



NEWSLETTER OF THE INSTITUTE FOR MATHEMATICAL SCIENCES, NATIONAL UNIVERSITY OF SINGAPORE

The Langlands Program and the Principle of Functoriality

From 17 December 2018–18 January 2019, the Institute hosted the program “On the Langlands Program: Endoscopy and Beyond”. The program organizers contributed this invited article to Imprints.

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From left: Wee Teck Gan, Dihua Jiang and Lei Zhang

For more than 50 years now, the Langlands program has been at the forefront of mathematical research, especially at the intersection of number theory, automorphic forms and arithmetic geometry. In 2018, its main protagonist, Robert P. Langlands, was awarded the Abel Prize for his visionary work. Quoting the prize announcement video,

“Some mathematicians are immortalised by a theorem. Others by a conjecture.

*But of the great mathematicians,
only Robert P. Langlands is immortalised by a program.”*

A 5-week long program on the Langlands Program: Endoscopy and Beyond was held at the IMS during December 17, 2018 to January 18, 2019. It was organised by Bill Casselman (University of British Columbia), Pierre-Henri Chaudouard (Paris 7), Wee Teck Gan (NUS), Dihua Jiang (University of Minnesota), Lei Zhang (NUS) and Chengbo Zhu (NUS). The program had been in the planning for the past two years, before Langlands’ Abel Prize award. So it was fortuitous, as far as timing goes, that the program was held in the same year of Langlands’ award, adding an extra joyous atmosphere to the proceedings.

The crux of the Langlands program can be boiled down to two main principles:

- The **Reciprocity Law**: this is a far-reaching generalization of the classical quadratic reciprocity law of Legendre and Gauss and the abelian class field theory

FEATURED

01

The Langlands Program and the Principle of Functoriality

Interview:

14

Tze Leung Lai

NEWS

06

Past Activities

22

Upcoming Activities

OTHERS

21

Lecture Note Series

24

Call for Proposals

of Hilbert, Takagi and Artin. In its modern incarnation, due to Langlands, the reciprocity law gives a precise dictionary between Galois representations (which are of arithmetic nature and of interest to number theorists) and automorphic forms (which are generalisations of classical modular forms and are of a more analytic nature).

- The **Functoriality Principle**: this is a principle which predicts precisely how automorphic forms on different groups are related to one another. An important special case of functoriality is the theory of Endoscopy. This special case was singled out by early works of Langlands, Labesse and Shelstad.

Both these principles are predicated on the introduction of the Langlands L-group in a well-known letter of Langlands to André Weil in 1967.

In the past 15 years, there has been a great deal of progress in the Langlands program, for both the reciprocity law and the functoriality principle, especially in the context of endoscopy. Much of this progress has been due to the theory of the stable trace formula developed by Arthur. To some extent, the theory of endoscopy has now been largely completed. The goals of the program were:

- to take stock of the current status and to explore applications of the theory of endoscopy as well as more refined questions.
- to look beyond endoscopy following the suggestions and work of Langlands, Braverman-Kazhdan, Ngo and Altug.

In the first 3 weeks of the program, there were 4 short courses on the following topics:

- Arthur packets, given by Hiraku Atobe (Kyoto University) and Wee Teck Gan
- the Braverman-Kazhdan program, given by Ray Zhilin Luo (University of Minnesota) and Lei Zhang
- The stable trace formula with emphasis on $SL(2)$, given by Abhishek Parab (Purdue University) and Tasho Kaletha (University of Michigan)
- The Altug and Arthur approach to Beyond Endoscopy, given by Julia Gordon (University of British Columbia) and Ali Altug (Boston University).

These courses were well attended by close to 100 participants, many of whom are graduate students or postdoctoral researchers. The lectures have been webcast on the IMS Youtube channel and the notes will appear in a proceedings to be published by the IMS. There were also a number of seminar talks on a wide range of topics, given mostly by young postdoctoral researchers, during this period.

The program in the first 3 weeks straddled the two long weekend breaks for the Christmas and New Year's vacation. These long weekends afforded the participants a very healthy work-life balance: 3 days' worth of intensive lectures followed by 4 days of rest and free time. The 4-day rest period was extremely helpful in the sense that it offered participants a chance to have fruitful discussions and closer interaction outside the lecture times. It also provided ample opportunities for participants to visit different sights in Singapore (and neighbouring countries) and to have food outings to savour the diverse local cuisines (such as the almost mandatory chilli or black pepper crabs as well as more exotic items like turtle soup and frog porridge).

The highlight of the program is the week-long conference held in the 4th week (January 7–11, 2019), when we welcomed even more visitors and speakers. It was quite intensive with 5 talks a day. The number of participants swelled to 120 or so during this week. The speakers hailed from many leading universities worldwide and reported on many exciting recent progress in the Langlands program. A highlight was the Distinguished Visitor Lecture Series by Bảo Châu Ngô of University of Chicago. Professor Ngô was one of the winners of the Fields Medal in 2010 for his work proving a crucial result in the Langlands Program known as the Fundamental Lemma. On this occasion, he gave two talks on slightly different topics. The first talk, which took place on January 9, 2019 in the Department of Mathematics at NUS, was on the Braverman-Kazhdan program on the theory of L-functions, while the second talk was held at the IMS a week later and was titled "On the Hitching fibration for algebraic surfaces".

The last main event of the program was a public lecture given by Professor Bill Casselman on "Mathematics in the Solar System". It was a very interesting talk with many computer simulations and was well attended by over 100 people, including many high school students. The public lecture provided a relaxing and fitting end to 5 weeks of intense mathematical activities.



