

Statistical Genomics, H1N1 Flu, and Quarantine Life in Singapore>>>



Terry Speed (extreme right) before the big "Q"

[Editor's Note: Terry Speed has been both an organizer and participant at IMS programs. In this lively article, he recounts his adventures as an unwitting participant in the control measures of H1N1 influenza during one of his recent visits to Singapore to participate in the IMS program on Statistical Genomics. This article was originally solicited by Imprints. It appeared in the August 2009 issue of Amstat News of the American Statistical Association. We are happy to report that Terry has since revisited Singapore (sans quarantine) to give a public lecture entitled "Keeping Afloat in a Deluge of DNA Data" on 22 September 2009.]

I arrived in Singapore from Melbourne, Australia, late on the Sunday, looking forward to a week's participation in the Statistical Genomics program at the *Institute for Mathematical Sciences* of the *National University of Singapore*. Not incidentally, Melbourne might well have been H1N1 flu capital of the world at that time, certainly of Australia. Before the first lecture on the Monday morning, a slide was put up asking all people who were in specified rows on specified flights into Singapore to contact the Ministry of Health (MOH). Someone in the middle of those

sets of rows had presumably tested positive for H1N1 flu, and contacts were being traced. My flight was there, but not my row. Phew: I'd dodged the bullet. There were four terrific lectures that day, lively discussions and a pleasant riverside meal that evening.

Just before the first lecture next morning, another H1N1 slide went up. A new flight, and new rows on old flights, including mine, but not my row. Again a sigh of relief. I didn't think it at the time, but two times lucky should have made me cautious. Once more the day saw four terrific lectures, and I had some excellent discussions. I was really getting into the workshop, looking forward to giving my talk next morning, and having more follow-up discussions, including ones with people from the *Genome Institute of Singapore*.

Out again for dinner that night, back to my hotel early to work on my talk. A message awaited me: "Will Prof Speed please phone Mdm L at the MOH". I did, and she had lots of advice for me: don't leave my room, don't give my lecture, await further advice from a representative of the Ministry. While stressing that this was just advice, it was made clear to me that as soon as the representative from the MOH arrived, this advice would turn into orders under the Infectious Diseases Act (Chapter 137). So I took the lady's advice, stayed in my room, and next morning went with the people who came to take me away to *Aloha Loyang*.

Aloha, a resort of 38 holiday bungalows and terrace houses for civil servants, has been set aside to quarantine mainly foreigners who may have been exposed to the new flu strain (*Straits Times*, May 29, 2009). We're on the north-east coast, just near Changi airport. Occasionally we can be treated to a fog-horn like sound blaring loudly every few seconds. That was slightly disconcerting on the first night. I thought it might be a large Eastern animal (a tiger?) wandering around looking for people who had left their rooms, but no, just a bull-frog looking for a mate.

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I'm *LT4/2*, in Terrace 4, which consists of 4 single rooms in which we are advised to stay, and a small courtyard, a communal kitchen and a lounge with TV which we are advised not to use. Through the lounge window is a barbecue area, a strip of grass, and the sea. I can gaze through the window at the sea, but only at the risk of being caught outside my room. Material intended for us, including meals, towels, etc is placed on a table outside our terrace door by face-masked carriers. Three times a day, we put on our masks, go out and get what's there, and retreat to our rooms once more. The first pick-up of the day is the best, containing the *Straits Times (ST)*, a 1.5 litre bottle of water, assorted tea-bags, coffee powders and biscuits, and new face-masks. I've stuck with my first mask, which has 4 ribbons to tie together behind my head, so my collection now numbers 14 new masks. I haven't yet learned how to tell when a face-mask is worn out or otherwise past its prime. I wish I had, as I'm looking forward to wearing the nifty kind that hook over one's ears, and don't need any ribbon tying. Later, I did.

2 Medically, we are left to ourselves after admission. I take my temperature 3 times a day with the *Digital Jumbo LCD Thermometer*, Lifetime Guarantee (its or mine, I wonder?), given to me by the MOH person. I take one 75 mg capsule of *Tamiflu* each day, and I watch myself closely for flu symptoms. One concern is that sitting all day in a hot room might bring something on, while sitting all day in a cold room might also, though perhaps something different. I turn the AC on and off many times each day, in the hope that nothing will come on.

One day I read in the *ST* that Singapore is home to the 30 highest-paid government officials in the world. I think I can safely say that these 30 don't holiday in my resort. The Spartan simplicity that I would put up with in an Australian beach house is less appealing when I can't leave my room for a swim. Every effort is made to keep us comfortable, within certain bounds, but it is hard not to think of it as a prison cell, if only because of our confinement. The similarity grows when I think of how I would behave if imprisoned in a low-security prison: just as I am now. To be fair, much of my life is spent as it is now, with the exception of compulsory confinement and reduced food choice, so I have little to complain about. Let me elaborate.

On my arrival at Aloha Loyang, I was handed a small black object, which turned out to be my cell phone. I approached it in much the same way as the apes in the movie *2001: A Space Odyssey* approached the mysterious black monolith that appeared before them. Like them, I learned to use it, and in the process found my intelligence awakening. Cell phones are the primary mode of communication between front desk and inmates such as me, but it also makes me accessible to the world beyond my resort. In no time friends, relatives and colleagues from all around the world, especially Singapore, were calling me to chat, commiserate, or ask for

advice. That was one unexpected and delightful aspect of my confinement. Later I was handed a small white object, labelled *Starhub*. This was my white monolith, and after a certain time experimenting with it, I discovered a moving part that permitted it to be plugged into a USB port, which I did. Then things appeared on my laptop screen, and after some downloading and installing, I found myself connected to the *outernet*. (I call it this, as the name *innernet* seems more appropriate to the workings of one's mind.) So here I am in a spartan room, with a phone and a net connection, sitting in a not very comfortable chair for hours on end, listening to music or the radio (ABC Classical FM), breaking only for meals, cups of tea, and reading a newspaper. Voilà, life as usual.

Almost. I miss two things: freedom and good food. I usually keep myself sane, perhaps even slightly more fit than I would otherwise be, by jogging in the morning. When I don't jog, I do a form of calisthenics, twisting, bending, pushing, etc, that takes a little effort and occasionally makes me break a sweat. Of course jogging isn't open to me, but the other form of exercise is, and I'm doing a lot of it. Interestingly, I've read that prisoners in gaols often spend a lot of time doing much the same thing, though perhaps for different reasons.

I am very comfortable eating rice and vegetables from time to time, indeed I frequently go out of my way to do so. But somehow it palls when served 3 times a day for more than about half a day running, and so the food is perhaps the most serious aspect of my confinement. However, the story picks up at this point. Two wonderful friends living in Singapore, who aren't, but for the present narrative shall remain nameless, have been bringing me supplies. (Again it's hard for me to omit pointing out that this is common practice for imprisoned people in many countries.) I have been given fresh pasta (spinach and ricotta ravioli, close to the sort I buy every Saturday in Berkeley or Melbourne), bread and cheese (ditto), Ben & Jerry's ice-cream (ditto²), Kettle's potato chips (ditto³), and other goodies to numerous to mention (mangosteens, lychees, oranges, cherries, biscotti, sticky bun, etc). The wine didn't get past the front desk, as after all this is a medical establishment. So my eating, while not quite back to normal, is pretty good, and not cause for complaint.

What can I complain about? Well, I missed the workshop, which was the reason I came to Singapore. I missed eating, drinking and chatting with all the workshop participants, and I missed jogging along the Singapore river, and other places (Bukit Timah, East Coast Park, etc.) The visit is not quite what I planned, but for the reasons I have given, it was remarkably close to my everyday life. Yes, I am a prisoner to my work.

Terry Speed. June 20, 2009.



Ewens Sampling Formula – an Illustration of the Value of Collaboration in Science >>>



Warren Ewens: The Sampler

[Editor's note: The Ewens Sampling Formula plays a fundamental role in statistical genetics. It provides the probability of the partition of a sample of n genes into a number of different gene types (alleles) under the assumption that the non-Darwinian theory is true, that is, when there are no selective differences between types. Warren Ewens, who discovered the formula in 1972, was an invited speaker at the Institute's program on Statistical Genomics in June 2009. He was specially invited to write this article.]

