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Kiyosi Itô: Father of Stochastic Analysis >>>


Kiyosi Itô at the Statistical Bureau of the Japanese Government in 1942

Kiyosi Itô has made great contributions to the advancement of the mathematical sciences by laying the foundations of the theory of stochastic differential equations and of stochastic integration in 1942. He has also played a leading role in the subsequent development of these areas into a core chapter in modern probability theory, known as stochastic analysis.

Since the early 1950s the theory of stochastic differential equations has been gaining new perspectives through interactions with various branches of mathematics, including partial differential equations, potential theory, harmonic integrals, differential geometry, and harmonic analysis. However, this theory has wound up reaching far beyond the confines of mathematics. Itô's theory of stochastic differential equations and the corresponding extension of classical calculus to highly irregular curves such as Brownian motion paths, now known as the "Itô calculus", are indispensable tools in analyzing random phenomena in fields as diverse as physics, biology, economics, and engineering.

The research on filtering initiated by R. Kalman could not have developed to its current stage without stochastic differential equations. In mathematical finance, in particular, in the research of F. Black, R. Merton and M. Scholes, for which Merton and Scholes received the 1997 Nobel Prize in Economics, stochastic differential equations and "Itô's formula" play crucial roles.

Itô has made significant contributions to many other topics as well, such as the Wiener-Itô chaos decomposition, one-dimensional diffusion processes, excursion theory for Markov processes, and infinite-dimensional diffusion processes. Itô's work in stochastic analysis, along with the central role he has played in its subsequent development, typifies twentieth-century mathematical sciences — having mathematical depth and strong interaction with a wide range of areas.

Itô was elected a member of the Japan Academy of Sciences in 1991 and a foreign member of the Académie des Sciences of France in 1989 and of the US Academy of Sciences in 1998. He has received many prizes which include the Japan Academy Prize (1978), the Wolf Prize (1987) and the Kyoto Prize (1998). He is also the recipient of the first Carl Friedrich Gauss Prize, awarded at the International Congress of Mathematicians at Madrid in 2006. He has also been conferred honorary degrees by Université Paris VI (1981), ETH Zürich (1987), and the University of Warwick (1992).

A symposium in honor of Kiyosi Itô will be held at the Institute for Mathematical Sciences at the National University of Singapore from 10 to 11 July 2008. This symposium is jointly

Continued on page 2

Contents

Continued from page 1

organized with the Research Institute for Mathematical Sciences at Kyoto. It is also a satellite conference of the 7th World Congress in Probability and Statistics, 14 - 19 July 2008, sponsored by the Bernoulli Society and the Institute of Mathematical Statistics, also to take place in Singapore.

The objective of the symposium is to gather together leading mathematicians and scientists to deliver expository lectures on Itô's work, the historical development of stochastic analysis, and the influence and impact of stochastic analysis in various branches of mathematics and science. It will be aimed at mathematicians and scientists in general.

The organizing committee of the symposium consists of Hans Föllmer, Masatoshi Fukushima, Ed Perkins and Yoichiro Takahashi. The invited speakers are: Alain Bensoussan, Donald Dawson, Masatoshi Fukushima, Shigeo Kusuoka, Pierre-Louis Lions, Terry Lyons, Shinzo Watanabe and Marc Yor.

Louis Chen
National University of Singapore

and

Hans Föllmer
Humboldt University of Berlin

The 2006 Gauss Prize presented to Kiyosi Itô by IMU President Sir John Ball (courtesy Kiyosi Itô)

When Atoms Catch a Cold >>>

Mathematicians and physicists condensed

We all have had on occasion the unpleasant experience of catching a cold. But have you ever wondered what would happen when atoms catch a (very severe) cold? In 1925, Satyendra Nath Bose proposed some rules ("Bose statistics") for studying light quanta (photons). When he encountered difficulties in getting his idea published, he sent his paper to Einstein, who recognized the merits of the idea and also applied it to construct a theory of how atoms would behave in a gas. The theory predicted that at temperatures very near absolute zero, a large fraction of the atoms would collapse to the lowest quantum mechanical energy level. When that happens, the affected atoms would lose their individual identities and quantum effects become apparent at the macroscopic level. The super atom-conglomerate in this state is called a Bose-Einstein Condensate (BEC) in honor of the first proposers of its existence. The first physical realization of a BEC took place in 1995 at NIST-JILA lab at the University of Colorado at Boulder. It was produced by Eric Cornell and Carl Wieman, who together with Wolfgang Ketterle of MIT shared the Nobel Prize in Physics in 2001.

Quantum behavior can often seem counterintuitive because our everyday experience lies with macroscopic objects. So it is not surprising that the realization of BEC, which brings quantum effects to the macro-level, fascinates researchers. After the initial breakthrough, BECs built of different atoms and exhibiting various properties have since been produced in a number of laboratories. Theorists have been kept busy building, refining and exploring models of BEC behavior. The field as a whole has been undergoing exciting and explosive growth on both the experimental and theoretical fronts.

During the last two months of 2007, the Institute hosted a program on *Bose-Einstein Condensation and Quantized Vortices in Superfluidity and Superconductivity*. Over a hundred local and foreign scientists, ranging from applied and pure mathematicians, theoretical and experimental

Continued on page 3

Continued from page 2

physicists, to computational scientists, shared their own expertise while interacting and learning from other participants of the program.

Two week-long workshops were held during the program. The first workshop focused on experimental progress, scientific modeling, mathematical analysis, numerical simulation and applications of BEC. The second workshop was on the topics of quantized vortices in BEC, superfluidity and superconductivity as well as kinetic theory.

Interspersed among the workshops were two weeks of tutorial lectures designed to provide graduate students and non-experts with background and introduction to various aspects of BEC. Weizhu Bao (NUS) and Dieter Jaksch (University of Oxford) and Francois Peeters (Universiteit Antwerpen) delivered lectures on mathematical modeling, numerical algorithms and basic physical theory of BEC, as well as work on optical lattice physics and the theory of quantized vortices in superfluidity and superconductivity.

In a public lecture on ``Quantum World of Ultra-Cold Atoms'', Christopher Foot (University of Oxford) described the tremendous advances in physics which made possible the realization of BEC. He explained how laser light was used to trap atoms and cool them to within a millionth of a degree above absolute zero. In a second public lecture entitled ``Applied Partial Differential Equations: A Visual Approach'', Peter A. Markowich (University of Cambridge, UK and University of Vienna, Austria) fascinated the audience with photographic illustrations of topics in science and engineering that are modeled by means of partial differential equations. The chosen topics, drawn from physics, biology and engineering, well illustrated the power of mathematics in the study of the natural world.

-- Weizhu Bao and
Denny H. Leung
National University of Singapore

Christopher Foot: Ultra-cool magic

Peter Markowich: Reducing dimensions

Fanghua Lin: Heat flows and eigenvalues

People in the News >>>

Béla Bollobás and Oliver Riordan Honored

Béla Bollobás and Oliver Riordan, both of the University of Cambridge, were honored by the London Mathematical Society in 2007. Bollobás was awarded the Senior Whitehead Prize "for his fundamental contributions to almost every aspect of combinatorics". Riordan was one of four recipients of the Whitehead Prize "for his contributions to graph polynomials, random graphs, extremal combinatorics, models of largescale real-world graphs, and percolation theory". Bollobás was chair and Riordan one of the co-chairs of the Institute's program on *Random Graphs and Large-Scale Real-World Networks* (1 May - 30 June 2006).

Eric Maskin, Nobel Laureate

Eric Maskin of the Institute for Advanced Study shared the Nobel Prize in Economics in 2007 for his work in Mechanism Design Theory – a theory of optimal allocation under institutional arrangements. Maskin delivered a lecture at the Institute's program on *Uncertainty and Information in Economics* (9 May - 3 July 2005). An interview with him was featured in the August 2005 issue of *Imprints*.

Programs & Activities >>>

Past Programs in Brief

Bose-Einstein Condensation and Quantized Vortices in Superfluidity and Superconductivity (1 November - 31 December 2007)

Website: http://www.ims.nus.edu.sg/Programs/bose07/index.htm

An article on BEC and describing this program in detail is found in this issue of *Imprints*.

