, so far as possible, to support students who wish to come. At present there is no plan to charge a registration fee, but members will have to cover their own costs.

In order to begin to organize both the meeting and sessions with respect to contributed papers, may I take this opportunity to invite all interested to write me at the Santa Fe Institute, 1120 Canyon Road, Santa Fe, NM 87501 (tel 505 984-8800). Let me know if you want to come, and want to submit a contributed paper or poster.

Above I raised issues which I believe are central to the membership. The Santa Fe meeting is the appropriate place for detailed discussions. In the meantime, if you write me with your views I will make sure that they are made publicly available at the Santa Fe meeting to help inform our deliberations.

Alan Perelson has now been elected President. His term will begin at the Santa Fe meeting, and I will become the Past President. I have been honored to serve as President. The Society is growing, in no small measure due to the activities of past presidents, the other officers, and most of all, the enthusiasm of the membership. Biology increasingly needs theory. May our successes continue.

Stuart A. Kauffman, President, SMB

MEETING REPORTS

Calculating Parasitic Diseases

(Communicated by Zvia Agur)

The interaction of biologists and mathematicians for the purpose of fostering an improved understanding of the control of infectious disease, both within individual patients and communities of people, was the aim of this workshop. The meeting was held March 18-20, 1990, at the Weizmann Institute of Science in Rehovot, Israel, under the auspices of the MacArthur Foundation Center for the Molecular Biology of Tropical Diseases. Mathematical models are beginning to play an increasing role in the formulation and testing of hypotheses concerning both infection and disease within individual patients, and the spread and persistence of infection plus disease in communities of people in developing and developed countries. Nowhere is the trend more apparent than in the field of immunology where models are beginning to provide a template for the synthesis and distillation of an ever increasing volume of observations, facilitated by advances in molecular biology and biochemistry. Concepts derived from the study of the population biology of infectious agents have established a broad mathematical framework for epidemiological study but these methods are now being directed, with increasing benefit, to the study of human immune system and the genomic organization of both infectious agent and host. The major need at present is for an increased dialogue between theoreticians and experimentalists, such that theory is based on biological insights, and experimentation is directed towards the analysis of pattern and process within a formal mathematical framework that facilitates interpretation and measurement.

The meeting was divided into five areas, each of which involved biologists and mathematical modelers. *Sequencing and Molecular Structure and Evolution* was introduced by Charles Cantor of the Human Genome Center, Berkeley, California. Dr. Cantor stressed the role of mathematicians and computer scientists in inferring protein structure and function from their linear sequences and from the few hundreds structural motifs of which they are assembled. He and other speakers expressed concern about the lack of encouragement at the NIH regarding active involvement of theoretical biologists in major research projects. The prospects of such an involvement were illustrated by talks on mathematical and statistical methods for analyzing genomic rearrangements, for inferring phylogenies for both parasites and hosts and for studying protein folding and unfolding.

In the *Population Dynamics* session mathematical models were presented, predicting the biological conditions for the emergence of parasitic virulence and for immunosuppression. Roy Anderson described the role of mathematical modelling in directing data collection and vaccination programs and in demonstrating the pitfalls in specific vaccination or chemotherapeutic programs. Using models he demonstrated how, if failing to meet the minimum coverage for efficient herd immunity, vaccination programs may become counter productive. By the same token he argued that chemotherapeutic agents should be licensed only after they have been shown to reduce infectiousness.

The theme of the session on *Pathogen-Immune System Interactions* was forcefully brought forward by Alan Sher, who suggested that theory could be of aid in diverting the focus of research from disappointing anti-parasitic vaccine developments towards immunotherapy. Sher proposed that the immune response to parasites, such as Leishmania or Schistosoma, is characterized by the balance between two competing subsets of T helper lymphocytes (Th1 and Th2). By formally describing the two networks related to these lymphocytes and their interactions, one could suggest how the anti-parasitic immune response might be reinforced. General approaches to modelling the immune response and a specific model explaining ordered parasitaemia waves in Trypanosomiasis illustrated the potential of mathematics in illuminating disease processes.

The session on *Vaccine Development* began with a report on *WHO* programs in the development and application of vaccine. Mathematical models were then presented for strategies for containing measles and for the effect of a major malaria control program in West Africa. Charles Delisi discussed the essential role of modelling in retrieving the structure of the ternary complexes involving T cell receptors, products of the major histocompatibility complex and antigen. He further suggested that the structure of these complexes, rather than that of the individual peptides, will constitute a useful tool for drug and vaccine design.

The final session was devoted to *Diagnosis and Chemotherapy*. A description was presented of the National Institute of Health's system of discovery and development of new potential AIDS therapies. An appeal was made to develop biostatistical and biomathematical methods for evaluating combination chemotherapies, for predicting occurrence of drug resistant strains in individual patients and for improving molecular modelling applied to protein-drug interactions. Several papers then described the effects on efficacy of the drug's administration timing: circadian rhythms and the administration of cancer chemotherapy; antibiotic perturbation of cell cycle, cell killing and the emergence of resistance; and a model by Zvia Agur, who organized the workshop, suggesting that toxicity of cell-cycle phase-specific drugs depends on the relation between the cell-cycle time and the frequency of drug administration. The latter approach has been experimentally verified in AZT and now is under clinical trials in AIDS patients.

The overriding impression left at the end of the conference was the feeling of excitement amongst both biologists and mathematicians of the suggestion role of mathematical and experimental techniques in both laboratory and field work in helping to improve our understanding of infection and disease, and in targeting research on methods of control toward the key processes that determine observed pattern. There seemed little doubt amongst the conference participants that mathematical techniques will play an increasing conceptual role in biological study, in a manner analogous to the development of other scientific disciplines such as physics in the early part of this century. What is needed in the future is a better appreciation amongst mathematicians of the opportunities opening up in biology for their skills, and a better understanding amongst biologists of the precision that mathematical methods provide in the formulation and testing of hypotheses.

Coherent and Emergent Phenomena in Biomolecular Systems

(Communicated by Michael Conrad)

Tucson was the site of this NATO Advanced Research Workshop, organized by Stuart Hameroff, Steen Rasmussen, and Jack Tuszynski, and January 15-19 was the time frame. The concentration of the meeting was punctuated on the second day by the announcement by Dr. Hameroff that hostilities had begun in the Persian Gulf. Though CNN clearly had a high rating among the participants on that particular evening, I think it became evident by the end of the meeting that the enervating news had not succeeded in detracting from the overall tempo and vitality of the scientific discussion.