I am very happy to take up the invitation to discuss some of my research work, since it gives me the opportunity to emphasize the value of collaboration in research, especially research in bioinformatics, where one often has to draw on experts from mathematics, statistics, computer science, genetics and medicine to complete any research task. I am particularly happy to take up this invitation because of the happy collaborations I have had with scientists at NUS and the Bioinformatics Institute of A*Star.

The DNA nature of the gene became known with the work of Watson and Crick in 1953. Genes are of various types: witness the ABO blood group genes, where three gene types, A, B and O are possible. I will generically describe possible types as possible colors (of genes), so that we may think of A genes as being red, B genes as being green, and O genes as being yellow. In general any number of possible gene types, or colors, are possible at any given gene locus. By the 1960's substantial information was becoming available about the degree of genetic, or color, variation in a population, and far more colors were seen, and with unexpected frequencies, than had been expected.

These data naturally led to the question of the reason for the variation observed. Was it due to selection, to a high mutation rate, or were the frequencies observed simply the result of random stochastic processes with no selective basis? At the end of the 1960's the non-Darwinian theory was put forward, claiming that in the great majority of cases the color patterns observed had no selective basis and were the result of purely random processes. As might be expected, this theory became controversial. In 1971 I

set myself the task of testing the non-Darwinian theory by using mathematical and statistical methods.

To do this it was necessary to find what color patterns would be likely to be observed if in fact the non-Darwinian theory were true. This proved to be a difficult task, since what we observe today in any population is the result of a long evolutionary process. Because of this, none of the standard formulae (often arising from physics) are applicable, because there is essentially no parallel in physics to the biological evolutionary process. Eventually I developed a formula, arrived at partly by intuition, giving the probability of any possible (color) pattern under the assumption that the non-Darwinian theory is true. However, I was not able to surmount the final mathematical hurdle in proving this formula. I asked many probabilists, and because of its unusual nature none believed that the formula could be correct. Eventually I asked my friend Sam Karlin, who was then one of the world's leading probabilists, to help me. Together with his colleague Jim McGregor he was able to push through the proof that the formula was correct. This was the first collaborative effort that I had concerning this formula: I could not have carried through this proof myself.

In the mid-1970's a second great probabilist, John Kingman, became interested in population genetics theory, and in particular in the probabilities of the patterns that the formula prescribed. These patterns form a partition: if one has a sample of n genes, each gene being of some color, then in that sample one will observe some number (perhaps zero) of colors that arise once in the sample, some number (again perhaps zero) of colors that are seen twice in the sample, and so on. This led him in two directions. First, he developed a theory of "partition structures": these are partition probabilities that have the property that if a random member of a sample (of size n) becomes lost, the probability structure of the remaining $n-1$ members of the sample is the same as that of an original sample of size $n-1$. This innocuous requirement turns out to be quite deep, and many partition probabilities do not have it. The concept of "partition structures" has proved to be very fruitful and has now entered into several areas of combinatorial mathematics.

The second direction that Kingman went in is more relevant biologically. As stated above, the properties of the formula that I arrived at are determined by a long evolutionary process. Kingman decided to investigate the history of the genes observed in a sample, going back generation after generation, to find out why, from an evolutionary point of view, the formula took the form that it did. In this he was successful, and more than that, his work changed the direction of research in population genetics theory. The theory until then had been largely prospective, that is "forward in time", following the direction of evolution itself. Kingman's work led to the development of "backward in time" retrospective theory, which now dominates population genetics both in theory and practice. Here we ask questions such as "When did the most recent common ancestor of all living humans live"? "How can we use genetic information

People in the News >>>

Programs & Activities >>>

Tony Chan assumes presidency of HKUST

Tony Chan became President of the Hong Kong University of Science and Technology on 1 September 2009. Tony has been an organizer, speaker and participant at several programs and conferences organized by IMS. An interview with Tony appeared in the third issue of *Imprints* in March 2004.

IMS associates honored by NUS

Several colleagues who have been associated with IMS in one capacity or another have been conferred honors by the National University of Singapore. Paul Matsudaira and Zuowei Shen have been appointed Distinguished Professors. Yeneng Sun has been appointed Raffles Professor of Social Sciences. Berthold-Georg Englert has been appointed Provost's Chair Professor. Hock Lim has been conferred the Outstanding Alumni Award by the Faculty of Science at NUS.

Paul Matsudaira and Zuowei Shen are serving members of the IMS Management Board, while Hock Lim was a past member of the Board. Both Zuowei and Hock have also been involved in organizing a number of programs at IMS in the fields of mathematical imaging and geophysical fluid dynamics. Yeneng Sun was Deputy Director of IMS from July 2001 to July 2004. He was also an organizer of programs and workshops at IMS in mathematical economics. Berthold-Georg Englert was an organizer of a workshop and program at IMS in the area of quantum physics.

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to track the 'Out of Africa' migration?" Only a probabilist of Kingman's stature could have developed the machinery that allows us to answer these questions.

Kingman was kind enough to call my formula the "Ewens sampling formula", but since it was finally proven by Karlin and McGregor, and since the practical use of it was largely in the hands of Kingman himself and population geneticists such as Griffiths and Watterson, it should be named after all these people. All of them have been my collaborators, and I owe a debt to all of them. Science has now become such a team effort, with each member of a team contributing what he or she can provide best, that collaborative efforts, such as those which I have been lucky enough to have been involved in, are now the order of the day. In bioinformatics these efforts will involve biologists and computer scientists as well as mathematicians, and it is important to recognize this and, among other things, to train the rising generation in such a way that collaborative work is encouraged and facilitated.

Warren Ewens, *University of Pennsylvania*

Past Programs in Brief

Statistical Genomics (1 – 28 June 2009)

Website: <http://www.ims.nus.edu.sg/Programs/genomics09/index.htm>

Co-chairs

Zehua Chen, *National University of Singapore*

Heping Zhang, *Yale University*

The program consisted of two workshops and a parallel summer school for graduate students. The topic of the first workshop was Gene Mapping, covering genome-wide association studies (family and population based), linkage analysis, and admixture mapping. The topic of the second workshop was Genomic Profiling, including inherited copy number variation (CNV) and its role in disease, somatic CNV in cancer genomics, motif detection, expression analysis, eQTL mapping, comparative genomics, origins of replication, epigenetic alterations, etc. The Summer School consisted of a 16-hour minicourse conducted by Zhaohai Li of George Washington University.



David Siegmund: Copy number variation



Heping Zhang: Genetic studies



Summer school feedback

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A statistically significant gene pool

Summer School in Logic (29 June – 24 July 2009)

Website: <http://www.ims.nus.edu.sg/Programs/09logicss/index.htm>

Co-chairs

Chi Tat Chong, *National University of Singapore*
Qi Feng, *Chinese Academy of Sciences and National University of Singapore*
Yue Yang, *National University of Singapore*

The Summer School in Logic is held annually and is in its fourth year. The Summer School consisted of two parts, one in recursion (computability) theory and the other in set theory, running in parallel. The lectures were conducted by Theodore A Slaman and W Hugh Woodin of the University of California at Berkeley. In addition to lectures, there were 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 at Berkeley, Chinese Academy of Sciences and NUS.



A school of logicians



Logical demonstration



Hugh Woodin: Set theory

Mathematical Theory and Numerical Methods for Computational Materials Simulation and Design (1 July – 31 August 2009)

Website: <http://www.ims.nus.edu.sg/Programs/09matheory/index.htm>

Co-chairs

Weizhu Bao, *National University of Singapore*
Qiang Du, *Pennsylvania State University*
Yuanping Feng, *National University of Singapore*
Fanghua Lin, *Courant Institute, New York University*

This program was interdisciplinary in nature. Leading experts in applied and computational mathematics, theoretical and experimental physics, materials science and computational sciences gave many interesting talks during the two one-week long workshops. A Summer School was also incorporated into the program. Distinguished researchers gave tutorial lectures on topics in physical modeling, mathematical theory, computational methods and applications related to computational materials simulation and design. In addition, we also had the privilege of having Sir John Ball (University of Oxford) and Fanghua Lin (Courant Institute, New York University) deliver public lectures.