Data-driven and Physically-based Models for Characterization of Processes in Hydrology, Hydraulics, Oceanography and Climate Change (6 - 28 January 2008)

... *Jointly organized with Pacific Institute for Mathematical Sciences, UBC*

Website: http://www.ims.nus.edu.sg/Programs/ocean07/index.htm

This 3-week program consisted of a full week of seminars/lectures, and two weeks of workshops. At the end of each activity day, there was a discussion on topics of the day. The main topics were: (1) Development of a fully integrated data driven and physical-based models for water resources management, (2) Dynamic and Statistical Downscaling on Climate Change Study and (3) Nonlinear Wave Dynamics and Tsunami Modeling. The Institute also saw a number of graduate students who came from China, Korea, Malaysia,

Continued on page 4

Programs & Activities >>>

Continued from page 3

Indonesia, Singapore, Thailand and Vietnam to attend the program. This is a continual effort of the Institute to provide training of graduate students and young scientists. On the last day of the program, a special arrangement was made for the overseas participants to visit Singapore Changi Water Reclamation Plant (WRP) and NEWater* Visitor Centre (NVC).

* NEWater is treated used water that has undergone stringent purification and treatment processes using advanced dual-membrane (microfiltration and reverse osmosis) and ultraviolet technologies. NEWater is mixed and blended with reservoir water and then undergo conventional water treatment to produce drinking water (a procedure known as Planned Indirect Potable Use or Planned IPU).

Hydro-modelers collected

Jim Zidek: Model reconciler

Shie-Yui Liong: Managing water resources

Hans-Rudolf Künsch: Predicting regional climates

Roger Grimshaw: Making solitary waves

Van-Thanh-Van Nguyen: Talking up downscaling

Tea-inspired water modeling

Upcoming Activity

Workshop on Stein's Method (31 March – 4 April 2008)

Website: http://www.ims.nus.edu.sg/Programs/stein08/index.htm

Stein's startling technique for deriving probability approximations first appeared about 30 years ago. It provides a tool for obtaining them in a wide variety of situations, including those in which dependence plays an important part. In contrast to many approaches, his method delivers estimates for the error in the approximation, and not just a proof of convergence in some limit. Nor is there in principle any restriction on the distribution to be approximated; it can equally well be normal, or Poisson, or that of the whole path of a random process. Since Stein's pioneering work, much has been done to refine and develop his method, but it remains a highly active field of research, with many outstanding problems, theoretical as well as in applications. The aim of this workshop is to bring together many of the mathematicians at the forefront of this effort, to report on the newest developments and to initiate further joint projects. Young mathematicians are encouraged to participate in the meeting, and to share in our enthusiasm for the field.

Next Program

Mathematical Imaging and Digital Media (5 May – 27 June 2008)

Website: http://www.ims.nus.edu.sg/Programs/imaging08/index.htm

Co-chairs
Tony Chan, *University of California, Los Angeles*
Zuowei Shen, *National University of Singapore*

Members
Say Song Goh, *National University of Singapore*
Hui Ji, *National University of Singapore*
Seng Luan Lee, *National University of Singapore*
Andy M. Yip, *National University of Singapore*

Continued on page 5

Continued from page 4

Mathematical imaging is a multidisciplinary field that synergizes many areas of science, technology and mathematics to provide solid foundation, new ideas and techniques and understanding of almost every aspect of imaging science, ranging from hardware design to image enhancement, from image representation to image understanding, and from modeling of pattern formation to synthesis of artistic graphics.

Digital media comprises hardware and software systems that enable real-time human-machine interaction. It involves a wide range of technologies that cut across various disciplines in sciences, mathematics, engineering and computer sciences with applications in diverse fields, including communications, education, medicine, finance, games, entertainment and lifestyle.

The purpose of this program is to conduct multidisciplinary studies involving mathematical perspectives and foundation of imaging science and digital media. The focus will be on the following themes.

1. Mathematical Imaging and Digital Media: Mathematical methods for computer graphics, computer vision, mesh generation, image restoration and reconstruction, image enhancement, image segmentation, object detection, image decomposition, image representation, image compression.

2. Wavelet Theory and Applications: Sparse data representation and approximation by wavelets and redundant systems, noise removal, stochastic wavelet analysis, inverse problems via wavelet methods.

Activities

Workshops:

I. Chinese-French-Singaporean Joint Workshop on Wavelet Theory and Applications, 9 – 13 June 2008
II. Workshop on Mathematical Imaging and Digital Media, 16 – 20 June 2008

Summer School: 26 May – 20 June 2008
Suitable for senior undergraduates and graduate students, the Summer School will consist of three weeks of tutorials and student oriented seminars which will cover basic mathematical theory of imaging, PDE and variational methods, wavelet methods and applications to digital media and biomedical imaging. Limited funds are available for support of participation of graduate students. For more information, please visit http://www.ims.nus.edu.sg/Programs/imaging08/index.htm

Programs & Activities in the Pipeline

Symposium on Pure and Applied Analysis (21 April 2008)

... Jointly organized with Department of Mathematics

http://www.ims.nus.edu.sg/Programs/pure_sym08/index.htm

Organizing Committee:
Louis Chen, *National University of Singapore*
Shih-Hsien Yu, *National University of Singapore*

The Symposium is organized to mark the initiation of academic exchange between IMS and the Liu Bie Ju Centre for Mathematical Sciences at the City University of Hong Kong. Professors Roderick Wong and Philippe G. Ciarlet, Director and Deputy Director of the Liu Bie Ju Centre respectively, will be among the speakers.

Summer School in Logic (30 June - 26 July 2008)

... Jointly organized with Department of Mathematics

http://www.ims.nus.edu.sg/Programs/logicss08/index.htm

Speakers – Theodore A. Slaman and W. Hugh Woodin,
University of California at Berkeley

The 2008 Logic Summer School will consist of two parts, one in recursion (computability) theory and the other in set theory, running in parallel. The lectures will be conducted by Professors Theodore A Slaman and W Hugh Woodin of the University of California at Berkeley. In addition to lectures, there will be classroom discussions of mathematical problems for participants led by senior graduate students. The Logic Summer School is a collaboration between researchers at the University of California, Berkeley, Chinese Academy of Sciences and the National University of Singapore.

Symposium in Honor of Kiyosi Itô: Stochastic Analysis and Its Impact in Mathematics and Science (10 - 11 July 2008)

... Jointly organized with Research Institute for Mathematical Sciences, Kyoto

Website: http://www.ims.nus.edu.sg/Programs/kiyosi08/index.htm

Co-Chairs
Hans Föllmer, *Humboldt-University of Berlin*
Masatoshi Fukushima, *Osaka University*

Members
Edwin Perkins, *University of British Columbia*
Yoichiro Takahashi, *Research Institute for Mathematical Sciences, Kyoto*

The objective of the symposium is to gather together leading mathematicians and scientists to deliver expository lectures on Itô's work, the historical development of stochastic analysis, and the influence and impact of stochastic analysis

Continued on page 6

Continued from page 5

in various branches of mathematics and science. It will be aimed at mathematicians and scientists in general.

7th World Congress in Probability and Statistics
(14 - 19 July 2008)

Jointly sponsored by the Bernoulli Society and the Institute of Mathematical Statistics
Jointly organized by the Department of Statistics and Applied Probability, Department of Mathematics and Institute for Mathematical Sciences of the National University of Singapore

Website: http://www.ims.nus.edu.sg/Programs/wc2008/index.htm

Chair of Scientific Program Committee:
Ruth Williams, *University of California, San Diego*

Chair of Local Organizing Committee:
Louis Chen, *National University of Singapore*

This meeting is a major international event in probability and statistics held every four years. It features the latest scientific developments in the fields of probability and statistics and their applications. The program will cover a wide range of topics and will include about a dozen plenary lectures presented by leading specialists. In addition there will be invited paper sessions highlighting topics of current research interest as well as many contributed talks and posters.