Participants of the Langlands Program

Scientific Advisory Board

New Chair

The Institute is pleased to announce the appointment of Professor Iain Johnstone as Chairman of the SAB with effect from 1 July 2019. He takes over from Professor Yum-Tong Siu who completes his term on 30 June 2019.

New Members

🌐 **Ngô Bảo Châu:** Professor Ngô holds the Francis and Rose Yuen Distinguished Service Professorship at the University of Chicago. He also serves as the Scientific Director of the Vietnam Institute for Advanced Study in Mathematics. He received the Clay Research Award in 2004 and the Fields Medal in 2010. He was conferred the order of *Legion d'Honneur* in 2011. Professor Ngô is a Fellow of the American Mathematical Society since 2012.



🌐 **Emmanuel Ullmo:** Professor Ullmo is Director of the Institut des Hautes Études Scientifiques (IHÉS) in Paris. He was awarded the Élie Cartan Prize by the French Academy of Sciences in 2006.



🌐 **Benoît Perthame:** Professor Perthame is Professor at Sorbonne University and member of the French Academy of Sciences. He headed Laboratory Jacques-Louis Lions from 2013 to 2019, and created the team Biology, Analysis, Numerics, Geophysics at Inria. In 2013, he was awarded the Blaise Pascal Medal and became a member of the European Academy of Sciences.



🌐 **Gim Pew Quek:** Mr Quek is currently the Chief Defence Scientist of the Singapore Ministry of Defence. He chairs the Temasek Defence Systems Institute in NUS and the Centre for Quantum Technologies. He also serves on the boards of A*STAR, the Defence Science and Technology Agency, DSO National Laboratories and ST Engineering. He is a Fellow of the Academy of Engineering of Singapore and an Adjunct Professor in the NUS Department of Electrical and Computer Engineering. His awards include the individual Defence Technology Prize in 1992, the Public Administration Gold Medal in 2007 and the NUS Distinguished Engineering Alumni Award in 2014.



Board of Management

New Member

🌐 **John Thong:** Professor Thong is currently head of the Department of Electrical & Computer Engineering at NUS. He is co-director of the NRF Quantum Engineering Program.



In Appreciation

The Institute would like to express its deep gratitude to Professor Yum-Tong Siu, Harvard University, who has been with the Board since 2009. Professor Siu has been the Chair of the Scientific Advisory Board since March 2011. As Chair, he has provided strategic guidance to IMS, and ensured that the institute's work contributes to its mission of fostering mathematical research and nurturing young mathematical talents.

The Institute would also like to thank the outgoing SAB members, Professor Wolfgang Hackbusch (Max Planck Institute), Mr Tong Boon Quek (Ministry of Trade & Industry), and Professor Hugh Woodin (Harvard University) and MB member Professor Andrew Lim (NUS).

IMS Distinguished Visitors

IMS arranges visits to the Institute by distinguished scientists who are prominent leaders in their communities. The program started in 2015. This initiative aims to enhance the diversity of people participating in our research programs, and provide mentoring/ inspire junior researchers and graduate students. Each distinguished visitor spends at least two weeks in Singapore, and participate in a variety of activities, including lecturing about their own research, give public talks, meet with faculty, and interact with program participants.

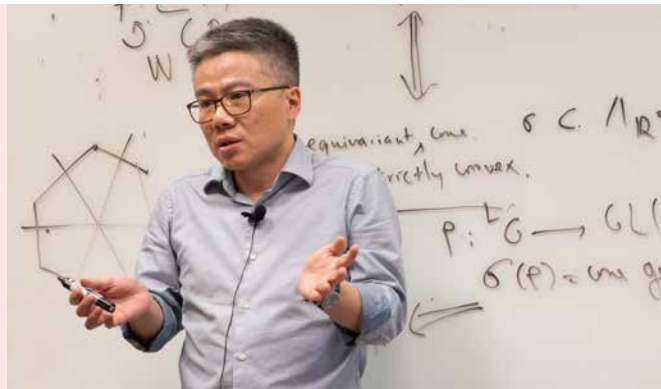
Under this program, the Institute has enjoyed visits from a stellar array of distinguished scientists. The list of distinguished visitors may be found on our website.



ASHOKE SEN

Professor Ashoke Sen is a distinguished Professor at the Harish-Chandra Research Institute, India. His major area of research has been superstring theory -- a theory that attempts to unify all the forces of nature into a single quantum theory. His work covers several aspects of superstring theory including strong-weak coupling dualities, black hole entropy, superstring perturbation theory and superstring field theory. For his contribution to the field he was awarded the Breakthrough Prize in Fundamental Physics, Dirac medal and the civilian award Padma Bhushan by the government of India.

Professor Sen visited IMS for the workshop on *String and M-Theory: The New Geometry of the 21st Century* (10–14 December 2018). He gave two talks on 11 and 13 December 2018.



NGÔ BẢO CHÂU

Professor Ngô Bảo Châu holds the Francis and Rose Yuen Distinguished Service Professorship at the University of Chicago. He also serves as the Scientific Director of the Vietnam Institute for Advanced Study in Mathematics.

Professor Ngô did his undergraduate study at the École Normale Supérieure and completed his PhD at the Université Paris-Sud in 1997. He was a member of CNRS at Paris 13 University from 1998 to 2004. In 2004, he became Professor at Paris-Sud 11 University and, in the same year, received the title of Professor in Vietnam. In 2010, he was awarded the Fields Medal for "his proof of the Fundamental Lemma in the theory of automorphic forms through the introduction of new algebra-geometric methods".