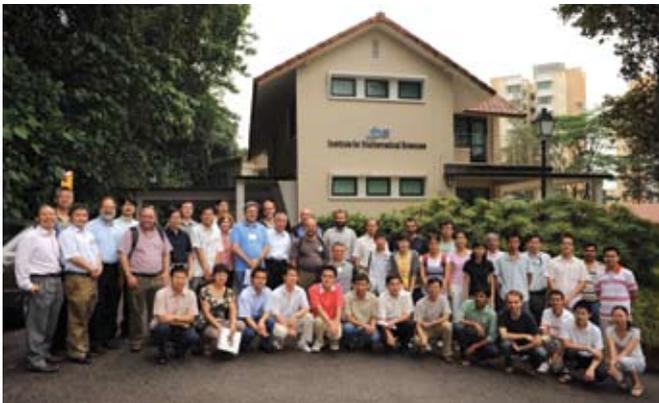


David Srolovitz: How grains grow

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Material men living in a material world: (from left) Shouhong Wang, Xiaoping Wang, Qiang Du and Xiao Fan Li



Computational materialists



Rohan Abeyaratne: Speaking dynamically on material interfaces

Next Program

Financial Mathematics (2 November – 23 December 2009)

... Jointly organized with Risk Management Institute, NUS

Website: <http://www.ims.nus.edu.sg/Programs/financialm09/index.htm>

Chair:

Paul Embrechts, Swiss Federal Institute of Technology (ETH) Zürich

Financial Mathematics is a fast-growing area of modern applied science. Over the last three decades, the subject

has grown into a substantial body of knowledge, where quantitative methodologies have become part and parcel of the functioning of the world's financial institutions. This program will be focusing on, but not limited to, the following areas:

- i. Risk measures and robust optimization in finance;
- ii. Pricing and hedging of environmental and energy-related financial derivatives;
- iii. Optimal stopping and singular stochastic control problems in finance.

Activities:

1. Topics on Risk Measures and Robust Optimization in Finance
 - Tutorials on Robust Preferences and Robust Portfolio Choice: 12 – 14 November 2009
 - Public lecture by Paul Embrechts, Swiss Federal Institute of Technology (ETH): 16 November 2009
 - Workshop: 16 – 20 November 2009
2. Topics on the Pricing and Hedging of Environmental and Energy-related Financial Derivatives
 - Round table discussion: 4 December 2009
 - Workshop: 7 – 8 December 2009
 - Special lectures: 9 December 2009
3. Workshop on Optimal Stopping and Singular Stochastic Control Problems in Finance
 - Workshop: 9 – 15 December 2009
 - Tutorial: 14 – 18 December 2009

Upcoming Activity

Workshop on Epidemiology of Infectious Diseases: Emerging Challenges (4 – 8 January 2010)

Website: <http://www.ims.nus.edu.sg/Programs/010wkepid/index.php>

Chair:

Alex Cook, National University of Singapore

Contagious diseases are one of the leading causes of death worldwide, resulting in more than 10 million deaths per annum. This is in addition to the social and economic burden of disease in humans and our livestock and agriculture. The current influenza pandemic demonstrates the speed at which emerging diseases can spread between and within countries. Mathematical modeling is a powerful tool in the fight against infectious disease.

The purpose of the workshop is to highlight on-going work that addresses the emerging challenges in the discipline, including technology, globalization, economics

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and climate change. In addition, it aims to enhance the working relationship between researchers and regional policy makers, by deepening policy makers' appreciation of modeling and targeting research at their needs.

Programs & Activities in the Pipeline

Complex Quantum Systems (17 February – 27 March 2010)

...Jointly organized with Centre for Quantum Technologies

Website: <http://www.ims.nus.edu.sg/Programs/010quantum/index.php>

Chair:

Heinz Siedentop, *Ludwig-Maximilians-Universität München*

The program will be organized in two related sections, but with different emphases, namely "Large Coulomb Systems" and "Quantum Information and N-Representability". The topics will include:

- Effective description of atoms and molecules (density and density matrix functionals, computational aspects)
- Models of relativistic quantum electrodynamics
- Stability of matter (including relativistic systems and the quantized photon field)
- Lieb-Thirring and other Sobolev type inequalities
- Reduced density matrices and the N-representability problem in quantum information theory
- Quantum and classical complexity theory of the N-representability and related physical problems
- Approximation methods for correlated states (Semi-definite programming, Matrix Product States (MPS), Projected Entangled Pair States (PEPS), fermionic PEPS)

Activities:

The first four weeks will emphasize the theory of Large Coulomb Systems, the last four weeks (there will be an overlap of two weeks) will emphasize Quantum Information and N-Representability. Each part will start with a kick-off workshop. Each workshop will be followed by working periods on the topics raised during the workshop. As part of the workshops, lead participants will give introductory talks on the current state of research. At the beginning of each period, there will be tutorial lectures followed by a working and collaboration session of three weeks. The tutorial lectures are planned to consist of five two hour sessions.

School and Workshop on the Mathematical Science of Understanding and Predicting Regional Climate (17 – 28 May 2010)

Chair:

Douglas W. Nychka, *National Center for Atmospheric Research, Boulder, CO*

Website: <http://www.ims.nus.edu.sg/prognosem.htm>

The basic goal of this program is to explore from a mathematical and statistical perspective how to improve inferences of regional changes in climate. This program will leverage on a large regional climate research effort centered in North America for methodology and some model simulations. The North American Regional Climate Change and Assessment Program (NARCCAP) is the largest-to-date suite of regional climate projections whose factorial design considers 4 distinct global climate models and 6 regional models for downscaling. Also part of NARCCAP are two cutting-edge high resolution (50km) global simulations that can address other areas outside of North America; in particular, Southeast Asia.

Activities:

Workshop: Three themes will be linked through a week long workshop.

- Climate impacts relevant to Singapore and Southeast Asia and the analysis of climate change impacts on Singapore regional climate experiments.
- Statistical models for computer experiments.
- Dimension reduction techniques for large spatio-temporal fields.

Short course: A week-long training and lab activity will be held before the workshop. The school will blend lectures with hands-on data experience using the **R** statistical language, with student teams working on some climate data relevant to Singapore.

Geometry, Topology and Dynamics of Character Varieties (18 June – 15 August 2010)

... Co-sponsored by Global COE (Center of Excellence) of the Tokyo Institute of Technology, Compview

Website: <http://www.ims.nus.edu.sg/Programs/010geometry/index.htm>

Co-chairs

William Goldman, *University of Maryland*

Caroline Series, *University of Warwick*

Ser Peow Tan, *National University of Singapore*

This program concerns character varieties of representations in a Lie group G of a discrete group π , for example, the fundamental group of a surface. These varieties have rich geometry and are related to interesting topological objects such as locally homogeneous geometric structures on

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manifolds, and moduli spaces arising in gauge theory. When π is the fundamental group of a surface group S , the mapping class group acts with a complicated and mysterious dynamics.

The program will bring together some of the leading experts from different backgrounds to explain their subjects and explore connections between them, to report on the latest developments and to chart out new directions. It is hoped that participants will also profit from the opportunity to interact and experiment with computer experts during the program.

Activities:

Tutorials on background material/Summer school:

28 June - 16 July 2010

Tutorials will form the core of a summer school, with several series of tutorial lectures on relevant topics.

Workshop:

19 - 30 July 2010 (An ICM Satellite Conference)

Participants will have the opportunity to present their work. Computer experimentation will be a significant part of the program, and the workshop will also include computer demonstrations.

Conference:

10 - 14 August 2010 (An ICM Satellite Conference)

Leading experts from around the world will speak on the main topics of the program.