Mathematical Horizons for Quantum Physics
(28 July - 21 September 2008)

Website: http://www.ims.nus.edu.sg/Programs/mhqp08/index.htm

Program Coordinator
Huzihiro Araki, *Kyoto University*

Co-chairs
Berthold Georg Englert, *National University of Singapore*
Kwek Leong Chuan, *Nanyang Technological University*

Secretary
Jun Suzuki, *National University of Singapore*

Quantum theory is one of the most important intellectual developments in the early twentieth century. Arguably, the field of Mathematical Physics, equally at home in mathematics and in physics, emerged from John von Neumann's seminal work on the spectral theory of linear operators in Hilbert space which was triggered by the birth of quantum theory in the mid 1920s. This is just one historical example of how the mathematical insights and tools that are developed in the course of answering challenging mathematical questions arising from physical problems have contributed to the advance of both mathematics and physics. In this tradition, it is the objective of this program is to bring together mathematicians, whose work has a bearing on quantum physics, with researchers in mathematical physics and theoretical physics, whose work will benefit from the mathematical progress. The collaboration between these scientists of different background, different expertise, and different scientific culture will bear fruit on the research of all participants by intellectual cross-fertilization.

Activities

The program will consist of four overlapping three-week sessions, each devoted to a selected topic. At the start of each session, there will be presentations by the discussion leaders to lay the groundwork. There follows an intense period of about 20 days of discussions and close collaborations among the participants. The session ends with talks summarizing the progress accomplished and a round-table discussion defining future problems and areas of close collaboration.

Session 1: Quantum Control and Dynamics
(28 July–17 August 2008 (weeks 1-3))
Session 2: Operator Algebras in Quantum Information
(11–31 August 2008 (weeks 3-5))
Session 3: Non-equilibrium Statistical Mechanics
(25 August–15 September 2008 (weeks 5-7))
Session 4: Strongly Interacting Many-Particle Systems
(1–21 September 2008 (weeks 6-8))

Highlights of Other Activities

Workshop on Mathematical Models for the Study of the Infection Dynamics of Emergent and Re-emergent Diseases in Humans (22 - 26 October 2007)

Website: http://www.ims.nus.edu.sg/Programs/infectious07/index.htm

This one-week workshop brought together researchers from a wide spectrum of mathematical and statistical epidemiology to integrate and synergize the strengths of mathematics, statistics and epidemiology to the understanding of disease dynamics and to propose control strategies. Invited speakers from Australia, Brazil, Canada, China, Hong Kong, Singapore, The Netherlands, UK and USA covered themes such as (1) vector-borne infections, (2) directly transmitted infections, (3) sexually transmitted infections and (4) antibiotic infections. Two public lectures were also held in conjunction with the workshop. The first lecture was given by Eduardo Massad of University of São Paulo and

Becoming infected by disease dynamics

Continued on page 7

Continued from page 6


Eduardo Massad: Vectors of diseases


Nina Fefferman: Taming of the flu


Paul Anantharajah Tambyah: Antibiotic questions


Infected enthusiasts of infection dynamics

was entitled “Mathematical Models of Dengue Fever”. The second lecture, “Real People, Virtual Worlds: Watching a Plague Unfold”, was delivered by Nina Fefferman of Rutgers University and Tufts University.

Fourth Asia Pacific Meeting of the Economic Science Association 2008 incorporating a neuroeconomics symposium (22 - 24 February 2008)

Jointly organized by Department of Economics, Institute for Mathematical Sciences, and Department of Marketing

Sponsored by Institute for Mathematical Sciences, Risk Management Institute, Faculty of Arts and Social Sciences, and NUS Business School

Website: http://nt2.fas.nus.edu.sg/ecs/wkshop/ESA/index.asp

The 4th Asia Pacific Meeting of the Economic Science Association was held at the National University of Singapore on 22 – 24 February 2008. Professor Barry Halliwell, Deputy President (Research and Technology) of NUS, gave the opening address at the Institute.


Building a chapter in economics

The focus of the symposium was neuroeconomics broadly defined, encompassing behavioral and experimental economics as well as incorporating methodologies from the biological sciences. The keynote speakers included Bernard Balleine of University of California, Los Angeles, Peter Bossaerts of Ecole Polytechnique Federale de Lausanne, John Dickhaut of University of Minnesota, Kenji Doya of Okinawa Institute of Science and Technology and Drazen Prelec of Massachusetts Institute of Technology.


Barry Halliwell: An economic exchange


John Dickhaut: Fine perspective of economic institutions


Peter Bossaert: Neurobiology of uncertainty

Continued on page 8

Continued from page 7

The meeting was organized to promote greater interest in laboratory based experimental research in economics and the social sciences in the Asia Pacific. It also marked the founding of an Asia Pacific Chapter of Economic Science Association (ESA).

Economic neurons in action

Workshop on High-dimensional Data Analysis (27 – 29 February 2008)

... Jointly organized with Department of Statistics & Applied Probability

Website: http://www.ims.nus.edu.sg/Programs/hidim08/index.htm

According to the executive summary of the 2004 NSF Report on the future of statistics, "among the highest priorities for statistics today is adapting to meet the needs of data sets that are so large and complex that new ideas are required, not only to analyze the data, but also to design the experiments and interpret the experimental results". The statistical community had clearly embraced this vision, which saw the Issac Newton Institute for Mathematical Sciences organize a large scale six-month program on *Statistical Theory and Methods for Complex, High-Dimensional Data* from January to June, 2008. To complement their program, the Institute organized a regional workshop, with participants from China, Taiwan, India and Singapore, and with the aim of promoting regional networking and collaboration. The workshop focused on three sub-themes, namely (1) Large dimensional random matrices, (2) Functional data analysis and (3) Sparsity issues and model selection in high dimensional problems.

Arup Bose: Spectral entities from higher dimensions

Ker-Chau Li: Statistical trilogist

Jin-Ting Zhang: Testing with two samples

Multi-dimensioned data analysts

Public Lecture

Avner Friedman, Director of Mathematical Biosciences Institute of the Ohio State University, who also serves on the Institute's Scientific Advisory Board, gave a public lecture on "What is Mathematical Biology and How Useful is it?" in December 2007. In the lecture, examples were shown of biological and biomedical problems that have been addressed by the use of mathematical models. They highlight the fast-growing applications of mathematical and quantitative techniques to the field of Biological Sciences.

Avner Friedman: Marriage of mathematics and biology

Mathematical Conversations

Ron Shamir: Unraveling Genes, Understanding Diseases >>>


Ron Shamir

Interview of Ron Shamir by Y.K. Leong

Ron Shamir made significant contributions to optimization and graph algorithms and is one of the leaders in bioinformatics and computational biology whose pioneering work contributed to the historic completion of the ambitious Human Genome Project in 2003.

He went from Tel Aviv University and the Hebrew University to the University of California, Berkeley for his PhD in operations research. While he is based mainly at Tel Aviv, he has held visiting research positions at top universities and research centers in Seattle, Rehovot, Rutgers and Berkeley. A full professor in the School of Computer Science of Tel Aviv University since 2000, he holds the Raymond and Beverly Sackler Chair in Bioinformatics. He was also the head of the School of Computer Science at Tel Aviv.

He is actively involved in organizational and committee work for international scientific meetings. He has been invited to give lectures at major scientific meetings, research institutes and leading universities throughout the world. He is well-known for his tremendous energy of scholarship in reviewing activities and in serving on the editorial boards of many leading international journals in discrete mathematics, computer science, bioinformatics and computational biology – among them SIAM Journal on Discrete Mathematics, Journal of Computer and System Sciences, Journal of Computational Biology, IEEE/ACM Transactions on Computational Biology and Bioinformatics.

As the leader of an active and internationally well-known group (ACGT) on algorithms in computational genomics at Tel Aviv, he sets the direction of and contributes extensively to the research that has produced algorithms and software for gene expression analysis, genotype analysis, graph-theoretic tools for modeling biological systems and statistical software for whole genome association studies. Among other things, he continues to contribute to one of the central problems of the post-genomic era, namely the determination of the function of genes and pathways.

He was an invited speaker at the Institute's program on *Algorithmic biology: Algorithmic techniques in computational biology* held from 1 June to 31 July 2006. *Imprints* took this opportunity to interview him on 18 July 2006. The following is an edited and enhanced version of the transcript of the interview, in which he talked about the excitement of switching from a mathematical realm in theoretical computer science to uncharted virgin territory in bioinformatics and computational molecular biology. Here he also gives us an insightful glimpse of the "brave new world" of modern biological sciences and its impact on human life.