Professor Ngô visited IMS for *On the Langlands Program: Endoscopy and Beyond* (17 December 2018–18 January 2019). He gave two talks on 9 and 16 January 2019.



W. HUGH WOODIN

W. Hugh Woodin is Professor of Philosophy and of Mathematics at Harvard University. Woodin has been an ICM speaker three times, is a member of the American Academy of Arts and Sciences, and for nearly 20 years has been a Distinguished Visiting Professor in the Mathematics Department at NUS.

Professor Woodin visited IMS for the program on *Higher Recursion Theory and Set Theory* (20 May–14 June 2019). He gave two talks on 6 and 10 June 2019.



TZE LEUNG LAI

Tze Leung Lai is the Ray Lyman Wilbur Professor of Statistics and, by courtesy, also of Biomedical Data Science and Computational & Mathematical Engineering at Stanford University, where he is the Director of Financial and Risk Modelling Institute. Before moving to Stanford in 1987, he was the Higgins Professor of Statistics at Columbia University where he received his PhD and an Assistant Professor appointment in 1971 and was promoted to Professor in 1977. He received the COPSS Award in 1983 and was elected to Academia Sinica in 1994. He is also the honorary dean of the Center for Financial Technology & Risk Analytics at Fudan University, a visiting chair professor of Southwestern University of Finance and Economics, and an advisory committee member of the Yau Center for Mathematical Sciences at Tsinghua University, the Center for Statistical Science at Peking University, the Department of Statistics and Actuarial Science at The University of Hong Kong, and the Institute of Statistical Science, Academia Sinica, in Taiwan.

Professor Lai visited IMS for the program on *Statistical Methods for Developing Personalized Mobile Health Interventions* (4 February–1 March 2019). He gave two talks on 27 and 28 February 2019.



THEODORE SLAMAN

Slaman received his PhD from Harvard University in 1981 with Gerald Sacks as his dissertation supervisor. After a two-year fellowship, he joined the faculty at the University of Chicago. In 1996, he moved to the University of California Berkeley and has remained there since. Slaman is a frequent visitor to Singapore, and holds a Distinguished Visiting Professorship at the Mathematics Department at NUS.

Slaman has worked primarily on topics in Recursion Theory. He has been involved in applying a recursion theoretic perspective in other areas, such as models of Peano arithmetic, Reverse Mathematics, Set Theory and Diophantine Approximation.

Professor Slaman visited IMS for two programs; *Equidistribution: Arithmetic, Computational and Probabilistic Aspects* (29 April–17 May 2019) and *Higher Recursion Theory and Set Theory* (20 May–14 June 2019). He gave two talks on 21 and 27 May 2019.



SUSAN A. MURPHY

Susan Murphy is Professor of Statistics at Harvard University, Radcliffe Alumnae Professor at the Radcliffe Institute, Harvard University, and Professor of Computer Science at the Harvard John A. Paulson School of Engineering and Applied Sciences. Her current research interests concern clinical trial design and the development of data analytic methods for informing multi-stage decision making in health, particularly in mobile health. She is a 2013 MacArthur Fellow, a member of the National Academy of Sciences and the National Academy of Medicine, both of the US National Academies. She is currently president of the Bernoulli Society and incoming president of the Institute for Mathematical Statistics.

Professor Murphy visited IMS for the program on *Statistical Methods for Developing Personalized Mobile Health Interventions* (4 February–1 March 2019). She gave two talks on 18 and 25 February 2019.

String and M-Theory: The New Geometry of the 21st Century

10–14 DECEMBER 2018

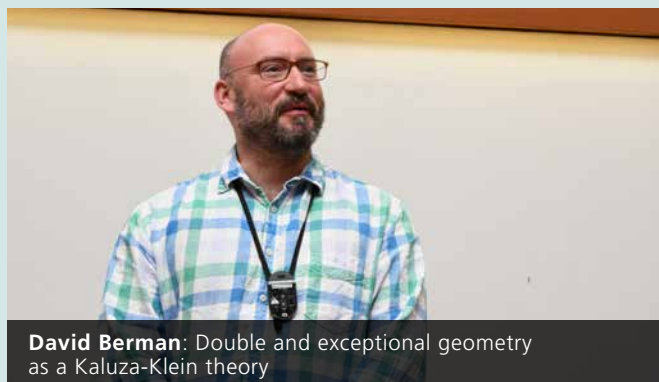
CHAIR:

Meng-Chwan Tan |
National University of Singapore

Apart from seeking the concept of “Theory of Everything”, this workshop aimed to help advance pure mathematics and theoretical physics in a nontrivial way. A better understanding of what the “new kind of geometry” that String/M-theory embodies would mean that new mathematics can be formulated, while current physical models which can be realized within the String/M-theory framework can also be more deeply understood. There were over thirty talks and more than fifty participants. This meeting has been relevant to the large community of condensed matter physicists in Singapore, especially in NUS.