Workshop on Recent Advances in Bayesian Computation
(20 – 22 September 2010)

Chair:

David Nott, *National University of Singapore*

Over the last 15 years there has been an explosion in the use of Bayesian methods in applied statistics. Due to advances in technology for data collection in many fields of science, engineering and the social sciences, applied statisticians increasingly have to deal with problems of combining data and information from different sources. This leads naturally to the use of richly structured hierarchical models, and advances in Bayesian computational methods have meant that a Bayesian approach is often the most easily implemented one for inference in such models. The purpose of this workshop is to bring together leading researchers in the area of Bayesian computational methods to discuss challenges and opportunities in the area, with a focus on dealing with large data sets.

Hyperbolic Conservation Laws and Kinetic Equations: Theory, Computation, and Applications (1 November – 19 December 2010)

Website: <http://www.ims.nus.edu.sg/Programs/010hyperbolic/index.htm>

Organizing Committee

Claude Bardos, *Université Paris VI*

Russel Caflisch, *UCLA*

Thomas Hou, *California Institute of Technology*

Petros Koumoutsakos, *ETH Zürich*

Cedric Villani, *ENS Lyon*

Shih-Hsien Yu, *National University of Singapore*

This program will provide a forum for people working in hyperbolic conservation laws, kinetic equations, mathematical physics, scientific computation, and engineering to jointly promote research on the kinetic equations for rarefied gas dynamics.

Activities:

Period I: 1 - 26 November 2010 (Tentative)

Asymptotic Theory in Boltzmann Equation and Mathematical Theory for Hyperbolic Conservation and Kinetic Equation.

Period II: 29 November - 3 December 2010 (Tentative)

International Conference on Nonlinear Partial Differential Equations: Mathematical Theory, Computation, and Applications.

Period III: 6 - 17 December 2010 (Tentative)

On Macroscopic and Microscopic Flows.

Highlights of Other Activities

Eleventh Asian Logic Conference (22 – 27 June 2009)

... Jointly organized with Faculty of Science in celebration of 80th Anniversary of Faculty of Science

Website: <http://www.ims.nus.edu.sg/Programs/09asianlogic/index.htm>



In celebration of logic and a logician

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Chair of Program Committee:

Qi Feng, National University of Singapore and Chinese Academy of Sciences

Chair of Organizing Committee:

Yue Yang, National University of Singapore

The Asian Logic Conference series features the latest scientific developments in the fields of mathematical logic and applications, logic in computer science, and philosophical logic. Singapore was chosen to host the 2009 Asian Logic Conference in honor of Professor C.T. Chong's 60th birthday. The one-week conference consisted of 17 plenary talks and 32 contributed talks and was attended by 86 participants from countries in Asia and beyond.



NUS Provost Eng Chye Tan (right) was the guest of honor at the conference which celebrated the 60th birthday of Chi Tat Chong (left)

Public Lectures

The Institute organized three public lectures between July and September 2009.

Sir John Ball of the University of Oxford gave a public lecture titled "Mathematics in the Public Eye - The Story of Perelman and the Poincaré Conjecture" on 22 July 2009. He talked about the Russian mathematician Grigori Perelman who sensationally declined the Fields Medal awarded to him by the International Mathematical



John Ball: Poincaré, Perelman and the Fields Medal

Union at the International Congress of Mathematicians in Madrid in August 2006. He had been awarded the Medal, regarded as the equivalent of a Nobel Prize, because of his ground-breaking work on the Poincaré conjecture, one of the most famous open problems of mathematics. The lecture described the conjecture, the unusual events surrounding its proof, and how this unfolding story of mathematics and personalities attracted unprecedented worldwide media attention.

Fanghua Lin of Courant Institute, New York University gave a public lecture titled "Roles of Differential Equations in Mathematics and Sciences" on 11 August 2009. In the lecture, he described some fundamental roles played by the theory of differential equations in both pure mathematics and applied sciences. Examining past themes and current developments, he discussed certain philosophical views and pointed out some new scientific directions and challenges.



Fanghua Lin: Looking at the world through differential equations

Terry Speed of the Walter and Eliza Hall Institute of Medical Research, Australia, gave a talk titled "Keeping Afloat in a Deluge of DNA Data" on 22 September 2009. He outlined the growth of technologies producing large amounts of DNA data, and talked about the corresponding efforts to store, display, analyze and interpret these data (called bioinformatics). His primary focus was on DNA sequence data, but genotyping and gene expression data were also discussed during the lecture.



Terry Speed: Floating on a sea of DNA

Mathematical Conversations

Eduardo Massad: Infectious Diseases, Vaccines, Models



Eduardo Massad

Interview of Eduardo Massad by Y.K. Leong

Eduardo Massad is internationally acclaimed for his work in the field of infectious disease epidemiology, both in the mathematical modeling of infectious diseases and in the introduction of successful disease control programs in Brazil.

Originally trained in medicine, Massad went on to obtain a degree in physics and a PhD in experimental pathology. Together with his collaborators, he did important work in the mathematical modeling of infectious diseases such as dengue, yellow fever, hepatitis A, vaccine preventable diseases, parasitology, HIV and antimicrobial resistance.

His extensive research work is contained in almost 200 joint papers and 4 books. During his distinguished research career, he has supervised 21 doctoral students. His scientific contributions extend beyond the theoretical aspects of modeling in infectious diseases and epidemiology to the successful implementation of disease control programs in Brazil. Fluent in six European languages, he also has research interests in evolutionary biology and telemedicine.

Massad is Professor of Medical Informatics at the University of São Paulo in Brazil and has been an Honorary Professor of Infectious and Tropical Diseases at the London School of Hygiene and Tropical Medicine since 2003. He is a Chartered Mathematician and Fellow of the Institute of Mathematics and Applications and a Chartered Scientist, Science Council, United Kingdom.

In 2003, the Courage Fund was set up in Singapore to meet the deadly challenge posed by the Severe Acute Respiratory Syndrome (SARS), and a grant of S\$3 million was presented to NUS to set up the Visiting Professorship/Fellowship in Infectious Disease and Epidemiology. In 2005, Massad was invited to Singapore as the inaugural Visiting Professor to initiate the building up of expertise in epidemiology management and control. In 2007, he was Chair of the Institute's *Workshop on Mathematical Models for the Study of the Infection Dynamics of Emergent and Re-emergent Diseases in Human* held from 22 – 26 October 2007. During his visit to IMS, he was interviewed by Y.K. Leong on behalf of *Imprints* on 29 October 2007. The following is an edited transcript of the interview in which he gave us a rare insight into the collective efforts of medical and academic specialists in the ongoing prevention and control of infectious diseases around the world. We also get a glimpse of how mathematics, statistics and computer science have put in their share of efforts in the continuous struggle to maintain the healthcare of humanity.

Imprints: You originally started with a diploma in medicine and then went on to concurrently obtain a bachelor's degree in physics and a medical degree. Why did you choose a degree in physics, why not chemistry, say, or even mathematics?

Eduardo Massad: Well, it's actually not that easy to describe. I did not choose chemistry because chemistry was not exactly what I wanted to do. I was in doubt between physics and mathematics. I chose physics because that course at my university at São Paulo was more applied than the mathematical one. I intended to be an applied scientist. I then chose the physics course degree because there was a balance of applications in that course.

I: Was your education taken mainly in South America?

M: Yes. I was trained in São Paulo and then I did my graduate study in England.

I: When you say graduate study, are you referring to ...?

M: I mean, as a postdoctoral graduate in England.

I: Which part of England?

M: I stayed for one year in Sussex University, and then for two years at Imperial College.

I: Was the training in physics directly useful in your subsequent research work in the medical sciences?

M: Actually it was not really useful; it was determinant because everything I do is professional nowadays. Thanks to my training in physics, it was very central indeed.

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I: So it's the training rather than the actual knowledge?

M: Yes, the form of training.

I: One of your research areas listed is "medical informatics". How different is it from bioinformatics?

M: Well, it's quite different because actually bioinformatics is part of medical informatics in a sense. Bioinformatics deals strictly with information from genomic science and the huge amount of data that is coming from the human genome project while medical informatics deals with information in medicine as a whole, with medical records, artificial intelligence as applied to medicine and so on.

I: It's a much wider science.

M: Much wider than bioinformatics.