Imprints: You did your PhD at the University of California at Berkeley in optimization. Could you describe the route that took you from operations research to biology?

Ron Shamir: I did my PhD in operations research, but with a very strong computer science tendency. One of my advisors, Ilan Adler, was from the operations research department and the other, Dick Karp, was from computer science. I joined the department of computer science in Tel Aviv a couple of years after that. I worked mainly in the field of optimization problems until around 1990. At that time I was on sabbatical in New Jersey at the DIMACS [Center for Discrete Mathematics and Computer Science] institute, and I did some work on temporal reasoning – in this problem one has to place events as intervals on the time line based on given constraints on the relations between event pairs. At some point there was a workshop and I presented this work, and the late Gene Lawler was in the crowd, and he told me, "Listen, this is very appropriate for modeling physical mapping of DNA." I didn't know what DNA was or what physical mapping was. Indeed, physical mapping just deals with constraints of intervals along the line, but the intervals are not temporal events but actual DNA blocks. So I started reading biological articles and got excited about this field. It was in the early days of the Human Genome Project, and I found myself part of this new field – in the beginning only partially, but eventually this became my main research interest. The first steps of this transition occurred in Rutgers,

Continued on page 10

Continued from page 9

New Jersey, but of course, a lot of things happened in the following years.

I: Was there a group doing research in that field?

S: Practically no. There was one colleague of mine, Haim Wolfson, who was working on structural problems related to biology from the geometric point of view and who got into the field a little earlier. But even so the term "bioinformatics" was not invented yet. We have set up our first formal bioinformatics program in the year 2000 at Tel Aviv University. We came a long way since, with a very strong and active bioinformatics community across the university, including over 15 groups in computer science, life sciences, medicine, physics and engineering.

I: Did it occur to you to continue your work in the United States?

S: No. I got several offers over the years, but never seriously considered accepting them. Israel is my home country, the home of my family, of my nation, and of my mother tongue. Of course, scientifically such offers were tempting, since the research conditions in the United States are better, but science is not everything to me.

I: What is the difference between bioinformatics and computational biology?

S: Actually I don't think there is a difference. It used to be thought that bioinformatics dealt more with the databases and software, and computational biology used to deal with algorithms. In the past, I used them as two distinct terms, but I do not make the distinction because people are using them interchangeably. We ended up calling our BSc and MSc programs (which should have been called "computational biology") "bioinformatics", because this is the term people are using. Semantically, there is also a technical difference. Bioinformatics is primarily informatics (computer science), and computational biology is primarily biology. But in the way people use these terms, it is the reverse.

I: Structural genomics is often considered as an investigation into the language of genes. Has linguistics or the study of human languages cast any insight into genomics?

S: I don't have much to say about this because I don't know linguistics well enough. The only aspect of it that I am aware of is natural language processing. It's not really linguistics. It deals with collecting the relevant words from large texts like the collection of millions of scientific abstracts and the like. So in that sense, the mechanics of trying to parse scientific texts has been used. I would say that, in general, such approaches were pretty successful, but of course they are not as accurate or provide "clean results" as human investigators would do on the same task. It is good as an initial filter but it lacks human intuition and broad context understanding.

I: Is it correct to say that gene determination is more of a computational and statistical problem rather than a systems problem?

S: It's a mixture. I don't think you can separate them. Gene determination using just statistical or just computational methods has been successful in a limited sense. A few years after the human genome has been completely sequenced, we still do not have the full picture of the genome because our prediction tools are not accurate enough. People have been using additional species to try to get better gene prediction. People have been using the systems approach. I think we are still a few years away from coming up with the ultimate set of genes. This can only be done with integrated methods that use what we will learn from systems biology and comparative biology approaches, and, of course, from classical experimental methods in biology.

I: Are there any general principles which help you to say that there are only 5 percent of the genes that remain to be determined?

S: Five percent is just a metaphor, not a solid number. It is a rough guesstimate based on extrapolation of what is already known. Five to ten years ago, we thought that most of the gene regulation occurs at the level of transcription, and now all of a sudden, we have this huge wealth of mRNA, siRNA, microRNA, etc. that changes the picture completely. Who knows what else there is that we are not aware of at this point? For example, there is very exciting work about ultra-conserved regions in the genome that we don't know the structure and function of and there must be a reason that they are so conserved. There is a lot of signal probably hidden at the level of the packing of the DNA and making certain regions more exposed and or accessible for transcription. There's definitely much more in the genome than what we know at this time. There are a lot of exciting revelations waiting for us. That is what makes the field so interesting.

I: In that case, it will depend a lot on the technological advances available at present.

S: Definitely, a lot of it depends on the ingenuity of experimental scientists and on technology development.

Continued on page 11

Continued from page 10

I: Has computational work on DNA nucleotides yielded general principles of genome evolution?

S: I think this is probably one of the oldest areas in computational biology because research on evolution and on phylogenetic trees has been an active research area since the 60s. It's a very old area, on the computational biology scale. I do believe we know much more about the selection forces that act on the DNA. At the time of Darwin the belief was that positive selection was probably the dominant force. The general belief now is that most of the evolution is neutral. There are exceptional cases of either positive or negative selection, but neutral evolution is now believed to be more dominant. Of course, there may be surprises in stock for us in the "junk DNA" region, which covers the majority of the genome, and of whose evolutionary role we understand very little now.

I: By neutral, do you mean that it is random?

S: Yes, most of the changes in the DNA do not affect the well-being of the phenotype; most of the mutations are neutral. Occasionally a combination of such mutations will have an effect – even a dramatic effect – on the phenotype.

I: Could it be that anything we don't understand, we say it is "random"?

S: We just don't understand it at this point. We are in the dark but it's definitely not random. Take the occurrence of ultra-conserved regions. It's definitely not random, it's statistically very significant, but we don't understand the role of these regions.

I: If I understand it correctly, much of the DNA of the human genome is considered to be "junk DNA" in the sense that they do not contain recognized functional elements. How can we be sure that indeed they do not contain "recognized functional elements"? Is it possible that they may contain such elements which we are ignorant of?

S: Definitely, yes. There are probably a lot of functional elements that we are not aware of either because we don't have the technologies to identify them or we simply didn't ask the right questions. What happened during the last 5 to 10 years has shown us that our knowledge is very limited. For example, what happens now with the genome-wide chips is that we used to think that expressions happen only in the regions coding for genes, and now all of a sudden we have evidence showing that a lot of expressions is going on in non-coding regions, contrary to what we thought before. The same thing happens with the binding sites of transcription factors. We used to look at them only in promoter regions. Now when you look at the binding in a genome-wide fashion, using ad-hoc chips and some of the techniques developed here in Singapore; you see that there is binding all over the genome, very far from known promoters. So definitely there is a lot of function out there that we are not aware of.

I: It may seem daunting for an outsider to go from biology into computational biology or from computer science into biology. From your experience, what is the least painful, if not the best, way to make such a transition?

S: Luckily for the young generation of students, there are already integrated programs. For example, in Tel Aviv University, we have, back in 2000, set up an undergraduate program where students get a full double major in computer science and biology plus a specialization in bioinformatics. So they can really speak both languages. We now also continue a similar program into the graduate level. For the young generation, it is simple. The transition for someone already educated in one of the three fields is indeed not easy. The different disciplines use different languages, both in terms of terminology and in terms of culture. I came from computer science and mathematics. To me a proof is something where you can write "QED" at the end. Once you've done it, the problem is solved. In biology, the notion of a proof is very different. A proof can be re-proved and un-proved. The notion of a definition that we cherish in mathematics does not exist in biology. The terms keep changing their meaning because of new light that is shed on them. A lot of the difficulties in the beginning were created since each area had its own culture and its own way of thinking. There are some cultural barriers in between. Many biologists of the previous generation are not that eager to try to speak the mathematical language. Many mathematicians are not eager to speak biology.