Neil Lambert: M-Branes lessons from M2s and M5s



David Berman: Double and exceptional geometry as a Kaluza-Klein theory



The mathematics of stringy objects



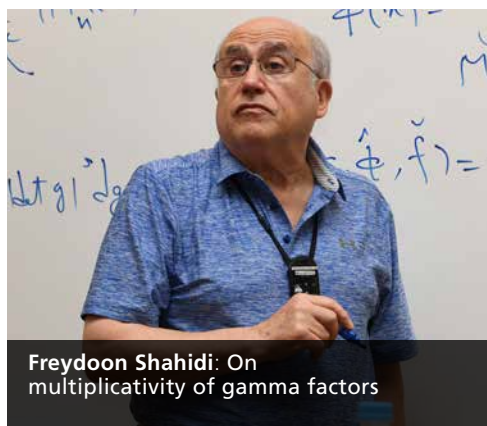
Rich description from the worldvolume perspective



Chong-Sun Chu: Holography, Weyl anomaly and induced string current in 6d BCFT



Mathai Varghese: Exotic equivariant cohomology of loop space



Freydoon Shahidi: On multiplicativity of gamma factors



Yiannis Sakelladris: Geometry of the moment map and the relative trace formula



Different definitions are equivalent for real classical groups

On the Langlands Program: Endoscopy and Beyond

17 DECEMBER 2018–18 JANUARY 2019

CO-CHAIRS:

Dihua Jiang |

University of Minnesota

Lei Zhang |

National University of Singapore

This program brought together researchers from different disciplines (i.e. Representation Theory, Trace formula, L-functions, Harmonic analysis) to work on the Langlands program. The program reported several current main approaches to attack the Langlands functoriality and explore its applications.

Introductory courses (over thirty hours in total) were planned in the first two weeks of the program. Almost all of the lectures were recorded and posted on the IMS YouTube channel. Following Professor Ngô Bảo Châu's approach to attack the Langlands functorial transfers in his talk, Professor Freydoon Shahidi investigated various examples, and made connections with the Langlands-Shahidi method in his presentation. Professor Jayce Getz explicitly constructed a kernel function in order to obtain the Langlands functorial for certain cases, while Professor Valentin Blomer applied the relative trace formula to obtain the refined results on the nonvanishing of central values of tensor automorphic L-function.

There were a total of 25 talks during the conference week. Junior participants and a few graduate students were excellent in communicating their ideas and research to a diverse audience. Local participants, including those from NUS (Department of Mathematics) and Singapore University of Social Sciences had a chance to work together. There were more than one hundred participants.



Tasho Kaletha (centre) engaging in discussions after his talk



Jayce Robert Getz: On triple product L functions for GL



On and beyond the Langlands functoriality conjecture



Enhancing learning and behavior change

**Anna Choi:** Mobile health technology in health applications**R. Todd Ogden:** Determining optimal treatments

Statistical Methods for Developing Personalized Mobile Health Interventions

4 FEBRUARY–1 MARCH 2019

ORGANIZING COMMITTEE:

Bibhas Chakraborty |

National University of Singapore

Ying Kuen Cheung |

Columbia University

Eric Laber |

NC State University

Jialiang Li |

National University of Singapore

Susan A. Murphy |

University of Michigan

Ambuj Tewari |

University of Michigan

In the era of “big data”, the large volume, quality and accessibility of patient-level data collected in mobile health applications has offered many opportunities for statisticians and data scientists. Work on mobile health (mHealth) is truly interdisciplinary and will benefit from the cross-fertilization of ideas from health-related domain sciences and mathematical disciplines in statistics and computer science (i.e causal inference, clinical trial designs and asymptotic theory, and reinforcement learning/artificial intelligence).

This program provided a platform for exchange between statisticians, computer scientists, as well as health/behavioural scientists working in the area of mHealth. By focusing on the theme of quantitative methods, participants learnt from each other about the cutting-edge study design and techniques in mHealth. The primary application area of focus was on the management of chronic diseases and conditions.

A one-week tutorial on the basics of personalized medicine, treatment regimes, reinforcement learning and

causal inference was planned before the main workshop, targeting at graduate students and professionals interested in personalized medicine and mobile health. The first workshop, which focused on the design considerations in the context of mHealth intervention studies (18–22 February 2019) had a total of 18 talks. The second workshop, which analyzed methods for data arising from mHealth studies (25 February–1 March 2019) had a total of 18 talks. There were more than 60 participants.

**Bibhas Chakraborty:** Dynamic treatment regimes and SMART design**Niranjana Bidargaddi:** Approaching mental health using mHealth systems

Roadmap for mobile health

**Sabrina Hsueh:** Applications of computational behavior science and interpretable AIML

Quantitative Finance I

18–22 MARCH 2019

Jointly organized with Risk Management Institute, NUS

CO-CHAIRS:

Min Dai |

National University of Singapore

Steven Kou |

Boston University

Quantitative finance is an interdisciplinary research area related to finance, mathematics, and statistics. This program will focus on three themes; 1) stochastic control in finance, 2) fintech and machine learning and 3) asset pricing and risk management. The first half of the



Participants of the 4th BPS Workshop on Quantitative Finance

program started with the 4th Berlin-Princeton-Singapore Workshop on Quantitative Finance (18–20 March 2019) which had 21 talks. Activities then continued on 21 March 2019 with another one-day workshop

which was jointly organized with RMI at the National University of Singapore and Humboldt-Universität zu Berlin, also known as the HUB-NUS Fintech Workshop. There were nine talks.

Equidistribution: Arithmetic, Computational and Probabilistic Aspects

29 APRIL–17 MAY 2019

CHAIR:

Theodore Slaman |

University of California, Berkeley

The program addressed recent advances and open problems in the theory of equidistribution by bringing together researchers from probability, number theory, computer science, and mathematical logic.