The session titles give a clear statement of the theme: dynamical structure and function of the cytoskeleton, communicative modes among cytoskeletal subunits, soliton and exciton models in proteins, soliton and exciton models in DNA, low level field effects in biomembranes, computation in biomolecular systems, long-range coherence, biomolecular cooperativity, self-organization in biomolecular systems, and technological approaches to nanobiology. A special session devoted to the questions, "What is Life, and Where is it Going?" was held (fortunately) on the first evening. Started off by Doyne Farmer's challenging talk on the future evolution of life, it served to provide an aerial view of the very specific physical-dynamical, computational, and biomedical questions addressed in the more specialized sessions.

It is not feasible to review the nearly fifty talks and nearly thirty posters presented. The overall gist reminded this reviewer of Salvidor Dali's appearance on the Mike Wallace interview show more than thirty years ago, shortly after the fall of parity. Wallace asked Dali what he admired most. "Weakness" came the answer from an artist who was obviously impressed by the fact that the weak interaction did not preserve reflection symmetry. This could not be the answer in a pure molecular biology meeting; there the great progress is based on the ability to manipulate strong (covalent) bonds in a precise manner. But the emergent information processing and control properties of biomolecular systems, from the subcellular to supracellular level, are based on weak interactions. The interactions responsible for protein folding and self-assembly are a classic example. Soliton and other quasi-particle dynamics, collective properties of hydrogen bonds in water-membrane systems, and coherent dipole oscillations in extended biomolecular structure are examples of possibilities now under active theoretical and experimental investigation.

It should not be surprising that a workshop dealing with the manifold subtle interactions that emerge from the more strongly bonded chemical structures in biological systems would encompass the computational properties of cells, on the one hand, and neoplastic behavior on the other. The question that presses for an answer is whether the methodological habits of classical molecular biology can retain their applicability in this more dynamic domain, where much of the relevant phenomena depends on the cumulative effect of multiple weak interactions and on the existence of tailored nonlinearities potentially capable of unmasking highly exotic effects. When we sequence a gene the effect of the observer need not be considered; when we look for a soliton in DNA, and its significance for the control of the genetic mechanism, this may no longer be the case.

International Symposium of Mathematical Approaches to Brain Functioning Diagnostics

(Communicated by Ivan Dvorak)

An International Symposium, Mathematical Approaches to Brain Functioning Diagnostics, was held in Prague, Czechoslovakia from September 3 to 7, 1990. It was organized as a part of the broader scientific meeting together with the International Conference Medical Informatics and Medical Education by the Association of Czechoslovak Medical Societies J. E. Purkyne under the auspices of the Society for Mathematical Biology and the International Brain Research Organization. International sponsorship was provided by UNESCO and IEEE - EMBS. The Symposium was also sponsored by commercial enterprises, EMS Wien and SimTest. Several local institutions participated in organization of the meeting, namely Psychiatric Center Prague; Charles University, Prague; Czechoslovak Academy of Sciences and Research Institute of Railway Health Care, Prague. Members of the Honorary Advisory Board were: F.H.Lopes da Silva (The Netherlands) - president, C. Dostalek, M. Katetov (Czechoslovakia) - vice-presidents, J. Andel (Czechoslovakia), E. Basar (Germany), A. Borsellino (Italy), J. Bures (Czechoslovakia), H. Cammann (Germany), L. Ciganek (Czechoslovakia), A. Holden (United Kingdom), P. Rapp (USA), E. Roy-John (USA), T. Radil (Czechoslovakia), and M. Zhadin (USSR). Local Programme Committee was headed by I. Dvorak.

The program of the Symposium was concentrated around four morning plenary lectures: General Mathematical Approaches to Brain Function Modelling, Analysis and Modelling of EEG Activity, Dynamic System Approach to Brain Functioning Analysis, and Event Related Brain Electrical Activity. The afternoon program was organized into six sections: Brain Activity Mapping, Computer Techniques in Brain Function Diagnostics, Neural Networks and Artificial Intelligence Approach to Brain Function Diagnostics, Computer and Mathematical Modelling of the EEG Formation, Chaotic Dynamics and Evoked Rhythmicities in the Brain, Mathematical Analysis and Modelling of Brain Perception and Cognitive Processes.

The meeting was accompanied also by exhibition of medical equipment and by demonstration of scientific software related to its topic.

About 140 participants came to Prague to attend the Symposium. During the meeting 54 lectures were read and 62 posters displayed. Invited lectures were delivered by H. Haken, A. V. Holden, P. Erdi, D. Lehmann, M. Matousek, E. R. John, J. Michel, E. Ducla-Soares, F.H. Lopes da Silva, K. J. Blinowska, V. Albrecht, W. J. Freeman, G. Mayer-Kress, J. Xu, I. Dvorak, P. Vos, S. Mateeff, R. Eckhorn, D. S. Ruchkin, S. Cerutti, Z. Kevanischvili, F. Ventriglia, A. de Callattay, M. Zhadin, and R. M. E. Sabbatini.

Invited lectures and all presented contributions demonstrated a variety of mathematical approaches used in the brain studies. Highly theoretical contributions concerning the brain theory were presented as well as very applied methods with direct impact on brain diagnostics. The aim of organizers to bring together theoreticians and experimentalists or even clinicians interested in computerized analysis of brain functioning was to a large extent successfully matched. Classical topics as EEG analysis by means of the theory of random processes or analysis of event related brain electrical activity were extensively presented as well as new topics currently very fashionable such as brain mapping. Possibly the largest attention was devoted to chaotic dynamics approach to brain dynamics analysis—not less than eight invited lecturers and many other contributors dealt this way or the other with this theme. Interest in this approach clearly documented that it is not a sidetrack, but a firmly established and very promising paradigm for analyzing and modelling the brain phenomena. Relatively less attention was paid to neural networks, as another conference devoted exclusively to this topic (Neuronet'90) immediately followed the Symposium in the same Palace of Culture in Prague.

Proceedings of the Symposium containing the invited lectures and several contributions that have aroused the greatest interest during the meeting will be published by the Manchester University Press.

The Symposium met in an extraordinary situation less than one year after Prague's "velvet revolution". Though the post-revolutionary situation brought some troubles to the organizers, the general impact of changing international atmosphere was very positive. In the spirit of growing optimism for the future, many old friendships were confirmed and many new acquaintances were made. Let us hope that it will have a long-lasting impact on the future scientific cooperation between developed countries and countries of the former eastern block. A bitter scent to the general enthusiasm was the absence of nearly all expected participants from the Soviet Union and Romania; economical situations in their countries did not make it possible for them to come. In spite of this, the majority of participants shared the opinion expressed by Prof. H. Haken during the farewell party—that the Symposium was another step not only in developing mathematics/brain interactions but also in confirming mutual understanding and scientific friendship.