I: Is this a very new kind of discipline?

M: Bioinformatics is new but medical bioinformatics has a history of 35 years.

I: Did it come about as a result of the computer revolution?

M: It's a compromise between computer science and medical doctors in the sense that there is a growing interest in applications of computer science to solve medical information problems.

I: In the early years, they were talking about expert systems.

M: Yes, expert systems is one of the specialties of medical informatics. There are a number of very interesting systems that are able to do medical diagnosis nowadays.

I: How recent is the field of mathematical modeling in the medical sciences?

M: In the sexual disease field, it's quite old in the sense that it was the first field to which mathematical thinking was applied in order to understand events in sexual diseases... Sir Ronald Ross in 1911, 1918 – he was the man who discovered that malaria was disseminated by mosquitoes. Then in the 20s, a couple of researchers started to apply more formally mathematics into the study of sexual diseases, and in the 70s, the field exploded. So it's about 40 years and it has consolidated since then.

I: Is it true that not many doctors are well equipped to do modeling?

M: No, not that many doctors. You see, it's very rare to have a doctor apply mathematics directly.

I: You are involved in training doctors to do the modeling?

M: Yes, yes. I have many doctor students.

I: Are there any general laws or principles that can be formulated in medical modeling like those in physics or chemistry?

M: Oh yes, certainly there are. There are some central principles that you can call general laws, like the law of mass action that is interaction between susceptible and infected people, the basic reproductive number.

I: Do epidemiological models depend on the size of the domain affected? In other words, are there such things as local models versus global models?

M: Very much so, yes. You have global models that are applied to explain diseases anywhere in the world. You have global models for certain kind of infection like vector-borne disease, and you have local models that are applied to specific communities, whereas the global models can be applied to any community whatsoever. You can distinguish between local and global models. There are certain models that are applicable only to certain communities.

I: How successful is computer simulation in predicting or preventing disease outbreaks?

M: I think it is very successful indeed. The problem is to convince the decision makers to believe in such a model. So the main problem in the actual application of such predictions is convincing the decision makers that the model is correct and reliable. The main problem is communication rather than the technology.

I: How do you convince the policy makers?

M: Normally, the logic behind some models can be explained to them, but if you make them too complicated, they tend not to believe you.

I: I think most of them would believe you if you can show them the results.

M: Yes.

I: I believe you have actually applied some of these models to solve problems in São Paulo.

M: Yes, we applied the models to real problems there.

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I: You have no problems in convincing the authorities there?

M: Well, some 15 years ago, we had one Secretary of State in São Paulo who really understood what our model was about and he was the one who supported the application of models as a whole in the state of São Paulo. We were lucky to find this man behind the job.

I: Have you applied your methods to formulate ecological models?

M: Yes, indeed. We applied some of our methods to simulate ecological models for vector-borne infections. The ecology of mosquitoes in the disease can be formulated according to the mathematical approach.

I: In your models, you have some kind of parameters where you have to measure something. How do you decide what these parameters are?

M: The parameters are determined by the model you structure. In a sense, the theoretical model anticipates the field work.

I: Before you formulate the model, do you collect the data first?

M: Yes. You know the problem and you know the natural history of the disease. Then you formulate a model that mimics this natural history. Then you go after the parameters in the field in order to check the model's position.

I: Does that mean you have to refine the model again and again?

M: You refine the model according to the data.

I: How do you know when you have reached the ideal model?

M: Normally if you know the natural history of the disease well, you don't have too many competitive models to choose from. You normally have only one model that mimics the natural history. The structure of the disease must be behind the structure of the model.

I: Are your models stochastic or deterministic models?

M: They can be either stochastic or deterministic. It depends essentially on the size of the population involved. For smaller populations, you have to apply stochastic models. For larger populations, you cannot apply a simply deterministic approach.

I: How do you pick up the necessary mathematical tools?

M: I was trained as a physicist. The essentials I know, but I work together with more accomplished mathematicians who help me on the project.

I: Are your models intuitively motivated?

M: Oh yes, intuition is very important indeed and is an essential part of the job.

I: Does that come from experience?

M: It can come from experience.

I: You have been highly successful in using modeling to control disease outbreaks in São Paulo. What was the greatest breakthrough behind those successes?

M: I think the greatest breakthrough is that we manage to succeed with the model which determines the introduction of the rubella vaccine in the state of São Paulo in 1992. At that time the health authorities have some doubts whether they should introduce the vaccine or not because, you know, rubella is a problem that affects pregnant women. And the vaccine causes a shift in the average age of infection. Before the introduction of the vaccine, the average age of infection for rubella is about 6 years of age. But when we start to vaccinate, this age shifts about. The fear at that time was that they did not manage to vaccinate the maximum portion of children in order to avoid the reproductive window which is between 15 and 40 years of age. We manage to calculate that and design a model which guided the introduction of vaccine in the form of a mass vaccination campaign. After the mass vaccination campaign, we introduced the vaccine in the local calendar of vaccination.

I: Was the result immediate?

M: Well, the immediate result was that the number of congenital rubella syndrome, which is something that affects the babies, dropped close to zero one or two years after the introduction of vaccination.

I: That is rather dramatic.

M: Yes, very dramatic indeed.

I: You collaborate with a lot of people. It's typical in biology, isn't it?

M: Yes, in biology it's common. Biology is team work. In the medical profession, even if you are working with some basic side of a medical problem, you have to work with a team of people in the background. We have doctors

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trained in infectious diseases, epidemiologists; we have mathematicians, statisticians, psychologists, meteorologists – a lot of different people working together.

I: Are diseases dependent on the actions of human beings?

M: Oh yes. Almost any infectious disease is behavioral dependent. It depends on how people behave in order to get the disease. It's important to know that.

I: How do you control the behavior of people?

M: You can't control the behavior of people. You just can only educate people.

I: What about intangible things like mindset and cultural attitudes?

M: That's the basic barrier in the HIV epidemic. It's a clear example of that – you know, to make educational contact in order to inform people what are the risks and the behavior that they should follow or what they should avoid and so on.

I: You have many research students. What is the secret of your ability to attract so many students into your research area?

M: Well, first it's because they were available. You know, full-time research in the medical school is a rarity. The sheer availability attracted some students. Second aspect is the novelty of this kind of method that I tried to apply some 25 years ago. So this attracted some students mainly because of their curiosity and the novelty of the approach. But, more recently, I'm not attracting so many students any more, mainly because I have to compete with microbiology and other novelties at this time.

I: These are the newer areas.

M: Yes, newcomers, and you have to compete with young and bright people with other interests.

I: What are your views about the prospects of controlling diseases in the future?

M: I think that vaccination is the key for any infectious disease. As soon as you find an effective and cheap vaccine, you can control any kind of infectious disease. The problem is that for some diseases, it is more difficult to develop vaccines, like dengue fever.

I: Vaccination is more like prevention. But once a disease has started . . .

M: Once a disease has started, you have to treat it. That is the greatest challenge of modern medicine – to find new antimicrobicide, antibiotics, anti-viral drugs.

I: What about global warming issues? Do you consider them?

M: Yes. At the moment, we are looking at one model that is trying to understand how the seriousness of diseases can be affected by global warming; in particular, those diseases that are transmitted by mosquitoes.

I: What is the impact of the human genome project on diseases?

M: The human genome project has a huge impact on the understanding of diseases – the fact that it can pin down the genes that are responsible for specific susceptibility to certain infection. Other parameters that are important are those genes that may facilitate the entrance of micro-organisms into our bodies and how they penetrate into our cells, how our organisms interact with this sort of micro-organisms, what is the best treatment with drugs in that specific genomic setting. Well, I would expect a huge impact.

I: What would be the ethical issues involved?

M: That is a very sensitive point because the ethical conscience would find new barriers for some kind of investigations. For instance, investigations with animal models are very much restricted nowadays for ethical reasons. And also observations on experimental human beings are very much constrained by ethical issues.

I: You mentioned animal models. Is animal testing done anymore?

M: It's still done, but each time on smaller and smaller animals. You can't do it experimentally on large animals like dogs, monkeys, cats. It's now unacceptable to carry out experiments on this kind of animals. It's restricted to large mice and guinea pigs at most.