Participants of each community were eager to understand the approaches of others. A conference (29 April–3 May 2019) was planned with 19 talks. The week after was planned with 12 focused talks. The problem of normality and Diophantine approximation in different bases, which was first posed by Yann Bugeaud, was presented in the workshop by Theodore Slaman. Discrepancy of sequences in different ambient spaces such as Cantor sets, fractals, dynamical systems. In particular, to give lower bounds of discrepancy for different sequences. The talk by Dmytro Bilyk on discrepancy bounds provided tools and references that were not known to many participants. The property of Poissonian Pair correlation in sequences



Dmitriy Bilyk: Discrepancy bounds and related questions



Verónica Becher: Normal numbers with digit dependencies



Uniform distribution of applications

of real numbers captured attention and many problems were posed around it. The talk by Zeev Rudnick and the discussion with him resulted in a list of open questions. There were more than 30 participants.



Computable constructions of real numbers



Level spacing and minimal gaps

SASI – Singapore-Abu Dhabi-Shanghai-India Probability Meeting

27–29 MAY 2019

CO-CHAIRS:

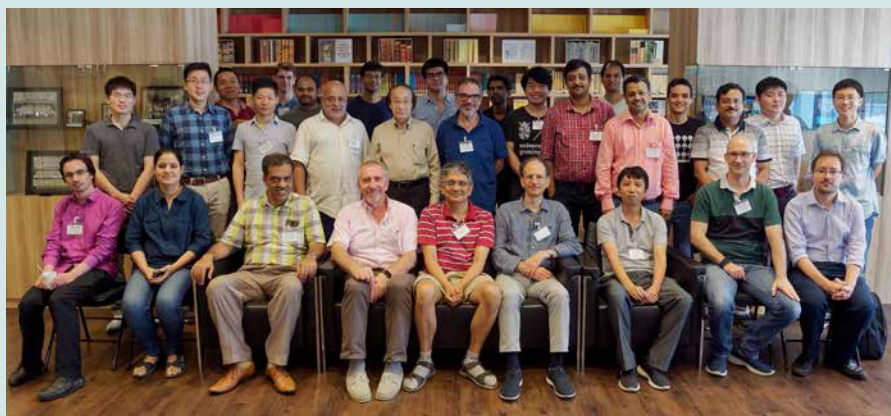
Adrian Röllin |

National University of Singapore

Sun Rongfeng |

National University of Singapore

This meeting aimed to bring together probability researchers from the Asia region, in particular from Singapore, NYU-Abu Dhabi, NYU-Shanghai and India, to foster research collaborations



Participants of the SASI 2019 meeting in Singapore

and discussions. There were ten talks and an open problem session which gave participants to present and discuss on various open problems. There were 26 participants.

Higher Recursion Theory and Set Theory

20 MAY–14 JUNE 2019

ORGANIZING COMMITTEE:

James Cummings |

Carnegie Mellon University

Andrew Marks |

University of California, Los Angeles

Yue Yang |

National University of Singapore

Liang Yu |

Nanjing University

The plan was to organize a program with a focus on higher recursion theory, definability in set theory and the interactions between these areas. Topics had included Martin's conjecture, higher randomness, the HOD conjecture, descriptive inner model theory and the Ultimate-L program.

The first week (20–24 May 2019) was planned with tutorials on hyperarithmetic theory, with applications to higher recursive



John R. Steel: Mouse pairs and Suslin cardinals



Ralf Schindler: MM++ implies (*)



Slawomir Solecki: Polishable equivalence

model theory by Antonio Montalban (University of California, Berkeley). This workshop on Higher Recursion Theory also had seven talks. The next two weeks (27 May–7 June 2019) followed with another workshop on Recursion Theory, Set Theory and their interactions, and had 25 talks. Last but not least, there was a third workshop on Set Theory (10–14

June 2019) which had nine talks. Paul Larson (Miami University) gave four ninety minute tutorials on AD+, synthesising a large body of mostly unpublished work by Woodin and others.

The talks were excellent, some of which announced solutions to some long standing open problems in the areas of focus for the program. Benoît Monin (LACL, Créteil University) reported his joint result with Ludovic Patey, separating SRT_2^2 from RT_2^2 in an ω -model. Adam Day (Victoria University of Wellington) reported on his joint work with Andrew Marks (University of California, Los Angeles), giving a complete solution to the Decomposability Conjecture under the assumption of Projective Determinacy. Richard Shore (Cornell



Domains beyond the set of natural numbers

University) spoke on joint work with Leo Harrington and Ted Slaman on Σ_1^1 . This implies many known basis and omitting types theorems. Slawek Solecki (Cornell University) spoke on a promising new approach towards proving the E_1 dichotomy in descriptive set theory. John Steel (University of California, Berkeley) reported on substantial progress in descriptive inner model theory. Ralf Schindler (Universität Münster) reported on a breakthrough result, MM^{++} implies $(*)$, which connects the two main lines in the search for strong axioms to control $\mathbb{P}(\omega_1)$. This solves a long standing problem posed by Hugh Woodin.

The workshops were scheduled to allow plenty of time for discussion and collaboration. The program was well attended, and attracted participants at all levels of professional development. There were over 70 participants. The schedule for the workshops can be found on the program website.



Questions of a set-theoretic flavor



Every ground model is definable



Undirected graphs come with uniform effective

Ng Kong Beng Public Lecture Series



17 JANUARY 2019

Mathematics in the Solar System

Astronomy represents one of the earliest applications of mathematics. Prof. William A. Casselman explained that Babylonians thought the gods were speaking to them through the stars and planets. They were therefore facing the difficult problem of having to predict planetary motion in order to understand what was being said to them. Of particular interest was Mars's peculiar retrograde motion — occasions when Mars seemed to wander backwards on the night sky, which happens roughly every two years. Here is a time series from the 17th century over a time span of 50 years, expressed in number of days between two consecutive oppositions, that is, two time points when sun, earth and Mars are aligned:

764, 767, 776, 803, 806, 780, 769, 765, 765, 771, 791, 812, ...