News from the Latin American Society

Jose Maria Cordero, of the Asociación Latinoamericana de Biomatemática, reports that the Fourth International Congress on Biomathematics was held in Lima, Perú, September 1989. The Nicolas Rashevsky Prize for 1987-89 was won by Carlos Luguizamón. This prize was established by the Latin American Biomathematics Society in 1987, and is awarded to the member of the Association who has done the best research work during the last two years. The Society also established a "Prize to the Best Research Work", for the best paper presented at the International Congress of Biomathematics organized by the Association. This was won by the paper "The Algebraic Theory for Relational Processes and the Continuous Periodic Effect Produced by Low Energy Irradiations" (by C.A. Leguizamón, A.N. Zeretsky, J.M. Cordero, and M.A. Allignani).

NSF Workshop on Mathematics and Biology Proposes Major Funding

The NSF Workshop on Mathematics and Biology chaired by Simon Levin last April in Washington has prepared its draft report, titled "Mathematics and Biology: the Interface." The report proposes that the NSF develop a major funding program in mathematical biology involving research support, infrastructure development, training and education. It identifies a number of areas where funding would be expected to facilitate major advances. These include:

- Genomics, including sequence analysis
- Global change and problems of ecological scale, including applications to problems of biological diversity and sustainable development
- Dynamic aspects of structure-function relationships, including the relation between morphology and physiological processes
- Multiple scale problems in complex hierarchical biological systems, from cells through neural networks
- Molecular evolution
- Structural biology

The draft proposes multiple modes of support, including support for interdisciplinary individuals, for collaboration between scientists from different disciplines, for mid-career and postdoctoral fellowships, and for graduate training.

Neurocybernetics Research in the USSR

Vitaly Dunin-Barkowski informs the *Newsletter* that as of January 29, 1990, he has been appointed Director of the Neurocybernetics Research Institute (NCRI) at Rostov State University (Rostov-on-Don, 344104, USSR). This is a unique research foundation in the USSR with a staff of approximately 300, occupying a new eight-story building. The main directions of research are neurophysiology and cybernetics, including neurobiology in general, nonlinear dynamics, connectionist models, and neurocomputer designs. In June, 1990, Dr. Dunin-Barkowski organized the USSR Academy of Sciences meeting in Rostov on Informatics, Physics, and Electronics of Neural and Neural-like Systems. Dunin-Barkowski was previously affiliated with the Institute for Problems of Information Transmission in Moscow, where for many years he has worked on structural-informational approaches to the analysis of neuronal systems, and in particular on network models of the cerebellum.

Assistant/Associate Professor of Biomathematics (tenure track). Evidence of research strength expected in mathematical biology, either in areas of relevant mathematical theory or biological application. Duties include research, teaching and graduate student direction. Letter of application, CV and 3 letters of reference should be sent by April 1, 1991 to: Dr. R. E. Stinner, Biomathematics Graduate Program, North Carolina State University, Campus Box 8203, Raleigh, NC 27695-8203. EOE/AA.

SMB MEETINGS

The 1991 Annual Meeting of the SMB will be held in **Santa Fe, NM**, August 18-21, 1991 (see *President's Message, p.2).* If interested in contributing papers and/or attending the meeting, contact: Stuart A. Kauffman, Santa Fe Institute, 1120 Canyon Road, Santa Fe, NM 87501 (tel 505-984-8800).

Symposium on Some Mathematical Questions In Biology

The Twenty-fifth Annual Symposium on Some Mathematical Questions in Biology will be held during the Annual Meeting of the Ecological Society of America, in conjunction with the American Institute of Biological Sciences (AIBS), August 4-8, 1991, in **San Antonio, Texas**. The symposium is sponsored by the American Mathematical Society (AMS), the Society for Industrial and Applied Mathematics (SIAM), and the Society for Mathematical Biology (SMB).

Robert H. Gardner (Oak Ridge National Laboratory) is the organizer of the Symposium, and the theme is *Theoretical approaches for predicting spatial effects in ecological systems.* There will be one afternoon session including six 30-minute lectures.

The names and affiliations of the speakers and titles are as follows (* denotes presenter):

Debra P. Coffin*, William K. Lauenroth, and **Ingrid C. Burke**, Colorado State University, *Spatial dynamics in recovery of Shortgrass Steppe ecosystems*;

Virginia H. Dale*, Frank Southworth, Robert V. O'Neill, and **Robert Frohn**, Oak Ridge National Laboratory, *Simulating spatial patterns and socio-economic and ecologic effects of land use change in Rondonia, Brazil*;

Bruce T. Milne, University of New Mexico, Albuquerque, *Renormalization relations for spatial models*;

Stephen W. Pacala, University of Connecticut, Storrs, *Neighborhood population dynamics models*;

John Pastor*, John Bunde, C.A. Johnston, and **R.J. Naiman,** University of Minnesota, Duluth, *A mathematical treatment of the spatially dependent stabilities of beaver ponds*;

Winfred F. Wolff, University of Tennessee, Knoxville, *A spatial individual-oriented model for a wading bird nesting colony.*

Proceedings of the symposium will be published by the AMS in the series *Lectures on Mathematics in the Life Sciences.*

For further information about registration and housing, contact: Betty A. Verducci, Conference Coordinator, AMS, P. O. Box 6887, Providence, RI 02940.

THE LANDAHL TRAVEL AWARDS

The Society for Mathematical Biology has funds for partial support of the travel of graduate students to meetings co-sponsored by the SMB. Graduate students who wish support may apply to: Michael C. Reed, Department of Mathematics, Duke University, Durham, NC 27706. The application, which should be received by May 25, 1991, should include a one-page research summary and one letter from a faculty sponsor.

Other Future Meetings

Stochastic Modeling and Statistical Inference for Selected Problems in Biology. This conference is a component of the Joint Summer Research Conferences in the Mathematical Sciences, to be held at the University of Washington, Seattle, from June 22 to August 2, 1991. The focus will be on problems of neuronal activity, the effect of radiation on single cells, DNA sequence analysis, and the transmission of infectious diseases. Co-organizers are Charles Smith (North Carolina State University) and Grace L. Yang (University of Maryland, College Park). For information contact: Summer Research Conference Coordinator, Meetings Department, American Mathematical Society, P. O. Box 6887, Providence, RI 02940.