I: What about using the computer to replace animal testing?

M: That's the great hope. We have to rely on experiments in a computing environment in order to substitute animal models.

I: Do you use the computer in your work?

M: We use the computers a lot because we have to simulate our models. Everything that we see as far as the dynamics

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of the project is concerned is carried out in a computing environment, so we can see how populations interact with each other.

I: In some sense, it's impossible to wipe out diseases; they usually morph into something else.

M: I think wiping out diseases is really very difficult. We should not aim for that. We have to better understand what is going on in these interactions between all these living beings, in particular, in the field of infectious diseases. I would not believe that we will eradicate all of them because there are so many new infections every week. The pathogens are evolving each time to be more infective, and we are evolving tools in order to be resistant. So this is a sort of arms race, and we have to keep maintaining the upper hand. That would be the aim.

I: You mentioned that vaccination is a sort of prevention, but what happens if the vaccine eventually becomes not so effective?

M: In some diseases, you have the vaccines, in particular those vaccines that apply living virus or bacteria, and sometimes it has a sort of reversion to the lethal state. We have vaccine side effects as well. It's not uncommon and it's a matter of much concern.

I: I remember that years ago people thought that tuberculosis has been wiped out, but recently they have second thoughts about it.

M: Yes, tuberculosis is still an infectious disease which kills the highest number of people in the world. It is the number one killer. We have about 3 million people dying every year from tuberculosis.

I: Is it mostly in the under-developed countries?

M: We have many problems in Africa and also in Russia, in confined populations like prison inmates and under-nourished children. It is still a global problem. Tuberculosis is still a challenge for us.

I: What is your advice to a student who wants to do research in your kind of area?

M: The advice is that you have to be prepared first of all, go after some formal courses on mathematics, statistics and computer science. Without these, it's very difficult even to interact with statisticians. The other way around, people from the mathematics background who wish to apply them should get some formal courses in biology. In order to apply



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Random Matrix Theory and its Applications: Multivariate Statistics and Wireless Communications

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at least the language to interact with other specialists, interdisciplinary background is important. The second important point is to mix with people from other backgrounds. You have to work with other specialists. This is a team work. It is very difficult to survive alone.

I: Do you talk to the mathematicians back home?

M: Yes, we talk a lot. I have several mathematicians in my group. They are all learning biological science as well. We have to speak the same language.

I: It's quite difficult for a mathematician to learn biology, isn't it?

M: I would think it's more difficult for a biologist to learn the mathematics than the other way around. It's easier for a mathematician to learn biology than for a biologist to learn mathematics.

I: But still, it's not easy to convince a mathematician to consider your problems.

M: No, it's not that easy but, you know, if the initiative of the mathematician is in applications rather than in such diseases, it's not that difficult to convince him or her to study some biology.

I: You have been very successful in that.

M: I think I have had some success, no complaints about it.

Fanghua Lin: Revolution, Transitions, Partial Differential Equations



Fanghua Lin

Interview of Fanghua Lin by Y.K. Leong

Fanghua Lin (林芳华) is world-renowned for his important contributions to classical analysis and its applications to nonlinear partial differential equations.

Lin graduated from Zhejiang University, China in 1981 and obtained his PhD from University of Minnesota in 1985. He was an instructor at the Courant Institute of Mathematical Sciences, New York University from 1985 to 1988 before going to the University of Chicago as full professor in 1988. He returned to New York University in 1989 and was awarded the Silver Professorship in 2002 by the Courant Institute, where he continues to produce outstanding research in the Courant tradition of hard analysis applied to nonlinear partial differential equations.

His research output includes more than 160 research papers and three books of lecture notes. Even before completing his doctoral studies at Minnesota, he had already made a reputation for writing many research papers. Among his many contributions are his fundamental work on the Ginzburg-Landau equations with a small parameter and his deep results on harmonic maps and liquid crystals.

His honors and awards are numerous, notably the Alfred P. Sloan Research Fellowship, the Presidential Young Investigator Award, AMS Bôcher Prize and S.S. Chern Prize (China). He was elected to the American Academy of Arts and Sciences and has been invited as distinguished speaker at important scientific meetings and conferences in U.S., China and Japan and in major universities throughout the world. Besides supervising a number of doctoral students and post-doctoral fellows, he serves on the editorial boards of leading mathematical journals, such as *Communications in Pure and Applied Mathematics*, *Analyse Non Linéaire*,

IHP, *SIAM Journal of Mathematical Analysis* and *Journal of Differential Geometry*.

Having established himself as a world leader in his field, Lin has not forgotten the moral obligation he has always felt towards China, his country of origin. For the past two decades or so, he has been actively engaged in promoting international scientific contacts and opportunities for the mathematical community in China. At a different level, Lin has a close association with NUS's Department of Mathematics and Department of Physics. He was co-chair of the organizing committee of the IMS program on *Bose-Einstein condensation and quantized vortices in superfluidity and superconductivity* held from 1 November to 31 December 2007. More recently, he also served as a co-chair of the organizing committee of the IMS program on *Mathematical Theory and Numerical Methods for Computational Materials Simulation and Design* (1 July – 31 August 2009) and of the program's Summer School (17 July – 19 June 2009).

He was interviewed by Y.K. Leong at IMS on behalf of *Imprints* on 10 December 2007. The following is an edited and enhanced version of the transcript of the interview in which he offered a glimpse of a student's life during the Cultural Revolution that swept through China during the 1970s and how he emerged from the throes of that period as one of the first batch of students to enter the reopened gates of Chinese universities and how he was sent as one of the pioneering group of students to do graduate studies in the US. In the interview, he exuded a passion for research and open-mindedness towards learning in mathematics and science.

Imprints: You went from Zhejiang University to University of Minnesota for your PhD. Why did you choose Minnesota and what was the topic of your PhD?

Fanghua Lin: The answer is very simple. I didn't choose Minnesota. My professor at Zhejiang University chose it for me. That has a lot to do with the history of the department. The mathematics department of Zhejiang University is historically very important in developing Chinese mathematics and has trained a lot of Chinese mathematicians. At the time I entered university, it was February 1978. The department had only a few professors. But, the professors made a decision to choose the top 10 students of the class of 77 and 78 and send them to US and Europe for their PhD and to get them to return to Zhejiang University. This was a rather strategic plan but as in many other schools in China, the plan was not carried out. Why would such an idea come up at Zhejiang University at that time? It has to do with the history of the department. The early professors of the department, Professor Chen Jiagong and Su Buching, both got their PhD from Tohoku University, Japan around 1930. At that time, you don't see so many PhDs in China. With only two PhDs, it was already such a great department. So the professors thought then, if we have

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10 PhDs, we will, you know, be even better. Because of this decision, I was chosen among the ten to be sent to US to study partial differential equations. Going to Minnesota was also decided by the professors. The professor visiting Minnesota then was Dong Guangchang who was doing PDE, and the chair of the department then was Professor Guo Zuorui. It's very hard to say I really chose the topic of partial differential equations. When you get to US, you basically follow whatever you like to study. It turned out that my thesis topic was not on partial differential equations. It was more on a geometric variational problem and my PhD advisor was Robert Hardt.

I: That was in the late seventies?

L: I went to Minnesota in 1981. I entered Zhejiang University in 1978. I had basically three years of undergraduate study, the last half-year learning English mostly.

I: Was it on a national scholarship?

L: I got a teaching assistant fellowship from University of Minnesota, so I had to spend half the time working and half the time studying. It was kind of challenging but interesting.

I: That was after the Cultural Revolution?

L: Yes, I was in the first class (the 1977 class) that entered university after the Cultural Revolution, but the class entered university in the spring of 78.

I: Did the events of the Cultural Revolution affect your studies before you entered university?

L: Certainly, I never really studied at all in elementary school or for that matter in high school. Actually, thinking back, I liked it because it was completely free. There was no homework, no exams. There was no serious exam before I took the university entrance exam. The elementary school then was like a political camp.

I: How did you study your mathematics in high school?