Babylonians were already able to predict these events, despite the fact that the intervals look quite random to the unexperienced eye. However, they did ultimately not understand the geometry behind this phenomenon. Even the Greeks, who were able to predict not only the intervals but the entire paths of the planets on the sky, did not correctly understand the arrangement of the celestial bodies in our solar system.

Based on works of Copernicus and Galilei, it was Kepler who first came up with the right model and mathematical language to describe planetary motion: The sun at the

centre and the planets circling around the sun in ellipses, rather than an elaborate system of nested perfect circles with Earth in the centre, as was the case in the Ptolemaic system since the Graeco-Roman era.

Newton later set the physical foundations of gravitational forces, explaining not only the appearance of Kepler's ellipses, but adding parabolas and hyperbolas to the set of possible paths celestial bodies can take around each other. Shortly after, Halley successfully applied Newton's theory to the study of comets, in particular what is today called *Halley's comet*.

As beautiful and elegant Newton's theory is, it is nevertheless difficult to predict some of the development of our solar system in the long run. As Prof. Casselman showed with the example of the comets *Lexell*, which was probably ejected out of the solar system after multiple close encounters with Jupiter, and *Helin–Roman–Crockett*, the *three-body problem* is still unsolved even in very simple and symmetric arrangements. The particular case of the Pythagorean *three-body problem*, also called *Burrau's problem*, shows the difficulties of making long-term predictions. Placing three bodies of masses 3, 4, and 5 at the vertices of a 3-4-5 right triangle, it turns out that one of the bodies eventually wanders off alone in one direction, while the other two wander off in the other direction, destined to circle around each other for eternity.

William Casselman of The University of British Columbia, Canada delivered the public lecture at NUS on 17 January 2019. A total of 139 people attended the lecture.



Mathematical means of interpreting the solar system

21 FEBRUARY 2019

Mobile Health Intervention Optimization

A few decades ago, most of the experimentation that went on in the USA, essentially in the form of randomized controlled trials, had to do with improving health; this is no longer the case. As Professor Susan A. Murphy explains, almost all of randomized experimentation nowadays is taking place on the World Wide Web, and it is being used to sell us things. One of the goals of *Mobile Health Intervention* is to adapt these new ideas and return experimentation back to improving health. One of these ideas are micro-randomized trials, and Professor Murphy illustrated it on the *HeartSteps* study she was involved with. Part of the study was to decide when participants, who were given wearable devices, had to be prompted with a suggestion to engage in some form of physical activity. The potential for disengagement through pushing too many prompts to the device is very high, and too many stimuli leads to habituation, resulting in the participants ignoring the prompts. Moreover,

availability has become a major issue — in certain settings, it is completely inappropriate to interrupt the user. For example, in the *HeartSteps* study, if the sensors of the wearable device would indicate that the user is driving, no prompt would be given during that time. Or if the user was already performing some physical activity, there would be no point in suggesting a new activity. The main question of the study was to determine whether these interventions had any near-term effect, and if so, did it deteriorate over time. Professor Murphy introduced her method of *Centered and Weighted Least Squares Estimation* to answer these questions appropriately from a statistical point of view. One of the conclusions of the study was that, while indeed a positive effect of activity suggestions on the number of steps in the subsequence 30 minutes was found, the study also showed that the effect deteriorated over time.

3 JUNE 2019

Can Every Mathematical Problem Be Solved?



Susan A. Murphy

"I didn't know there were any open problems in mathematics. I thought you people knew everything!" These were the words of Professor Magidor's father after his graduation ceremony at the Hebrew University in Jerusalem, and they reflect the attitude of many even well-educated people. But, as Professor Magidor points out, there are many open problems in mathematics. A famous one is the *Twin Prime Conjecture*, which asks whether there are infinitely many pairs of prime numbers which are only two apart from each other. While progress has been made, the answer to this question is still unknown. Another one is the *Goldbach Conjecture*, which claims that every even number greater than 4 can be expressed as the sum of two odd primes. Again, it is unknown whether this conjecture is true or false. And one of the most famous conjectures is of course *Fermat's Last Theorem*, which was only proved in 1994, and so it took 350 years to settle this specific question. In view of these examples, Professor Magidor asks the simple question whether every mathematical problem actually has a solution. David

Susan A. Murphy of Harvard University, USA delivered the public lecture at NUS on 21 February 2019. A total of 61 people attended the lecture.

Hilbert [1862–1943], one of the greatest mathematicians of his time, believed very strongly that, while it may take a long time to find it, every mathematical problem has a solution, and he even tried to find a proof for this very statement itself. This became known as *Hilbert's Program*, which is an attempt to create a formal language in which every mathematical statement could be phrased and proved or disproved. This program was disrupted by Kurt Gödel [1906–1978], who was able to prove that in any consistent formalized mathematical system, rich enough to support basic facts about Arithmetics, there is a mathematical statement for which there is neither a proof nor a proof of its negation. While thought to be rather obscure at the time, it was later shown that these statements, which can be neither proved nor disproved, can be turned into statements about certain equations having natural numbers as solutions.