The Canadian Society for Theoretical Biology (CSTB). June 8-11, 1991, Queen's University, Kingston, Ontario, held under the auspices of the Canadian Federation of Biological Societies (CFBS). A Symposium on *Mechanical Engineering of the Cytoskeleton in Developmental Biology* has been organized by Dick Gordon (Department of Botany, University of Manitoba, Winnipeg R3T 2N2 Canada) and Brian Goodwin (The Open University, Milton Kaynes MK7 6AA, England). Chuck Schom (St. Andrews Fisheries Research Laboratory, P. O. Box 608, St. Andrews, New Brunswick E0G 2X0 Canada) has organized a seminar on *Forests and Forestry; More Than Just Cutting Trees*, which fits in the theme for the Presidential Symposium at the CFBS meeting: "Can Biological and Biomedical Research Solve Major Problems Resulting from Global Change?" Donald R. Forsdyke (Department of Biochemistry, Queen's University) and Dick Gordon are planning a forum on *Alternatives to the Present Granting System*. If you would like to contribute to any of the sessions noted above, contact the cited organizers. For a registration package contact: Ms. Crystal Hache, Administrative Assistant, Canadian Federation of Biological Societies, 360 Booth Street, Ottawa, Ontario K1R 7K4, phone: (613) 234-9555; fax: (613) 234-6667.

Summer School and Advanced Workshop on Neurocomputing and Systems Control. The European Centre for Peace and Development, established by the University for Peace of the United Nations, is organizing a summer school on neurocomputing from June 10-12, 1991, to be followed by a workshop from June 13-15. Workshop topics include the biological basis for neurocomputing, control mechanisms at the molecular, cellular, and brain level, artificial neural nets, new logics for neurocomputing, as well as implementation technologies and applications to control systems. Both events will be held in Sveti Steven, Yugoslavia, just south of Dubrovnik. For further information contact: European Centre for Peace and Development, Division of R&D in High Technology, Kneza Mihaila 7/11, 11000 Belgrade, Yugoslavia (fax: +(38 11) 623-169).

Pacific Coast Resource Modeling Conference (PCRMC). Humboldt State University (Arcata, CA) is the venue for the tenth PCRMC from June 19 to 21, 1991. This year's conference will again provide a forum for presentation of recent progress in mathematical modeling of renewable resources, with particular emphasis on biological processes, population dynamics and bioeconomics as they relate to fisheries, forestry, pest and wildlife management, and water resources. There will be a panel discussion on population viability and conservation planning for endangered species, and a session on modeling success stories.

Five speakers will be featured: Colin Clark (University of British Columbia) will give the keynote address on behavior, population dynamics, and conservation; Anthony Charles (St. Mary's University) will speak on aquaculture and fishery models: applications in the developing world; Russell Lande (University of Oregon) will speak on genetics, demography, and biological conservation; Jon Conrad (Cornell University) will speak on economic activities, buffer zones, and biodiversity; and Marc Mangel (University of California, Davis) will speak on behavior models for fish patterning and response to global climate change.

The registration fee before May 1 is $50 for RMA members and $70 for non-members. Students are $15. Anyone registering after May 1 will be charged $10 extra. May 1 is also the abstracts deadline for 20-minute contributed talks.

For further information, contact: Dr. Roland Lamberson, Department of Mathematics, Humboldt State University, Arcata, CA 95521-4957, phone: (707) 826-4926, E-Mail: ROLLIE@CALSTATE.

4th Interdisciplinary Conference on Natural Resource Modeling and Analysis. June 15-18, 1991. For the first time in the RMA's history, a European university will sponsor an RMA conference. Barcelona, Spain's sophisticated second largest city and greatest industrial center, will be the site of the conference. The meeting—whose objective is to facilitate communication among biologists, ecologists, economists and other scientists who share an interest in resource modeling—will have two-and-a-half days of invited and contributed talks on fisheries, forests, soil, water, wildlife and other natural resources. The meeting is hosted by the University of Barcelona.

Invited speakers are Colin Clark (University of British Columbia) on mathematical models in renewable resource economics; Alain Laurec (IFREMER, Paris) on population dynamics in fisheries; Ramón Margalef (University of Barcelona) on ecology; Martin Sykes (University of Uppsala, Sweden) on management models in forestry; Michael Usher (University of York, U.K.) on succession models in forestry; and Jorge Wagensberg (University of Barcelona) on theoretical biology and non-equilibrium thermodynamics.

The abstracts deadline for papers is May 31. Registration fees before May 31 are $45 for RMA members, $65 for non-members and $25 for students; after June 1, the fees will be $70 for members, $90 for non-members and $40 for students.

The conference organizers are Emilia Gutiérrez, Jordi Lleonart and Pere Rubiés. For registration, submission of abstracts or further information, contact: Pere Rubiés, Instituto de Ciencias del Mar, P.º Nacional s/n, 08039 Barcelona, SPAIN; phone: 34-3-310 64 16; fax: 34-3 319 98 42; E-Mail: CCICM@CEAB.ES.BITNET.

ICIAM. The Second International Conference on Industrial and Applied Mathematics, July 8-12, 1991, Washington, DC. (See February 1990 Newsletter for earlier announcement.) For further information, contact: ICIAM 91 Conference Manager, c/o SIAM, 3600 University City Science Center, Philadelphia, PA 19104-2688, phone: (215) 382-9800; fax: (215) 386-7999;
E-Mail: iciam@wharton.upenn.edu.

IMACS '91 High Performance Computing in Biology and Medicine. IMACS is the International Association for Mathematics and Computers in Simulation. The next World Congress will be held in Dublin, July 22-26, 1991. The biology and medicine sessions are being organized by Matthew Witten (University of Texas System—CHPC, Balcones Research Center, 1.154 CMS, 10100 Burnet Road, Austin, TX 78758-4497, USA).

Resource Management and Behavioural Ecology: A Conference in Celebration of the 60th Birthday of Colin Clark. This conference will be held at the University of British Columbia July 24-26, 1991. The program includes invited hour lectures, contributed talks, and poster sessions as well as social functions. Registration and accommodation information are available from Ms. Nancy Oikawa, Secretary, Institute of Applied Mathematics, University of British Columbia, 222-1984 Mathematics Road, Vancouver, B.C. V6T 1Y4, phone: (604) 228-4584, fax: (604) 228-6074.

Biomed 91. The objective of this first International Conference on Computers in Biomedicine is to bring together scientists who work on the applications of computers in biomedical systems and engineering. The conference will be held from September 24-27, 1991, at the University of Southhampton, UK. For further information contact Dr. C.A. Brebbia, Computational Mechanics Institute, Wessex Institute of Technology, Ashurst Lodge, Ashurst, Southhampton, SO4 2AA, UK.

Fifth International Congress on Biomathematics will be held in Santiago, Chile, from October 14-19, 1991. For further information contact: Carlos A. Leguizamon, Gerencia de Investigaciones, Comision Nacional de Energia Atomica, Av. del Libertador 8250, Buenos Aires, Argentina, phone: 54 1 782 8843.

Biocomputing. The Hawaii International Conference on Systems Sciences will include a mini-track on Biocomputing (Theory, Implementation, and Applications). The conference will be held in Kailua-Kona, Hawaii, from January 7-10, 1992. Full camera-ready papers are due before October 1, 1991. Papers should be submitted to Prof. Dr. Djuro Koruga, Molecular Machines Research Center, University of Belgrade, 27. Marta 80, 11000 Belgrade, Yugoslavia (Phone and fax: +(38 11) 320-207).