The transition that I went through – going from computer science and mathematics to computational biology – is easier than the transition required for a biologist if he or she does not have any basic training in computation, because first of all, the language of computation is very formal and very hard to pick up in an informal way. You really have to go to classes or digest the textbooks. Also, mathematics is very structured. You cannot learn "B" before you learned "A". Almost everything is very dependent on prior theory, in contrast to biology which is much more "flat". Another advantage for someone making the transition from the computational side is that biologists have wonderful textbooks – they are very clear and full of illustrations. The textbooks in computer science or mathematics are much less

Continued on page 12

Continued from page 11

friendly; so trying to learn from the literature in mathematics or computer science, if you don't have any prior training, is much harder than trying to learn biology from the books. Even so, it is not easy. It's a difficult process. If you ask, "What is the easiest path?" the easiest path is to be 18 now. Then you can learn it in an integrated way. There are very good programs both in Europe and in the United States. I don't know if you already have such programs here for undergraduates.

I: We have started to some extent, but we are at quite an elementary stage and still developing.

S: I would suggest – I don't know whether you have considered it or not – even if you don't train the next generation of biologists in computational biology, train them in computation. Have them learn one or two courses on basic principles of computation so that they will have basic knowledge in this "foreign language". It is worth the effort to include it into the biology curriculum. Also, give mathematics and computer science students one or two courses in life sciences, just the principles, so that they will be closer in language. Then, in graduate school, if they decide to go into the other area, they will have an easier start.

I: What about asking computer scientists to write better books?

S: That would be great, but you need people who will be willing to put in the effort. I think it's mainly a marketing issue. There are very good books for software manuals, simply because there are many thousands of people who will buy it. Biology is taught to millions of students. Computer science students are ten-fold or twenty-fold fewer; so there is not enough demand. There is not sufficient reward to simplify these texts; it's really hard work to turn something complicated into friendly and simple concepts. And in the end, there is only so much that you can simplify – mathematics is a formal language and a formal discipline.

I: How much benefit has the complete mapping of the human genome yielded to the medical and clinical sciences?

S: Tremendously, and it's only the beginning. For example, we know by now, as a by-product of the Human Genome Project, the causal genes for the majority of the Mendelian diseases. A tremendous amount of knowledge that we now take for granted wasn't there without the Human Genome Project. It has already made a tremendous difference and it will continue to. For example, the hapmap projects which aim to map all the single nucleotide polymorphisms, are still under way. They have already revealed millions of mutations which make the difference between all of us – different features, different life expectancy and so on. Getting such information would have been inconceivable without the reference human genome. We talk about "the human genome" as if it is a unique genome, but it's just a reference. But once you have a reference, you can start zooming in on individual mutations to see how they relate to diseases. I think we are going to reap the benefits of this visionary project for many decades.

I: This sounds like a reductionist view in biology – that everything can be reduced to the genes.

S: Well, not everything. If you can explain 50 percent of diseases just by looking at the genotype and the other 50 percent by other causes, this is a great step forward. In 5 or 10 years, you will be able to have your full genome sequence, for a reasonable cost, and the doctor can tell you, "Look, you don't have to worry about smoking because with your gene combination, it will not make any difference. On the other hand, you should be very worried about your cholesterol or whatever." I don't think the genes are everything, but they account for quite a lot. They will tell us whether someone is more likely to have a particular disease than others, and if a certain lifestyle is going to make a difference for him or her in terms of quality of life. Of course, all this is a blessing but also a curse because the genetic information must be used and not abused. To a large extent, this is not only a thing of the future but is already here today. People have been doing pre-natal tests to identify all kinds of defects, and they will be able to do much more – and more post-natal tests in the future. We can't stop this knowledge, so we'd better use it for the best of our understanding.

I: Maybe in the future we will be able to look at a person's genome and say that he or she will have a stroke at a certain age.

S: I don't think it will be able to tell you that – but it can give you probabilities. You will be able to tell someone that changing the lifestyle will make a big difference in her case. Definitely. Eventually, it's all probabilistic. There are relatively few cases of combinatorial fate. It's up to us. The more we know, the more we can control it.

I: Is there a gene that determines the lifespan of an individual?

S: Probably much more than one gene. In mice, scientists found a gene that affects longevity very significantly. We

Continued on page 13

Continued from page 12

know that this has a lot to do with the shrinking of the telomeres during the life of a creature. It's not a single gene but quite a few genes affect longevity.

I: In that case genetic engineering can lengthen lifespan.

S: That's one of the dreams. I think real genetic engineering in humans is still far ahead, but in principle, we might be able to do so.

I: It seems that in biblical times people had long life spans by modern standards.

S: I think that they just counted differently... They talk about Abraham and Sarah, and Sarah had a baby when she was 90. They probably lived, in modern way of counting, to the age of 30 to 35. Life expectancy at that time was much shorter than it is today.

I: Research in genomics and proteomics usually involves multi-disciplinary team effort whereas the tenure system in the universities (at least in the United States) centers round individual achievements. For that reason, a prominent biologist has said that progress in modern biology will come from institutes of research rather than the universities. Do you agree with this viewpoint?

S: No. First of all, the university system is not that blind to joint effort. Credit will be given to several partners in case of joint work. Even in publications from research institutions, there is the first author, the second author and the last; so credit is not spread totally equally. Institutions outside universities have other advantages over the universities because they may be more flexible, and resources can be moved more easily, but I don't think the issue of credit for work is the primary issue. In my own university we at Computer Science School have a lot of joint projects with colleagues in the Medical School and the Life Sciences Faculty. If we are successful, then everybody takes credit for the success. The question of how this credit is partitioned is there, but it is not specific to universities. I don't think that the tenure system is an obstacle to interdisciplinary research.

I: For the younger faculty, the emphasis is on single papers rather than joint papers. In that sense, a younger faculty will not want to risk going into another field.

S: But on the other hand, I have some young colleagues in my university, some of whom were my students in the past. In bioinformatics and computational biology, a lot of what they do is joint work. On one hand, it's not single-author papers, but on the other hand, they are involved in more projects, so they have more papers. It balances out. How many research projects can you carry out just by yourself? If you work with other people, you can be involved in more projects because you only do part of each project. I may be naïve about it, but I don't know of cases where this is the main obstacle.

I: You are heavily involved in many projects at the same time. How do you manage to do it?

S: I've been very lucky to have wonderful students. In the last few years, I was also heading the School of Computer Science in addition to running my group and teaching, etc. The secret is really to have wonderful students. You don't need to guide them on every little detail. Once the group has a critical mass, there is joint effort and there is a lot of assistance by the mature students to the younger ones. Also, it's more fun to do more diverse things. I may be doing a little too much, but I have 4 or 5 different areas that I try to be active in. As long as each of these areas is exciting to me and as long as I have such wonderful students, I will continue. As my group is quite large, I seldom work on my own. I work with others, mainly students and also colleagues. Students do individual projects, they get individual credit for them and write theses. It's mostly individual work but it's done in a framework of a supportive and unified group.

I: If I may say so, mathematicians are quite notorious in working mainly on their own without getting involved with others.

S: You are right. It's a different culture in computational biology. In my early years, my papers had only one or two authors, but my papers of today may have 4 or 6 or sometimes 10 authors. Part of it is because it is the culture of a different field. Part of it is because the projects are more complex and have more aspects and require more diverse expertise. They are not as deep as pure mathematics projects but they are complex and therefore there are many people and sometimes several groups involved.

I: You hold a number of patents. Do they pertain to the algorithms or the source codes of the software?

S: Only algorithms. The codes are typically protected by copyright, which is a different type of protection. Actually all these issues are handled by the technology transfer unit at Tel Aviv University. They define what justifies patenting and also copyrighting for software. All the tools we develop are completely free for academic use, and we make an effort to make our tools useful for the academic community.

Continued on page 14

Continued from page 13

Occasionally, there is interest from the pharmaceutical and biotech industry. In that case, licensing and patenting have to be addressed. But for me, the issue of patenting is of low priority. It is more important for me that our tools will be useful to others. Our software is not as robust and as convenient as commercial software. We don't have the resources to do this, and I also cannot give academic credit to students for doing work that is purely technical, like graphical interfaces. This work is more appropriate for a company. If at some point, some company would like to take the algorithms and the basic software and package them into something fancy, that would be great. We package the software to make it useful for us, and also, we hope, useful for other academic groups and occasionally to pharmaceutical companies.