Professor Magidor continued to discuss the different types of infinite sets, a topic initiated by Georg Cantor [1845–1918]. The impact of Gödel's work was very concrete in this area, as it helped to answer — to some degree — the *Continuum Hypothesis* question, which asks whether there is an infinite set that is, in some mathematical sense, between the set of integers and the real line. It turns out that this question can be neither proved nor disproved within the standard framework of mathematics. As a consequence, one can ask the question on how to expand the current set of axioms such that the *Continuum Hypothesis* can be settled in one way or another. Of course, adding the hypothesis itself or its negation is one way out, but one would hope that only much more basic axioms need to be added. Coming to the end of his presentation and showing quotes of various famous mathematicians, Professor Magidor seemed to make the point that we should not be afraid of extending the standard set of axioms in order to solve currently unsolvable problems. If these new axioms in turn generate new unsolvable problems, then that's a (worthwhile!) price we need to pay.

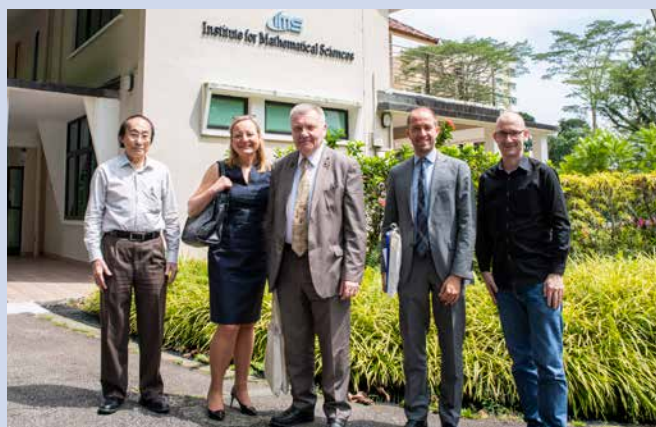
Menachem Magidor of The Hebrew University of Jerusalem, Israel delivered the public lecture at NUS on 13 June 2019. A total of 94 people attended the lecture.



Menachem Magidor

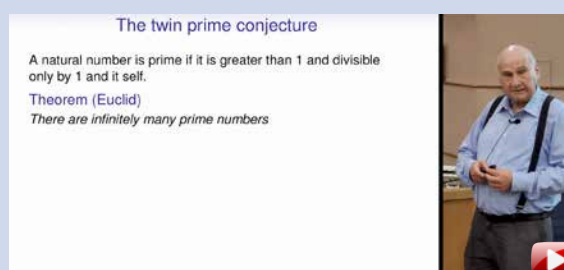
Visit by delegates of the European Research Council

March 12, 2019. While on an official trip to Singapore, President of the European Research Council Professor Jean-Pierre Bourguignon and his colleagues took the opportunity to visit NUS and the Institute for Mathematical Sciences, where they were hosted by former IMS Director Professor Louis Chen and Deputy Director A/Professor Adrian Röllin. After a brief introduction to the Institute, its organisational structure and after highlighting some of our past and upcoming programs, both sides exchanged ideas and discussed opportunities for further collaboration.



From left: Emeritus Professor Louis Chen, Ms Sabine Simmross, Professor Jean-Pierre Bourguignon, Mr Jean Pierre De Meerleer Sánchez and A/Prof. Adrian Röllin

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TZE LEUNG LAI:

FROM ACCIDENTAL
STATISTICIAN TO INTER-
DISCIPLINARY STATISTICIAN
WHO COMBINES THEORY
WITH PRACTICE

**Interview of Tze Leung Lai
by Y.K. Leong**

Tze Leung Lai is well-known for his far-reaching contributions in sequential statistical analysis and wide-ranging applications in engineering, finance and biomedical sciences.



Starting with a reluctant switch from economics to mathematics in his early undergraduate years, Lai graduated with first class honours in mathematics from the University of Hong Kong (HKU). After a one-year stint as demonstrator in mathematics in HKU, he went to Columbia University for graduate study in statistics essentially out of convenience in an application process. Subsequently, again as a matter of convenience, he stayed and taught at Columbia for 16 years. Destiny has it that while he was teaching a new course on time series in his early faculty years, he was accidentally roped in as a statistical consultant into a medical project on the sudden infant death syndrome in the Pediatric Pulmonary Division of the Columbia Presbyterian Medical Center. This marked the beginning of an enduring interest and prolific contribution to multidisciplinary research in a wide spectrum of areas in the biomedical sciences, engineering and financial mathematics.

He has published over 300 papers and 12 books, and has supervised 74 Ph.D. theses at Columbia, Stanford, and Stony Brook and University of Padova in Italy (where he visited). He has served on the editorial boards of leading international journals such as *Journal of the American Statistical Association*, *Zeitschrift für Wahrscheinlichkeitstheorie und Verwandte Gebiete*,

Probability Theory and Related Fields, *Statistica Sinica*, *Annals of Mathematical Sciences and Applications*, *Sequential Analysis*, *Journal of Statistical Planning and Inference*, and *Journal of Multivariate Analysis*.

Among his many contributions to sequential statistical analysis is the development of a comprehensive theory of sequential tests of composite hypotheses, unifying previous approaches and providing far-reaching extensions to cope with the practical complexities that arise in the applications to group sequential clinical trials. He has also done ground-breaking work in (i) the solution of the long-standing “multi-armed bandit problem”, (ii) stochastic approximation and recursive estimation, (iii) adaptive control of linear stochastic systems and Markov decision processes, (iv) saddlepoint approximations and boundary-crossing probabilities in Markov random walks and random fields, and (v) survival analysis.