L: I entered school at the third grade basically because the first two years was the start of the Cultural Revolution. We didn't really learn anything except Chairman Mao's quotations. At the fifth grade, we were starting to study the solving of equations. A lot of my classmate experienced difficulties with the problems, but I found them particularly easy. I found it started to get interesting because there was something else, not just something mechanical. My elementary school teacher thought that I did have some natural talent. I spent a year or two in elementary middle school (sixth and seventh grade) studying a lot of mathematics and physics too, basically by myself. I happened to meet a very good teacher. He was our physics teacher and he gave me the books published before the Cultural Revolution and

some special books in mathematics. I read most of them and found them not too difficult to learn from. But then I really didn't spend too much time studying in high school because it was still during the Cultural Revolution and you didn't see the end of it. You didn't see much future then and therefore you didn't do much work – eventually you would become a farmer. But I enjoyed the free time however, never really followed any rules or studied anything systematically.

I: Maybe it's not that bad for creativity.

L: Yes, in some way. Because of that I was always interested in thinking about problems and trying to solve them by myself instead of reading them in the books. Of course, there are advantages and disadvantages.

I: Except for a short stint at the University of Chicago, you are essentially based at New York University. What is the attractive factor of NYU?

L: Many reasons. First, New York City is very unique. You feel at home there. Everybody feels at home there. It has so much to offer: music, art galleries, museums, movie theatres, restaurants. It's just fantastic. I'm a lazy person. I always want to get things very easily – live near to food, get to work easily and everything should be very accessible. The other thing is that the Courant Institute is one of the greatest institutes in the world. You feel very warm and you find a lot of colleagues, so educated, and from different cultural backgrounds. I feel the friendliness.

I: Did you feel any culture shock?

L: I didn't feel much of a culture shock. I'm always very open. When I was a graduate student at Minnesota, I interacted mostly with students from other countries, a couple from Hong Kong. Of course, the culture thing is a much deeper matter. As time passes, I find I'm still very Chinese – some things never change. However, you don't feel like a foreigner at the [Courant] Institute. People simply respect you if you do a good job. Faculty is very happy when you accomplish something. People congratulate you and so on. This is a particularly friendly place. You don't have to prove to your colleagues that you are good or so excellent, which sometimes happens in some other places. I like other places too, like Chicago. I love the University of Chicago very much. It's a very English society – gentlemen, treat you very nicely. It's great. The weather is very tough however, particularly at the time I was there. I enjoyed it very much and that is why later my family went back there again. I've been at Berkeley for half-a-year as a post-doctoral, Princeton for one sabbatical year and the Institute for Advanced Study for half-a-year as post-doc.

I: Have you gone back to China since then?

L: Yes, many times. My first return to China was in 1989 just before the Tiananmen Square incident. That was a

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cornerstone. That was my first visit to China after 8 years in the US. A lot of things were changing and it was very nice. After that I practically went back to China every year and spent a couple of months; in recent years, always two months or more. I go back in summer to give courses to graduate students and try to find post-docs and good students. At the beginning, none of us who became professors would return to China, we would settle in the US. It's hard to say whether it's good or bad. But I think, in general, I'm still very positive that we can still go back to serve the country in some way. China has changed drastically over the last ten years in particular. If it was 20 years ago, I would have gone back to China already. When I graduated in 1985, it was a very different time.

I: Your research spans both pure and applied mathematics. Were you already interested in applications to physics right from the beginning?

L: Physics is always a subject that I liked ever since high school. In the college admission test, I got my best score in physics. But I never really got seriously interested in physics. I always see myself as a mathematician. I am always interested in mathematical issues which may or may not be related to natural phenomena or science. After many years at the Courant Institute, my philosophy and point of view have been changing. To me, as your age grows, you realize that when you are young, whenever people tell you some problem or you see a problem, you just jump in and try to solve. But you gradually realize that there are simply too many problems, infinitely many problems, and "a man should know his limitations". You cannot solve all of them. And therefore, you have to be very selective. As age grows, your view changes and you spend more time selecting the problems. To me the type of problems is very important. At any point of time, there is only a small set of really interesting problems. When you look at the publications 50 years ago, you say, "Oh, why are the papers on such bizarre subjects?" You can be sure 50 years from now, people looking at our publications will say the same thing. What this means is that the problems that are interesting now may not be interesting in the future. So one has to choose a problem that is not just mathematically interesting but also relevant to what is going on in science. Science is always developing; it's not just imagination and creativity, it's driven by practical needs.

I: How do you select your problems you want to work on? Do you get them from journals or do you talk to people?

L: You choose a problem depending on your training, background and interest and by reading and talking to people – for me a lot of time reading non-mathematical articles in *Nature*, *Science* and so on. You know what is relevant and that is very important. Of course for some mathematicians, you can simply ignore what is going on in the world and do whatever you like. You know, science develops so drastically and is so diverse that if you don't pay attentions to the whole picture you are going to miss out quite a lot.

I: Courant Institute is mostly inclined to applied mathematics, am I right?

L: Yes, but we have faculty in both pure and applied mathematics, probably stronger in applied. But we have a very strong group in pure mathematics too. In the University of Chicago, I was regarded more as an applied mathematician, but at the Courant Institute I'm probably more on the pure side of mathematics.

I: Would it be fair to say that partial differential equations used in modeling physical phenomena are often based on simplified and ideal assumptions. As such do these equations actually reflect reality?

L: First of all, I would like to answer in a philosophical mode. Absolute truth or reality doesn't exist or is probably not so important to us. Even if it exists, when we try to understand natural phenomena, it's through our perception. So when we talk about reality or truth, it's always an approximation. If we know the absolute truth or reality, we probably understand the problem so well and therefore the problem is not worth studying. We model by using partial differential equations and other mathematical methods. A model is a model. Therefore you have to simplify and make certain fair assumptions. But between different models one can sometimes distinguish between good models and not so good models. So what is the distinction? First of all, we want simple models because we can understand simple things better. If the model is as complicated as the real problem, what is the use of the model? A good model should always capture the essence and characteristics of the issues you want to address. A minimum requirement of a good model is to be real enough. How much you want is a practical trade-off for your needs. Yes, partial differential equations always use simple models. The good thing is that most of the time when we understand these models, we also understand the general situation.

I: Would you consider modeling more of an art rather than a science?

L: It's a bit of both. You cannot forget the fundamental issues you want to capture or understand; this aspect is science. How you do it – you do it nicely and elegantly or you just do your very best – that is art, and it also depends on the technology available.

I: Is there any recipe for doing good modeling?

L: I'm not a specialist in modeling. I think it's like doing physics or mathematics. Unconsciously, people use some very basic principles.

I: Which type of problems is more tractable? Evolutionary problems (i.e. parabolic or hyperbolic type) with given initial values or elliptic boundary value problems?

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L: It's very hard to make a distinction or comparison between different types of problems and say one is easier or more difficult than the other. The problem can be extremely difficult for simple questions. The problem can be relatively simple even though it addresses a complicated system of equations. Really it is what you want to achieve. If you want to access a large space of phenomena, even for very complicated systems, it is easy to come by. If you want to understand very delicate, very detailed information of some specific issues, then you have to look into very detailed characteristics of the problem and it can become difficult to solve. I think the difficulty depends on the issues you ask or the final conclusion you want to draw from the problem. It is not the type of problem (stationary or evolutionary) posed that is easier or harder.

I: Are the difficulties merely technical?

L: Some problems technically could be very tough. Other problems you simply don't know how to approach. In that kind of situation, one has to be very original and have deep insight into the problem.

I: It seems there is a tendency to resort to computational methods when analytical solutions seem to be beyond reach. Is this a new paradigm in applied mathematics? Has this approach yielded new insights or breakthroughs?