I: Have you ever gone back to your original field in optimization?

S: I never really left it. I still find it interesting and I still try to find the optimization or graph-theoretic problem behind any computational problem that we address. Over the years, I realized that you have to compromise in terms of elegance what you do in order to be useful to the biologists. Perhaps 99 percent of the problems in bioinformatics are NP-hard, and only occasionally you can develop approximation algorithms for them.

I: Typically, in spending your time, do you want to dwell on the theoretical aspect of the problem or do you want to find something that works?

S: According to my training, I would, when I just started out, devote 100 percent of my time to the theoretical aspect of the problem. But if you really want to get new findings in biology, you have to compromise: you will not have time to prove everything rigorously, and you need to develop codes and not just algorithms, because the algorithms by themselves are not useful to the biologists or the medical people. But I still think of many of these problems in terms of optimization. Interestingly, in Operations Research, there is a strong emphasis on modeling. You have a real-life problem and a big challenge is to formulate it mathematically in a useful way – for example, as an optimization problem in integer programming. In recent years, I realized that in biology, a big and sometimes crucial part of the research is getting to the right problem formulation. In that respect, I am more appreciative now of the emphasis on modeling than I used to be when studying operations research. In addition to optimization, I find myself doing much more statistics than I was trained to, since the bioinformatics area requires it.

Publications >>>

The main objective of the Lecture Notes Series is to make available to a wider audience the notes of the tutorial lectures given at the Institute's programs in their original or revised form. The Series will occasionally include special lectures and workshop proceedings organized wholly or jointly by the Institute.

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I: Is computer simulation done in bioinformatics?

S: Some people do it, particularly for modeling the dynamics of networks. There is also a lot of the use of Monte Carlo methods (I don't know whether you would call them simulation in the strict sense). When it is very difficult to theoretically analyze a particular distribution of outcomes, you can just sample it and see how the results are distributed. It's quite efficient in practice. Of course, there is also the whole field of molecular simulation where you try to study the dynamics of folding and interactions between molecules and which is a huge area that requires tremendous computational resources.

I: From a simple-minded point of view, is it possible to have a model to simulate the rules of combination of the genes by random selection from a large pool of the building blocks of genes?

S: In principle, probably yes, but we are still very, very far away from that.

Leonid Bunimovich: Stable Islands, Chaotic Seas >>>

Leonid Bunimovich

Interview of Leonid Bunimovich by Y.K. Leong

Leonid Bunimovich has contributed to the fundamental understanding of dynamical systems and made important applications of probability and statistics to geophysical hydrodynamics, neuroscience, operations research, statistical mechanics, mathematical biology and numerous other scientific areas.

Bred in the great Russian tradition of probability, statistics and mathematical physics of the well-known and influential mathematician Yakov Sinai, Bunimovich began his research interests in Moscow University and quickly developed his own original and independent approaches to various problems in genetics, geophysics, biology, statistical physics and other scientific areas outside mathematics – problems that he encountered in his scientific journey that crossed the high seas and great continents. Even before the political convulsions that shook and broke up the former Soviet Union in 1991 took place, his seemingly chaotic path in academia finally found a niche for him in the School of Mathematics of the Georgia Institute of Technology. Holding the Regents' Professorship, he was the director of the Southeast Applied Analysis Center at Georgia Institute of Technology, and continues as the director of its successor program – the Applied & Biological Contemporary Mathematics Program. He is a winner of the Humboldt Prize and serves on the editorial boards of numerous leading international journals on applied mathematics and mathematical physics. He is actively engaged in organizational work for many scientific meetings around the world. He has traveled widely to major research centers as visiting professor and been invited to speak at major scientific meetings around the world.

Bunimovich was in the organizing committee of the Institute's program on *Dynamical chaos and non-equilibrium statistical mechanics: From rigorous results to applications in nano-systems* held from 1 August to 30 September 2006. He was interviewed on 17 August 2006 by Y.K. Leong on behalf of *Imprints*. The following is an edited and enhanced version of the transcript of the interview in which he traced the unusual scientific odyssey that took him physically to many places and scientifically into numerous disciplines which speak the language of mathematics. He gives us a first-hand account of scientific discovery and a bird's eye view of the enigmatic landscape at the interface of physics and mathematics which underlies the tantalizing field of chaotic dynamics. He also gives us an insight into the politics of a monolithic ideology that impeded the development of the biological sciences in the vastest political empire that dominated the world in the 20th century.

Imprints: Your PhD in Moscow was in probability and mathematical statistics while your Doctor of Science was in theoretical and mathematical physics. Was there a switch of research interest or was it more of a "natural" transition of research interest? What motivated it?

Leonid Bunimovich: It was not a switch of research interest. I graduated from the department of probability theory and was a student of Professor Sinai who is the major person in dynamical systems and one of the greatest mathematicians of our time. He was a student of Kolmogorov. I was working on the statistical properties of dynamical systems. This again goes back to Kolmogorov. The general view is that there are random phenomena, and there are deterministic phenomena, but in his short paper of 1958, Kolmogorov built a bridge between the world of random systems and the world of deterministic systems. This was the major event that started the revival of ergodic theory, which is the statistical theory of dynamical systems. At that time, it was considered to be essentially a finished area of mathematics. All of a sudden it started to evolve and grow enormously. This is considered to be one of the major developments in science, not only in mathematics, in the 20th century. My thesis was in stochasticity of dynamical systems, where a new mechanism of stochasticity, later called a mechanism of defocusing, was discovered. Ergodic theory was created in the works of Boltzmann and Gibbs on statistical mechanics. My Doctor of Science dissertation was on applications of these new ideas in ergodic theory to statistical mechanics.

After getting my PhD from Moscow University, I didn't work a single day as a mathematician in the Soviet Union because of political reasons. This is why there was such a long gap between my two dissertations as well. I "was allowed" to defend my Doctor of Science dissertation after perestroika started and there was some kind of transition, but scientifically, there were no real changes besides a possibility to travel to scientific meetings abroad. I worked

Continued on page 16

Continued from page 15

in many areas, but because of the strange, not usual way, I did not work as a mathematician after graduating from what was considered the best university in the world and defending an outstanding PhD. The same thing happened to many young mathematicians of Jewish origin. So I worked in many places. Maybe that is why my scientific interests and the questions I worked on are broad and perhaps even strangely broad.

I: You were actually applying a lot of mathematics to other problems after your PhD.

B: That is exactly what happened. I needed to work somewhere and couldn't find a job, not only me. The political situation was very bad and I believe that the disintegration of the Soviet Union started at that time; it was just concluded in 1991. I had to support my family, I was already married. So I found a job – it was 32nd place where I applied. It was at the Institute of Psychiatry of the Academy of Medical Sciences. They wanted to hire a mathematician because the institute had a computer. Two years later, when the computer broke down, they asked me to repair it. They thought that since it was a mathematical machine, mathematicians must be able to repair it. By then I had done some work in psychiatry and genetics. They realized that I could do something there besides repairing computers. So they hired an engineer to repair it, and I retained and continued my job there.

I: It seems that your scientific journey from Moscow University to Georgia Institute of Technology has been a very long one. Was it a planned one or did it just happen?

B: It was not planned at all. It was life with all its turns and changes, so on and so forth. For instance, my first job was in psychiatry and I applied mathematics to real problems in psychiatry and genetics. It is again the history of the Soviet Union. I was the only mathematician speaking at the First All-Union Conference of Medical Genetics. In Stalin's time, genetics was considered as capitalist science; it was forbidden, and many researchers working in this area were sent to camps. In high school we never studied genetics. I learned it only after coming to the Institute of Psychiatry and was fascinated by it. There were already new developments. Geneticists who had spent some time in prisons and camps and survived there came back and were working again on genetics, which again became an "allowed" science. They were much older than me. I was then under 30. When there were PhD defenses, it was very interesting for me. There were two people needed to read the thesis – the first was usually very senior, and the second sometimes was me if mathematics was used in the thesis. After the defense, it was the Russian tradition to have a banquet. That was where I learned a lot of real history of Soviet genetics. I wasn't doing mathematics, but I was doing an exciting science, and many people suffered much more than me. I couldn't complain.