3rd Conference on Population Dynamics (preliminary announcement). The 3rd Conference on Population Dynamics will take place in Pau, France, and is scheduled for May/June 1992 (organizers: O. Arino, D. Axelrod, M. Kimmel). Previous conferences in this series were held in 1986 (University of Mississippi, USA), and 1989 (Rutgers University, New Jersey, USA). The conference is intended as a forum where specialists of various fields interested in population dynamics can meet. The main emphasis is on applied mathematics, and more precisely on evolution problems arising from structured populations. More detailed information will follow at a later date. Persons interested can contact: O. Arino, Lab. de Mathématiques Appliquées, I.P.R.A., Av. de l'Université, 64000 Pau France, (e-mail: Arino@FRUPPA51).

Future RMA Conference Venues. The 11th Pacific Coast Resource Modeling Conference will be held at the University of California, Berkeley, during the spring of 1992 (anticipated May). The conference will be organized by Wayne Getz and Peter Berck. The 5th Interdisciplinary Conference on Natural Resource Modeling and Analysis will be held later that year (probably August) in St. John's, Newfoundland. The conference will be organized by Ransom Myers, Peter Shelton and Michael Wernerheim.

Ilya Prigogine—Pursuer of Conceptual Consistency

(interviewed by Michael Conrad)

I vividly recall my first meeting with Ilya Prigogine in the early 1970s. The occasion was his visit to the Institute for Information Processing (part of the physics faculty) at the University of Tübingen. I had for many years been well acquainted with Professor Prigogine's elegant formalism for irreversible thermodynamics, which was playing an important role in my own work on biological adaptability. I was also well aware of the work of Prigogine and his school on dissipative structures—complex spatial and temporal patterns created by the dissipation of energy in the presence of suitable nonlinearities. It was a time of rekindled interest in nonlinear dynamics. On the mathematical side René Thom's theory of structural stability was emerging on the broader scientific horizon. The 1960s renaissance in dynamical systems theory was bringing itself to bear on questions of biology and economics. On the physical side models based on collective and coherent dynamics, such as the synergetics models of Haken and the dipole oscillation models of Fröhlich, were attracting attention. From physical chemistry and molecular biology came the hypercycle model of Eigen. These and congener ideas mixed with concepts of evolution, morphogenesis, and immunity (in particular Jerne's network theory) to create a vibrant mix that still colors work in theoretical and mathematical biology today.

Prigogine's work on dissipative structures, for which he subsequently won the Nobel Prize, stood out, I believe, because it contemplated nonlinear kinetic models in a conceptually coherent thermodynamic context. The analysis made a three-point landing on the methodology of the mathematics, the generalities of the physics, and the particularities of chemistry, and in addition addressed the broad issues of order and evolution in a way that could reach across to basic questions of biology. But Prigogine's talk in Tübingen dealt not with this, but rather with new work on the fundamental relation between dynamics and thermodynamics.

The approach followed the methodology that has dominated physics since the advent of relativity theory at the beginning of the century: to seek descriptions that are invariant to schemes that transform the "perspectives" of different observers into one another. Prigogine's talk introduced a rather radical extension of this approach, to transformations between dynamical and thermodynamical modes of description. The physical motivation is quite reasonable since the main point of statistical mechanics is to construct averaging procedures that make dynamic and thermodynamic descriptions equivalent, at least in those regions where good thermodynamic observables are available. The extension perhaps seemed overly radical to most of the audience since the required transformation is nonunitary, therefore entropy increasing. Since the macroscopic description is clearly irreversible the implied microscopic dynamics must also exhibit elements of irreversibility, leading to a breakdown in the classical concept of a trajectory, in clear contradiction to features inherent in both the classical and quantum mechanical equations of motion.

For reasons connected with my own scientific interests (part of my doctoral dissertation concerned the connection between quantum measurement, irreversibility, and evolution) I followed the development of Prigogine's transformation theory over the years, and have had the opportunity to discuss the theory directly with him on a number of occasions. My impression is that his physical interpretation of the theory, which was only in very preliminary form at the time of the Tübingen talk, has undergone a substantial evolution. My aim in this interview (conducted through two telephone discussions) was to elicit his current views on this, and to explore his thoughts about implications for biology.

Perhaps, I thought, the famous debate between Ostwald and Boltzmann would bring the issue to center stage. My understanding was that Ostwald held that entropy increase is irreducible, while Boltzmann argued that it should be put on an atomistic basis, a view that is commonly associated with an ignorance interpretation of entropy increase. I recalled reading Sommerfeld's account of this debate, and his stated preference for the atomistic position. Who would Prigogine side with?

The response was that my descriptions of the positions, especially Boltzmann's, were only partially correct. Ostwald was a positivist and an energeticist. His position was motivated by a rejection of the atomistic interpretation. Boltzmann was the first theoretical physicist to give a microscopic interpretation of irreversibility, to bridge the gap between thermodynamics and dynamics. One has to go back to 1865, when Clausius presented his entropy theory. Physicists said this was just a nice tool for engineers and physical chemists. Nothing very new. Laws with broken symmetry, such as the Fourier law, were known. So most physicists reacted by ignoring the problem. Boltzmann was the exception. He was influenced by Darwin, by Darwin's ability to explain biological evolution through the concept of populations. The nineteenth century, Boltzmann thought, would be the century of Darwin. He sought a population dynamics, like Darwin's, but for a population of molecules. It was very successful, yielding kinetic equations and the H-theorem. The really interesting point, though, is that something strange appeared. The basic equations of motion were time reversible and thus people became concerned with the origin of irreversibility.

Boltzmann thought he could derive irreversibility from dynamics. But, continued Prigogine, the reaction of Poincaré and the other big scientists of the day was negative. Poincaré thought it was a conceptual contradiction. Boltzmann retracted, at least implicitly, by treating irreversibility as a question of probabilities. Irreversibility was identified with the progressive change of occupation number. The implication is that irreversibility is only apparent, just a question of time scale. Time then is an illusion, and this was the opinion of the leading scientists, such as Einstein.

Prigogine allowed that he was always amazed that this negative conclusion did not create a crisis in science. For a pendulum you don't know what is earlier or later; but not so for a chemical reaction which approaches equilibrium.

Is nature timeless, or not describable as a pendulum? According to Prigogine ideology has dominated the thinking on this. Scientists wanted to think not in terms of events, but rather in terms of universal laws of nature that had more the character of theological knowledge. It is closer to God, as Prigogine phrases it, if you can know present, past, and future.