L: In some way, I could say "yes". Historically, computation is an auxiliary tool. When we have difficulties understanding something, let's do some computation or we do some computations to verify. So therefore computation is always something supplementary to facilitate certain ideas and prove they work or do not work. With the development of science and technology, the situation is changing drastically, particularly over the last 10 or 20 years. The use of supercomputers in modeling is not only to understand certain issues and to do computations or numerical simulation; it is also becoming a preliminary kind of science. For example, in earlier times, we do a lot of experiments in materials. Then from the experiments we propose some empirical model according to our physical intuition and theory. From the equations there could be something new. Then you test the theory with the experimental data and then you modify and add in more parameters and so on. This is the classical way of doing things. But now it seems you don't go through the theoretical part so clearly at the preliminary stage. Some simply feed into the computer various parameters, effectively hundreds of experiments, at the same time. So you have much more data collected and how to handle these data and from these data get a reasonable mathematical model has become a sensitive issue in itself. The use of computers to model has become a necessity. It is not necessarily separated... I have this wonderful idea that I want to test using computers. No, you can also get the idea from the computational experiments.

I: So simulation will give rise to new ideas?

L: Right. Simulation itself will give insight into the problem as well as understanding of the problem. The computer can generate tons of data. Afterwards, you have to understand what these data are. You use statistical methods or other methods. With some models you can still do a testing. This process creates a lot of new mathematics. Some of the ideas that people have these days are from ancient times and they dropped out after Newton-Leibnitz's calculus worked so nicely and simply in ideal situations.

I: But Newton did not depend on simulation to come up with the calculus.

L: Mathematics does have a unique position in science. Sometimes it's indeed surprising that something that you somehow have purely from the imagination and logical deductions has to do with the real world. It may be because imagination is a part of the real world.

I: Is there any discovery of yours that you find intuitively surprising?

L: It's very hard to say. Sometimes when you prove something or create something you find it surprising. But after several years of deeper thinking and understanding, you realize that it's so natural. I find most of the things I did are indeed very natural. At a certain stage, something happens and one is surprised once in a while. For example, sometimes by looking at seemingly more complex problems, one can do much better. In the beginning it was a kind of surprise, but after years of thinking and understanding one realizes that it is very natural.

I: In your work on partial differential equations, do you put much emphasis on the beauty of the model rather than the technical details?

L: I'm personally much more interested in the ideas and methods that solve the problem. Sometimes there are certain technical computations you cannot avoid and you have to be able to handle such difficulties. Sometimes the technical things are the real things. But sometimes you are interested in the idea and the approach to the problem – which may be more beautiful and useful.

I: I believe some physicists believe that if a theory is beautiful, it must be correct.

L: In a certain way. If something is very simple, very beautiful, you say, "It's fantastic." Sometimes one can understand it from basic mathematics. But simple things could involve very deep and complicated mathematics. So you never know.

I: Is the Ginzburg-Landau equation completely solved in dimension 2?

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L: There are a lot of papers and books on the Ginzburg-Landau equation in 2-d and 3-d. In a certain sense we understand quite a lot about these equations and their solutions. In partial differential equations, it seems you have so many equations to work on. But the good thing is that only a few equations are really fundamental and interesting. These equations will appear now and will appear later again and again. So I won't say that we completely understand the Ginzburg-Landau equations. It depends on what kind of questions asked and what kind of issues you want to address. For example, the Laplace equation – people worked on it for 200 or 300 years, we practically understand every aspect of it, but once in a while people will tell you something new about the equation. Because the Ginzburg-Landau equation is one of the fundamental equations to model basic physical phenomena, it is a nonlinear partial differential equation and I think it will appear again and again. Even for 2-d, there are some issues we don't understand. So I won't say it's completely solved.

I: The Navier-Stokes equations are extremely difficult to solve. Is it due to the fact that it is difficult to formulate radically new concepts within the framework of classical physics?

L: They are probably one of the most fascinating partial differential systems I know of. I have personally spent some time thinking about them, but not really a lot because you get nowhere. We realize there are a lot of difficulties in understanding the issues but we don't know how to overcome these difficulties. Unlike a lot of mathematical questions, when you really understand the real difficulties of the problem you may try to find a way to overcome them. And sometimes you are lucky to solve them. For this one, looking at the difficulties from various views and angles, we understand it in a certain way but we don't know how to overcome them. Is it because of mathematically technical reasons or is it the formulation at the fundamental level? I really don't quite know. I won't be surprised maybe some day some people say, "This system is only one part of a grand physical system which may be solvable even though we don't understand this particular one." This may go back to the fundamental level of formulation of the problem. Maybe there is something missing from the very beginning. On the other hand, the Navier-Stokes equations are, from the mathematical point of view, already consistent and well-posed. In other words, it is a closed system and you don't need extra information from outside. But however, sometimes extra information from outside could lead to some fundamental or more radical ideas which may assist.

I: Is the existence part of the problem partly solved?

L: We understand existence under the so-called weak conditions, but we want a classical solution. People always tell you that it may not be important to real physics. But it is a very intriguing question, a simple mathematically

formulated problem, and we simply do not know the answer. It's very mysterious.

I: But the physicists do not worry about the existence of solutions.

L: To the physicists, the physical system must exist but they may not talk about classical solutions. It's hard to say what one should really believe in. This is part of the difficulty.

I: The Navier-Stokes equations are classical and not quantum mechanical, isn't it?

L: Yes, there are many, many ways to derive that equation. Of course, from the mathematical point of view, you can forget whatever way you derive it.

I: Do the Navier-Stokes equations apply to all fluids?

L: Yes, but there are compressible or incompressible fluids, or visco-elastic fluids... One can derive similar equations in many real problems of physics.

I: Have they been extended or modified in some sense?

L: There are more complex forms of these equations and modified forms. But for the classical Navier-Stokes equations somehow the modified equations are couched in such a way that it is no longer interesting because the very difficulties of the original equations disappear. This is not the way to find a mathematical theory.

I: What are the chances of solving the equations in the next 30 years say?

L: It's very hard to make a prediction. Personally I don't like to make a prediction. But I would say it cannot be done in a relatively short period of time and may last a long time. For generations the best trained minds have attempted the problem and it has defied all attempts.

I: It seems that applied mathematicians are generally more gregarious in research in the sense that they collaborate more among themselves than pure mathematicians do. Why is that so?

L: Yes, I also tend to believe that applied mathematicians are more gregarious than pure ones. I'm not surprised. But you also see more and more pure mathematicians joining efforts together to solve problems. It depends very much on the nature of the problem. Traditionally the mathematician works individually. But as the problems become more multidisciplinary and complex, it is natural to have groups of people working together to attack a common problem. In applied mathematics, the problems are by nature across the fields – it's mathematics applied to other sciences – and come from different disciplines. So it's not surprising. It should be this way.

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I: What is your advice to the beginning graduate student who is interested in both pure mathematics and applied mathematics?

L: Just because you want to be cross-disciplinary, you try to understand a little bit from each field. That is, unfortunately, not the way. It is like that you are trying to understand the art better than they do. There is no reason you would do a better job than the experts from different fields; they can do much better than you do. Even if you do cross-disciplinary research, you have to be a specialist in one or two things – the insight, the ability to separate the problems. When you have that, you need to have an open mind, to learn things and get interested at the beginning. Even if you work in pure mathematics you shouldn't work alone in research. I may be more practical in a certain way but I'm interested in what is going on in pure mathematics and science and so on. If you have this kind of attitude and you specialize in one field, have an open mind in expanding your horizons to learn more things, you will do a very good job. People from different disciplines think in different ways. It's very interesting and good to know. Intellectually it's very satisfying. One would also find that there are many things in common.

I: Do you have any students?

L: At the moment I have four students – two are going to graduate, maybe next year. I have maybe 10 or 11 students who have already graduated. I also have some post-docs working with me.

I: Do you think that Chinese students are inclined more towards the applied side?

L: I don't think that way. They could be neither pure nor applied. The training in China generally seems to have certain disadvantages because students tend to focus and concentrate very early on one very special topic and remain so for most of the time. Once in a while you see a very top student but he is narrowly focused. If you are too focused very early on, then your ability will be very narrow also. If you don't expand your horizons and knowledge, then you lose your chance. Later on, when you see a problem you would say, "Oh, it's outside my field." Always take more topics courses. It shouldn't be that you take a course just to apply it to something. Of course, when you work on a problem, you will use whatever tools you have to solve it.



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