I: Is the banquet after the defense organized by the department?

B: It's usually organized by the person who made the defense. It was just a traditional celebration. It is paid for by himself, but more often by his parents. It was the tradition that parents were very happy to have educated kids and sacrificed a lot.

I: Your research interests are wide ranging. Do you think that the Russian system of education has something to do with the range of your research interests and inclination?

B: It depends. In my case, yes. As everybody knows, Kolmogorov was one of the greatest mathematicians of the last century. Take his work on turbulence – it's the basis of turbulence theory for physicists. He was a mathematician, but he laid the foundations of modern turbulence in a 4-page paper. This is the style that I always admire. New clear ideas lead to some clear implications for real world problems. The longest time that I worked in the Soviet Union was in the Institute of Oceanology. This is, in fact, my third trip to Singapore. The first time that I came here was as a sailor essentially. Twenty-six years ago, I came with a scientific ship. I came here the second time, two years ago, and the changes in Singapore were very impressive.

I: Did you do any kind of experiments on board the ship?

B: I was a theoretician there, but almost everybody was an experimentalist. It was a long journey, about 4 months. I was young and strong and could help to carry heavy instruments, not just do theory. Most of the journey was devoted to the experimental studies of the oceans. On the way back, it was another thing. I had only a short time to somehow think over the results and to come up with simple models that would show that the results of measurements were correct and novel. I learned also to value the work of the experimentalists and how to talk to them, although they talked a different "language". Kolmogorov had also been on such a journey earlier on. He was there when his theory was under investigation. He really wanted people to check his theory with experiments. Then he published another paper which took into account the measurements. Of course, it was his influence. It was the style of his school. For example, when I was an undergraduate, my supervisor Professor Sinai would tell me about some dynamical system and said, "This is an interesting system. Look into that." But he did not always tell me what I should prove. By the way, some of the problems Sinai brought up came out of the research of one of the organizers of this program, Professor Zaslavsky, who was a physicist at Novosibirsk at that time.

I: The Russian tradition seems to be that theoreticians, even pure mathematicians, have a close interest in data and experiments.

Continued on page 17

Continued from page 16

B: It's actually not like that. A great majority of pure mathematicians, because of the same reasons as mine, did not work as mathematicians but worked in some applied institutions. They naturally didn't like that and were not much interested in what was going on around them. Most of them were really pure mathematicians and didn't really understand what the physicists and engineers were talking about. They don't give definitions. It's a kind of personal thing whether you are willing to understand the things which are not exactly defined. For me, a formulation of a new mathematical problem and proof of that for some natural (hopefully visual as well) examples is much more important and exciting than trying to prove this for more and more and more general classes of systems. More and more technical ideas are needed for that, often combinations of various techniques, but I always prefer simple proofs. Now, sometimes a mathematical community gets embarrassed if a simple proof is found for a long-standing problem, whereas it should be to the contrary.

I: Would you consider yourself to be some kind of theoretical physicist?

B: In fact, some of my friends and colleagues call me a physicist. I don't think there is a big difference. I don't have a broad training and background in physics though it was part of our education. But I'm really interested in physical problems. It also depends on your scientific taste. Many of my results are just examples, and you can build a lot of generalizations on them. I'm more interested in the phenomena, maybe it's a more physical approach. I think all this is science. What I don't like in the US, for instance, is that they always say "Mathematics and Science". What is really part of the Russian mathematical system is that there are no sharp borders between scientific disciplines. If you remember, Francis Bacon, founder of natural philosophy, said, "Any science reaches a really high level only when it manages to use mathematics."

I: Is chaotic dynamics a recent development of the chaos theory of the seventies?

B: "Chaos" is (actually was for a long time) a very good selling word. Chaos is just a part of that new branch of science which Kolmogorov founded in 1958, twenty years before the word "chaos" was coined. It was called stochasticity of dynamical systems, which means that dynamical systems, purely deterministic systems, can demonstrate the same behavior as purely random systems. It was a real physical and even philosophical discovery. To the general public or people who give funds, what is "stochasticity of dynamical systems"? It is something vague. So "chaos" was coined and chaos is only part of this general area of stochasticity of dynamical systems. Chaotic dynamics is just one face of complex dynamics. The first book on this subject was published by George Zaslavsky in 1970 under the title "Stochasticity of Dynamical Systems". But "Chaos" completely took over. You know, when something becomes more fashionable, you give up something else.

I: The term "chaotic dynamics" seems to suggest more of a physics discipline.

B: It's not only a branch of physics. It's a branch of science – it's also chemistry, biology, geology, geophysics and many other disciplines. But, of course, first of all, physics. Physicists are mathematically trained and they can use the computer better than mathematicians. This is why it was first used in physics. There are many physical systems that develop chaotic behavior. What is the basis of that? Historically, what people knew for centuries, starting with Laplace and even before, is that if you knew exactly the initial conditions of your equations, and the functions involved are sufficiently smooth, then there is a unique solution that can completely predict the evolution of the system. But in practice, if you have any measuring device like a thermometer in physics or medicine, you never have complete precision. You know approximately how you drive your car, approximately 50 mph, maybe 51, but not 51.603. In any practical situation, you work with some such small set of data, not a point. You study the evolution of this small set, and very often it does not look like the evolution of points. This is where all the chaotic dynamics occurs. You have very good precision at the beginning, but with time you lose it. Your prediction can only be statistical.

I: What are some of the central problems and recent advances of chaotic dynamics?

B: This is a kind of natural evolution and development. The major discoveries were in the late 50s and 60s by Kolmogorov, Sinai, Smale, Arnold, Moser, Anosov. Dynamical systems evolution can be very complicated. Another of Kolmogorov's work said that not only a dynamical system's evolution can be complex, but the simplest (integrable) dynamics in Hamiltonian systems is actually stable. It is the celebrated Kolmogorov-Arnold-Moser (KAM-) theory. In practice, you see all those things that are stable under small perturbations. There was a general belief though in physics that if you take a surface (manifold) of constant energy, then the motion is ergodic there, uniformly distributed, but KAM-theory said that it's the opposite situation if you have integrability. Integrability is stable, chaoticity is stable as well. The studies so far took care of these two polar situations – complete chaos and near integrability. The most challenging problem now is: what is in between? The system is neither integrable nor chaotic. Instead, it has a mixed behavior – sometimes it's divided phase space – you have islands of stability in phase space that are called KAM- islands, situated in a chaotic sea. It is much more difficult to study such intermediate

Continued on page 18

Continued from page 17

systems. Some methods were developed to study the chaotic dynamics, another totally different methods were developed to study stable dynamics. But, at the border of these islands in chaotic seas, you cannot apply any of these methods. This is the major challenge and development.

Dynamical systems behave like stochastic processes. First of all, we are looking at the simplest random processes – coin tossing, independent random variables. But most often, in applications you don't see independent random variables, you don't see Markov processes, but you see processes with infinite but decaying memory. This is a much more difficult problem. There were some breakthroughs. For instance, the simplest examples were found which demonstrate the co-existence of islands and chaotic dynamical systems. By studying these examples, one can completely analyze the system and generalize the theory. The basis of the theory of dynamical systems and ergodic theory often comes from some simple classical examples. One of the major efforts now is the study of the so-called Arnold diffusion – if you start in the chaotic region, how does the particle move between the islands? Does it move fast or slowly, can it move far and so on?

Another development is related to general questions in communications theory and biology, and it has to do with interacting dynamical systems, like systems of neurons, communication networks. We now know rather well how finite-dimensional dynamical systems may behave. But suppose you have several such systems that are connected. Then some new general questions appear. How does the whole system behave? It's space-time dynamics. Not only dynamics in time, but in space because you have different local systems (elements of a network). How do networks behave? It raises questions about different types of synchronization, space-time chaos, etc.

I: Are there are general results for such questions?

B: There are very few results so far; only for some special classes of dynamical networks. But there is no general theory. This is a major challenge.