But for Prigogine the paradox of time only became stranger and stranger. It appeared in three fields. The first is nonequilibrium thermodynamics. This was a turning point since the whole idea of dissipative structures is that nonequilibrium regimes give rise to structure. Irreversibility is in a sense a new parameter, and the idea that it is artificial becomes difficult.

Second, there is the rediscovery in dynamics of chaotic systems, of dynamics that can lead to stochastic-appearing behavior. One can no longer speak about trajectories for these systems. Is this a matter of computational limitation? Yes, answers Prigogine, but hastens to add that he will say it is also a matter of fundamental importance.

The third appearance is in physics, where theory deals with laws and not events. General relativity, for example, is a timeless theory. But the big bang is an event. Quantum mechanics, with its necessity for an observer, is another example. Measurement is an event, and it implies irreversibility.

The problem of time thus "emerged in a new and urgent way," and for Prigogine in a way that clearly strains the concept of time as illusion. When Prigogine says that his effort "was first to convince himself that time is real" it might be rather surprising to the student cramming for an exam. But it shouldn't be surprising to the student cramming for a physics exam.

Where, then, could irreversibility be hidden in dynamics? The key idea is dynamic instability. The approach traces back to Kolmogoroff, Arnold, and Moser, and to progress in the field of nonintegrable systems. Intregable systems, the usual dynamics, in principle form a complete description of planetary or other periodic motions. Consequently, Newtonian physics appears closed, affording no opening for the arrow of time. But this is not true for nonintegrable systems. Here new solutions can be extracted from classical equations. Nonintegrable systems are not closed, and as a consequence a second type of time becomes possible—a topological time connected with the number of foldings or deformations that must be introduced. The connection to chaos is evident (just think of Rössler's rotating taffy machine, where the rotations, stretchings, and foldings can pull neighboring points on the taffy far apart, and make neighbors of far apart points). As he and his coworkers have shown, integrability for "nonintegrable" systems is possible in the complex plane, and one senses Professor Prigogine's enthusiasm about the progress that has been made by his group in this area over the past few years (see References). The physical connection is through resonances, since fields interacting in a resonant way are a source of nonintegrability.

But Prigogine can illustrate his point with a more commonplace example: a glass of water. It can be a young glass or an old glass. It depends on correlations. Time flows in the direction of an increasing number of particle correlations. Aging means that there are more correlations, and it is in this concept of aging (I believe) that Prigogine sees the unification of dynamics and thermodynamics.

Can this model account for quantum measurement? Would it not be a hidden variable theory and (according to Bell's theorem) entail some sort of action at a distance, therefore a major departure from classical dynamics in any case? No, answers Prigogine; it is a solution at the level of probability distributions, not at the level of the wave function. There is no implication so far as hidden variables are concerned.

Does the model allow evolution theory to have a fundamental status? After all, if the probabilities that contribute to the variation in variation and selection are fictional we would have t conclude that the fundamental conceptual scheme of biology is ultimately just as much a matter of illusion as time in the classical physical models. Prigogine's response was that evolution theory would only be meaningful in an unstable dynamical world, therefore only in terms of chaos. Again, there should be an internal dynamical level which includes time, just in the topological sense mentioned above. Presumably the answer would be the same if I had posed the question in terms of the antinomy of determinism and indeterminism.

What about psychological time? Prigogine presumes that this also has its ultimate basis in correlation, but quickly points out that this cannot be direct, since too many levels of complexity are involved.

Do the laws of physics have to be expanded (to accommodate biology)? Prigogine reiterates that the Newton/Schrödinger type models only describe a small fraction of the universe, the integrable systems. The enlargement that he contemplates clearly involves the assimilation of unstable dynamics. My question was perhaps not complete enough to elicit a direct answer, but I am not at all left with the impression that he is contemplating, for example, any sort of broken symmetry that uniquely manifests itself in biological phenomena.

Are there practical implications? It is only the beginning, Prigogine points out. One goes from trajectories to diffusion. Nonintegrable systems are all around; they include interacting fields as well as all problems treated in nonequilibrium statistical mechanics. The program is to make a noncontradictory universe in which time symmetry breaking is just at the basis of the description. For treating such phenomena as intelligence, the procedure for removing the contradiction should not make a big difference. The new model does not invalidate present approaches to mathematical and theoretical biology, since these can be dealt with at a higher macroscopic level. The reason is that there are two types of chaos: the chaos that leads to equilibrium through attractors, and the more fundamental dynamical chaos that is connected with the correlations. The uncertainty we see, the variations in behavior, reflect the contributions of missing dynamics. But I sense that the answer is ambiguous. Certainly Prigogine is saying that culling up these missing dynamics is not going to invalidate phenomenological models of evolution, morphogenesis, immunity, and intelligence. But he is also saying it is just the beginning, and at least for this interviewer it is irresistibly amusing to contemplate whether it would indeed always be possible to completely bury missing dynamics in higher level parameters. And if not, would the approximate burial achieved by phenomenological models be adequate to span the functional capabilities of organisms?

Is there an example, aside from the glass of water (and aside from the resonances not discussed here)? I recall that Prigogine's talk at the 1983 Synergetics Meeting in Pushchino elicited this question from an irritated member of the audience. Unhesitatingly came the reply: "The whole world."

References

T. Petrosky, I. Prigogine, and S. Tasaki: "Quantum Theory of Nonintegrable Systems", Physica A, to appear.

T. Petrosky and I. Prigogine: "Alternative Formulation of Classical and Quantum Dynamics for Nonintegrable Systems", Physica A, to appear.

T. Petrosky and H. Hasegawa: "Subdynamics and Nonintegrable Systems", Physica A, 160(1989) 351-385.

I. Prigogine and T. Petrosky: "Poincaré's Theorem and Unitary Transformations for Classical and Quantum Systems", Physica A, 147(1988) 439-460.

AN OPEN LETTER FROM NSF

Dear Colleague:

Promoting collaboration among the biological, computational, and mathematical sciences represents a special challenge for the National Science Foundation. Striking advances in biology, computer science, and mathematics are creating opportunities for important collaborative work. Biological fields such as molecular biology, neuroscience, and ecosystems offer challenging computational and analytical problems. Meanwhile, revolutionary developments in analytical methods, computation theory, and computer hardware are widely thought to have important application to these problems. However, establishing and supporting an environment for effective interdisciplinary research requires the cooperative action of the research community and the research programs at NSF. This letter is the first of several to enlist your participation in a broadly based research effort in mathematical and computational aspects of modern biological problems. We will also use these letters to keep you apprised of our plans and progress toward this goal.

It is interesting that present collaboration between biological scientists, on the one hand, and mathematical and computer scientists, on the other hand, continues a long tradition of biological influence on the basic models and methods of computing and mathematics. For example, many of the models of computation studied by computational theorists over the past forty years are explicitly motivated by biological systems. Entire subdisciplines, such as artificial intelligence and neural network processing, have developed in part from the desire to provide a computational explication of overtly biological phenomena. In the more distant past, the work of Darwin and Mendel transformed biology and dramatically broadened the horizon for biological research, generating new problems that attracted the attention of mathematicians and statisticians. In particular, the mathematical efforts of Galton, Pearson, and Fisher to resolve biological questions helped form the field of modern statistics.

Today, widespread technical and popular discussions are calling attention to such intriguing problems as the following: (1) unraveling the meaning of the billions of nucleotides that make up the human genome using analytical and algorithmic methods, (2) visualizing how the folding and knotting of DNA affects its function, (3) representing in a scientific database biological diversity by millions of elements with changing and sometimes ill-defined components, (4) modeling the complete human nervous systems with its 10^{15} connections representing nonlinear relationships among 10^{12} components. In nearly all major biological subdisciplines, the underlying processes of interest are now thought to be "information rich" and in need of study by computational and quantitative tools and methods.

Following the recommendations of several NSF sponsored workshops at this interface, it is our intention, over the next several years, to increase NSF support for interdisciplinary research in computational and mathematical aspects of the biological sciences. We are specifically interested in new research that makes significant contributions to biological, computational, and mathematical research.

We believe that the best ideas for research within a field of science originate from the investigators themselves. Therefore, the examples mentioned in this letter are given only to illustrate, not to limit, the scope of this interdisciplinary support.

For the coming year, proposals addressing computational and mathematical problems in biology should be directed to the "regular" research programs, i.e., in mathematics, computer science, or biology. (A description of all NSF programs can be found in the publication,, Guide to Programs: Fiscal Year 1991, NSF 90-25.) In most cases, advance discussions with NSF program officers will help investigators determine the best programs for their work. Interdisciplinary teams are especially encouraged to apply. Only one proposal for any project need be submitted. We are committed to cooperation in the review and possible funding of interdisciplinary proposals.

We are particularly concerned with promoting infrastructure in the scientific community to facilitate the work of biological, computational, and mathematical scientists in work at interdisciplinary interfaces. The development of shared vocabularies, research goals and methods, conferences and journals, and value systems are, in our view, an essential part of any such collaboration. Accordingly, we have a special interest in fiscal year 1991 in supporting activities that lead to improved infrastructure. These activities might include highly directed "summer schools", workshops or symposia that seek to increase the joint awareness of scientists in the basic problems and research modes of the others' disciplines. By the same token, proposals whose aim is to make it easier and more desirable for young scientists to undertake such interdisciplinary research, are of interest.

We believe this is an exciting venture that will further biology while leading to advances in mathematics and computer science that will prove to be of as great and lasting significance as the works of Galton, Pearson, and Fisher in mathematics or von Neumann, Wiener, and McCulloch and Pitts in computer science. We encourage you to participate by contacting NSF program officers for further information and discussions of your ideas, for interdisciplinary (team) research proposals as well as for infrastructural support.

Sincerely,

Richard A. DeMillo, Director, Division of Computer and Computation Research, (202) 357-9747.

Yi-Tzuu Chien, Director, Division and Information Robotics and Intelligent Systems, (202) 357-9572.

Judith S. Sunley, Director, Division of Mathematical Sciences, (202) 357-9669.

John Wooley, Director, Division of Instrumentation and Resources, (202) 357-9880.

AWARDS

Nancy Kopell, Professor of Mathematics at Boston University, has been awarded a MacArthur Fellowship and will receive $290,000 from the Chicago-based John D. and Catherine T. MacArthur Foundation over the five-year course of the award.

Dr. Kopell uses and develops methods of dynamical systems to attack problems of applied mathematics. She is especially interested in questions involving self organization in physical and biological systems. With L.N. Howard, she has written a series of papers on pattern formation in oscillating chemical systems. Recently, with G.B. Ermentrout, she has been concerned with developing mathematics appropriate to analyzing neural networks that govern rhythmic motor activity, such as walking, swimming and breathing. Such systems are, roughly, large collections of units, each of which is an oscillator or a close mathematical relative of an oscillator. The aim of the mathematics is to help sort out which properties of the units and their interactions have implications for the emergent properties of the networks. The techniques include extensions of invariant manifold theory, averaging theory and geometric methods for singularly perturbed equations. The current work has led to the formation of a highly interactive group of physiologists and mathematicians, headed by Dr. Kopell. In addition, she is also currently interested in geometric techniques in dynamical systems.

Nancy Kopell

Literary Events

Theoretical Biology for Science and Technology. This is a book series newly established by Chapman and Hall, and edited by Michael Conrad, Werner Ebeling (Institute of Theoretical Physics, Humboldt-University, 1040 Berlin, Fed. Rep. Germany), and Koichiro Matsuno (Dept. of BioEngineering, Nagaoka University of Technology, Kamitomioka, Nagaoka, 940-21, Japan). The series encompasses fundamental issues in theoretical biology in a manner that is pertinent to nature and science in general and to biotechnological applications in particular. It is intended as an outlet for books dealing with the conceptual foundations of biology, and with computional, mathematical, and physical approaches to these foundations. Proposals should be submitted to one of the editors listed above.

Nanobiology. This new quarterly international bioscience journal (to be published by Carfax Publishing Company) will focus on the basic mechanisms of living systems at the nanoscale, including biochemical, electromagnetic, quantum mechanical, and logical aspects which collectively lead to self-organization, communication, and computation within living cells. The Chief Editor is Per Anders Hasson (CST Ltd, 67 Shakespeare Road, London W7 1LU, UK).

Chaos, Solitons and Fractals. To be published by Pergamon Press in 1991, this new journal will deal with nonlinear science and applications in science and engineering. The Executive Editor is Professor M.S. El Naschie (Sibley School of Mechanical and Aerospace Engineering, 105 Upson Hall, Cornell University, Ithaca, NY 14853, USA).

Ecological Applications. This new quarterly journal from the Ecological Society of America focuses on researach dealing with the integration of ecological science and concepts with their applications and implications. The Editor-in-Chief is Simon Levin (Section of Ecology & Systematics, 347 Corson Hall, Cornell University, Ithaca, NY 14853-2701).

International Symposium on Mathematical Models of Cellular Processes. This special issue of Biomedica Biochimica Acta (Vol. 49, No.8/9, 1990) contains twenty-eight of the papers presented at a meeting held in 1989 in what was then the GDR. The meeting was organized by Reinhart Heinrich and Hermann-Georg Holzhütter.