I: Is there any theory for infinite-dimensional dynamical systems?

B: Again for some classes, such a theory exists, but usually it is not something which is likely to have real applications. But it is very important to find a class (even a narrow one) of systems where we can understand everything. It helps to build intuition on what to expect in the evolution of more general networks.

I: You did some work on chaotic motion of billiards. Is it related to the Hadamard billiards introduced more than one century ago?

B: Hadamard was one of the pioneers in studies of chaotic dynamics. What is now called "Hadamard billiards" is not really billiards. What "billiards" means is that you study the motion of a point particle, mechanical particle, or an acoustic wave propagating in some medium. It gets reflected from the boundary. If there is no boundary, it is not a billiard. Systems without boundaries are the simplest – they are just geodesic flows and were studied before billiards. Hadamard's fundamental work is not really about billiards. I was surprised to hear this name "Hadamard billiards". It was given by a physicist working in chaos theory. It's kind of confusing, but it's in the literature now. Unfortunately there is much confusion in giving names in chaos theory. Many people are working with billiards in applications because it is a very natural physical model in mechanics, in statistical physics as well as for light and sound propagation, in mesoscopic and in atomic physics.

I: What about some of the advances in percolation theory?

B: In percolation theory, I was only working tangentially and would be embarrassed to talk about it as I'm not an expert.

I: Are there any surprising or counter-intuitive discoveries in your research work?

B: There were quite a few. The first was right after my PhD – there I proved a theorem for a rather general class of systems of billiards. But after it was published, I realized it had some consequence which was very counter-intuitive. I published a very short paper, which is a special case of the research conducted in my PhD, and this paper had a hundred times more citations than the general paper. This result is very easy to explain.

Consider a narrow parallel beam of rays emitted by some flash light. Let this beam propagate in two-dimensional planar region (a billiard table) with mirror walls. It gets reflected from the mirrors. Question is whether the entire region will be illuminated – that is, for all points inside the region, some ray will pass through them. If all mirrors are convex inwards – this was introduced by Sinai – the beam becomes broader and illuminates much more. But if it is a concave mirror, like a circle, it illuminates less. Therefore there was a universal understanding that if you have dispersion at the boundary, then it is strongly chaotic – it illuminates everything and you lose precision fast. In a circle, the beam of rays just goes around and there is no illumination of the central part of the circle. I considered a perturbation of the dispersing boundary by small focusing pieces; then it will still be chaotic. It doesn't sound surprising. It occurred as though there is another mechanism of chaos generated by the focusing boundary.

Continued on page 19

Continued from page 18

For instance, if you take a circle, cut out a small piece by a chord and consider a billiard inside such table, then it is strongly chaotic because of defocusing: between any two consecutive reflections a beam of rays will pass through a focusing point and become divergent, like in billiards with dispersing boundary. Eventually it will illuminate the entire region. This was a real discovery – nobody thought about that, I didn't expect it either. The funniest thing is that everybody refers to this short paper rather than to the one from which it follows. This mechanism of defocusing was found in many other systems. It revealed that chaotic behavior is much broader phenomena than people thought before.

I: Are there some strange physical consequences of that kind of behavior?

B: There are; actually, experimental physicists in many physical labs constructed this type of devices and studied this phenomenon. This is what I like. When you come up with some clear examples, physicists go to their labs and build real physical analogs of these "purely mathematical" toy models.

Another example is from a totally different area, in psychiatry. My first papers were published in genetics journals. At that time, there was a theory by an outstanding geneticist in the Soviet Union that any hereditary disease is confined to genetic families (consisting of all ancestors); that is, roughly speaking, if two persons are carriers of a hereditary disease, then there is a high probability that they are relatives (in the genealogical tree). There was such a strong claim based on some computations in genetic populations. It is a fundamental problem for the organization of health care. Dealing with it, I introduced a new class of models in population genetics, which was called hierarchial models of human population. Models that were considered before assumed that the population is mixed, people get married randomly or there are several such populations with (horizontal) migrations between them. But we see that people from small villages usually migrate to cities, from small cities to bigger cities, and so on. Migrations in the opposite directions are essentially negligible. Of course, there are not so many layers, roughly speaking four or five even in the developed countries. However, this hierarchial structure is very important and changes the behavior of the population very essentially. My computations for such hierarchial populations gave the distribution of the special genes that are carriers of hereditary diseases.

Several years later I was at a conference in mathematical physics, and a physicist from Germany asked me whether I had a brother. "Yes, I have a brother," I said. "Oh, your brother is working in population genetics," he said. "No, it's me, not my brother". He was very surprised, and said that he had a friend who worked in demography, conducted experimental studies in Germany and could not explain the results and measurements, especially in urban areas. Then somebody told him about my model and everything was explained. It was exactly the same situation – there are many relatively big cities close to each other, coal miners were living in Essen, Dortmund, Duisburg, etc. Thus several big and well-developed cities are extremely close to each other, and form the rich high level in the hierarchy of migrations. The demographers there said the population structure did not fit any model, but the hierarchial one worked quite well.

I: You were already working on problems in biology and medical science long before the Human Genome Project. Have you applied your ideas to bioinformatics?

B: Actually I'm working in bioinformatics in Georgia Tech. We have a big effort in bioinformatics there. In Georgia Tech we had the first Master of Science program in bioinformatics in USA. Now we have also a PhD program in bioinformatics. You know, bioinformatics is another buzz word in a sense. I like it; it's better than chaos. But still, some people ask, what is bioinformatics? To me, it is analysis of medical and biological information in a general sense. But often people refer to it merely as the computer analysis of long molecules like in the Human Genome Project – DNA, proteins. A few years after the Human Genome Project, we know the letters but not the language; you don't know what is written by these letters. I think it's extremely tempting to bring in mathematics at this level and this is what people are trying to do. I believe that one of the major problems with biology is that there are no biologists who, like physicists, know and understand mathematics. All areas of mathematics are based on calculus or analysis. Historically, all the examples there were taken from mechanics and physics. Biology majors are not interested in calculus courses because there are no examples from their science. This is one of the major obstacles we need to overcome and this is what we are doing in Georgia Tech. We have developed new courses and now have several sections of calculus: traditional for engineering students and a new one for life sciences students. It's not a big deal. We just collect examples from biology, chemistry, biochemistry, genetics as a basis of this course. I hope that in 5 years' or 10 years' time, a new generation of biologists educated in mathematics will appear. A new thinking is needed.

I: Biology is changing very fast nowadays.

B: Yes, but still very slowly. Computers are now used and many people believe they can compute everything. But you should understand what you have computed. Here mathematical modeling is necessary.

Continued on page 20

Continued from page 19

I: How much of the computer do you use?

B: I don't use it myself but I really appreciate this possibility to conduct mathematical experiments. It's great. You have some idea and you can see whether it works or not by simulations. My students and collaborators use them.

I: Do you have a lot of graduate students?

B: At Georgia Tech, I usually have 3 graduate students. On the average, in our department, there is one graduate student per faculty member. I don't know whether 3 is a lot. In some other places, people have more.

I: Can you tell us something about the Southeast Applied Analysis Center?

B: Actually, it doesn't exist anymore. It was created by the Georgia Tech Department of Mathematics which became one of the leading research departments. We won a tough competition for a NSF grant with other departments in US. We were running projects and lectures for a lot of universities and colleges in the Southeast informing them about new developments in mathematics. We also had postdocs and some of them became visible researchers and won prestigious prizes. We are now trying to launch another center which will be more oriented to biology and ecology. The Southeast Applied Analysis Center was more oriented to probability and discrete mathematics. There are no more funds for this program now. In US, if there are no funds, it is just a name. So SAAC naturally disappeared.

I: The new center you mentioned is a kind of successor?

B: Yes, it is a successor. It is a kind of natural and major development for Georgia Tech where biological studies became a high priority area.

I: What will the new center be called?

B: I suggested "ABC Mathematical Center". A stands for "applied", B for "biological" and C for "contemporary mathematics" – contemporary in the sense that ABC will be more oriented to the studies of new contemporary topics like biological networks, systems biology, evolution biology, cell biology, bioinformatics, infectious diseases and ecology.

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