Mathematical Models in Medicine, ed. by Matthew Witten, Pergamon Press, Oxford, 1988. This is the second volume of the series, *Advances in Mathematics in Computers and Medicine*. Topics covered include lymphocyte differentiation, cytometric issues, cancer related topics, disease modeling and simulation, and analytical approaches to mechanisms of thrombopoiesis.

Biological Complexity and Information. ed. by H. Shimizu, World Scientific, Singapore, 1989, 328 pp. Information, brain complexity, semantics, and consciousness are the themes addressed in this proceedings of a conference held in Japan. A unique feature of this volume is that it includes papers that seek "the amalgamation of the Eastern and Western ways of thinking."

Modeling and Computer Methods in Molecular Biology and Genetics (USSR Academy of Sciences, Siberian Branch, Novosibirsk, 1990). These are the abstracts of an international conference on bioinformatics, organized by the Institute of Cytology and Genetics in Novosibirsk from August 27 to September 1, 1990. The editors are N.A. Kolchanov and V.A. Ratner. Topics include computer analysis of nucleotide sequences; computer analysis and modeling of protein structure; molecular evolution theory, modeling of molecular-genetic systems; molecular biological data banks; program packages for molecular genetic and molecular biological data analysis; and new computer techniques in molecular biology and genetics (expert systems, other artificial intelligence techniques, and knowledge bases).

Interdisciplinary Training in Computational Neurobiology

The National Science Foundation has newly established an innovative program for students investigating the neurobiology of cognition. The program's focus is the interpretation of cognitive functions in terms of neuroanatomical and neurophysiological data and mathematical modeling. Such functions include perceiving, attending, learning, planning, and remembering in animals and humans. A carefully designed program of study prepares each student to perform original research investigating cortical function at multiple levels of analysis. State of the art facilities include: computerized microscopy, electrophysiological instrumentation, the Pittsburgh Supercomputing Center, and brain scanners. This is a joint program between the University of Pittsburgh, its School of Medicine, and Carnegie Mellon University. Each student receives full financial support, travel allowances, and a computer workstation. Applications are encouraged from prospective graduate students and post-doctoral fellows with interest in biology, psychology, engineering, mathematics, physics, and computer science.

For information contact Walter Schneider, Program Director, Neural Processes in Cognition, University of Pittsburgh, 3939 O'Hara Street, Pittsburg, PA 15260, or Bard Ermentrout, Department of Mathematics, University of Pittsburgh, Pittsburgh, PA 15260 (EMAIL: phase@pittsvms.bitnet).

In Memoriam

David Garfinkel, *May 18, 1930—February 8, 1990*
(Contributed by Michael C. Kohn)

David Garfinkel died one year ago after an eight-month fight against cancer. David was a pioneer in the techniques of computer modeling of metabolic systems, an interest he developed as a postdoctoral fellow when computers first became widely available. He was often told that his ideas were too advanced; the problems in which he was interested were too difficult to be addressed using the existing machines. Yet, even then he saw the potential role computer simulation could play in elucidating the biochemical mechanisms underlying the behavior of complex biological systems.

David received his A.B. degree in biochemistry with highest honors (equivalent to *summa cum laude*) from the University of California at Berkeley in 1951. He was elected to Phi Beta Kappa. He received his Ph.D. in biochemistry from Harvard University in 1955. His dissertation, "The Raman Spectra of Amino Acids, Peptides, and Proteins," was completed under the guidance of John T. Edsall and pointed towards a career as an experimentalist. Indeed, David was one of the first to isolate cytochrome b_5 from liver (D. Garfinkel, *Biochim. Biophys. Acta.* **21**:199, 1956). However, he soon became more interested in theoretical subjects.

Except for a brief period as a research biochemist at New York State Psychiatric Institute, David spent his entire professional life at the University of Pennsylvania in Philadelphia, initially at the Johnson Research Foundation and later in the Department of Computer and Information Science. Almost immediately his research suggested novel regulatory mechanisms. In a computer simulation of intermediary metabolism in ascites tumor cells, he proposed that the enzyme phosphofructokinase is subject to feedback activation by fructose bisphosphate (D. Garfinkel and B. Hess, *J. Biol. Chem.*, **239**:971, 1964). This was later confirmed experimentally.

One of his major research projects was the simulation of metabolism in perfused rat hearts. His models yielded remarkable insights into the metabolic response of the tissue to changes in fuel or work loan and to stress such as anoxia or reduced perfusate flow rate. An especially satisfying prediction was that an increase in work load stimulated a transient increase in glycogenolysis and, hence, output of the waste product lactic acid. Prior to this work, glycogen was not considered an important source of fuel for the heart. The original experiments (performed in the early 1970s) on which the model was based did not show the predicted spurt of lactate production, because no measurements were made in the first 30 seconds following the increase in the work load. The experiments were repeated with a new sampling schedule, and the predicted spurt of lactate was observed (M.J. Achs, D. Garfinkel, and L.H. Opie, *Am. J. Physiol.*, **243**:R889, 1982).

Repeatedly, David's models suggested that lactate output was under metabolic control; the acid did not passively diffuse through the lipid of the cell membrane as many contended. David established a collaboration with an experimenter, who measured the kinetics of lactate export. The results clearly indicated the presence of a permease specific for short-chain monocarboxylic acids (S.C. Dennis, M.C. Kohn, F.J. Anderson, and D. Garfinkel, *J. Mol. Cell. Cardiol.*, **17**:987, 1985). As predicted by the heart models, lactate and pyruvate compete for transport on this carrier. The transport rate is largely governed by the pH gradient across the plasma membrane.

David strongly believed that mathematical and computer approaches to studying complex systems must be accessible to nonspecialists. He was instrumental in the development of new computer techniques and implemented them in easy-to-use programs. These include the BIOSSIM program for metabolic modeling (G.-C. Roman and D. Garfinkel, *Comput. Biomed. Res.*, **11**:3, 1978) and the widely used PENNZYME program for optimization of parameters in enzymatic rate laws (M.D. Kohn, L.E. Menten, and D. Garfinkel, *Comput. Biomed. Res.*,**12**:461, 1979; S.D. Schremmer, M.R. Waser, M.C. Kohn, and D. Garfinkel, *Comput. Biomed. Res.*,**17**:289, 1984). His research group applied the engineering method of "decomposition" to modeling complex biological systems and automated the technique in the DEMOS program (L.E. Menten, M.C. Kohn, and D. Garfinkel, *Comput. Biomed. Res.*, **14**:91, 1981). Toward the end of his life he was working on application of relational data bases and expert systems to biochemical modeling.

David's life stands as a testimonial that theoretical concerns do matter in biological science. As our knowledge of living systems increases, they are revealed in their exquisite complexity. When intuition fails to uncover the hidden patterns in our observations, computer modeling is another key to unlock Nature's door.