He was Higgins Professor of Mathematical Statistics before moving to Stanford University in 1987 as Professor of Statistics. During the past three decades at Stanford, he served as Director of the Interdisciplinary Program in Financial Mathematics and Co-director of the Biostatistics Core, Stanford Cancer Institute. Currently, he is the Ray Lyman Wilbur Professor of Statistics and by courtesy, also

of Biomedical Data Science and of Computational and Mathematical Engineering. His capacity and energy for multidisciplinary work is legendary, as can be seen in the numerous hats he is now wearing: Director of Financial and Risk Modelling Institute (FARM), Co-director of the Center for Innovative Study Design (CISD) and core member of the Comprehensive Cancer Institute, Center for Innovation in Global Health, Center for Precision Mental Health and Wellness, and Center for Population Health Sciences in the School of Medicine.

Since the late 1980s, Lai's tireless efforts have also made their imprints on the development of the statistical sciences in China. He is also the honorary dean of the Center for Financial Technology & Risk Analytics at Fudan University, a visiting chair professor of Southwestern University of Finance and Economics, and an advisory committee member of the Yau Center for Mathematical Sciences at Tsinghua University, the Center for Statistical Science at Peking University, the Department of Statistics and Actuarial Science at the University of Hong Kong and the Institute of Statistical Science, Academia Sinica in Taiwan. Notable among the numerous honours and awards he received is the prestigious COPSS Presidents' Award, the annual award given by the Committee of Presidents of Statistical Societies (COPSS) to statisticians below the age of 41 and sometimes referred as the "Nobel Prize of Statistics".

Lai's association with the National University of Singapore (NUS) dates back to 1989-1993 when he was its external examiner in mathematics. He is an old friend of Louis Chen, former director of NUS's Institute for Mathematical Sciences (IMS) and was the Ph.D advisor of Hock Peng Chan and Tiong Wee Lim, respectively the current Head and a Deputy Head of NUS's Department of Statistics and Applied Probability (DSAP). Lai visited DSAP in January–March 2017 as Saw Swee Hock Visiting Professor and was back again at NUS for the IMS program on Statistical Methods for *Developing Personalized Mobile Health Interventions* (11 February – 1 March 2019) in which he gave two IMS Distinguished Visitor Lectures on (i) *Real World Data, Real World Evidence, and Decision Analytics for Precision Medicine and Health*, and (ii) *Latent State Modeling in Mobile Health and Diagnostic Classification: Recent Advances in the MCMC Approach*.

During his visit to DSAP, he was interviewed on 15 February 2017 by Y.K. Leong on behalf of *Imprints*. This was updated by an email interview on 1 March 2019 when he was visiting IMS. The following consists of two parts. Part I is an edited and enhanced version of the transcript of the interview on 15 February 2017, and Part II is an updated email interview given during his second visit to NUS in March 2019. Part I describes in vivid details how he became a statistician "by accident" while Part II describes his multidisciplinary work and, in particular, his involvement with AI (artificial intelligence) in medicine and finance.

Part I. The Accidental Statistician

IMPRINTS I As an undergraduate at The University of Hong Kong, your declared major was originally economics, but you later switched to mathematics. Why did you switch to mathematics?

TZE LEUNG LAI L First of all, I must tell you about the University of Hong Kong (HKU) in those days because it was very unlike now. I entered HKU in 1964. At that time it was the only recognised university in Hong Kong. Then later, after I graduated, The Chinese University of Hong Kong (CUHK) became the second university. In my days, not everybody had to go to the university to get a very good job, but a degree from HKU could serve as a "licence" for certain high-level jobs.

I I think most of the university graduates end up as civil servants.

L Yes. That was why I declared economics as my major. [Laughs] Actually I didn't really intend to go to the university. You probably know that Donald Tsang, the second governor of Hong Kong (after it became the Special Administrative Region of China), did not go to the university. He became a civil servant very early and rose through the ranks. After he held several positions in finance and trade as Chief Executive Officer, he was sent

by the British colonial government in 1981 to the Kennedy School of Government at Harvard, where he received a master's degree in public administration before returning to Hong Kong. I was in Tsang's age group albeit nine months younger.

When I was in Form 6 (Lower 6 and Upper 6 – it's the British system), I could have studied science, which most of my classmates did, but I took up arts just to build up my language skills and also because I didn't have to work that hard. [Laughs] I applied to the Housing Authority when I was in Upper 6, but I was not selected. It was too late to apply to the university, so I taught at a private school for a year and that was when I acquired my teaching skills. It was in the following year that I entered the university to study economics in the Faculty of Arts. The Faculty of Medicine was the most glamorous at HKU in those days, followed by engineering, science and arts in that order. The first-year examination consisted of four papers (subjects). I wanted to major in economics; hence I took economics and statistics. The two other subjects were (a) first-year mathematics and (b) history of mathematics and number theory. The most difficult subject was first-year mathematics because I did not have the background as I could not attend mathematics classes in Form 6 and relied on self-study to pass the Matriculation Examination in mathematics that I registered for. When I was in Form 6, I had to attend English literature classes for the arts students, which were held at the same time as mathematics classes for the science students. I asked

my teacher, a Scotsman, whether I could attend some mathematics classes and read English literature on my own. He answered that he would think about it. The next day, when he was lecturing on Shakespeare's *Twelfth Night*, in which Lady Olivia's steward Malvolio had "conceited" fantasies of marrying Lady Olivia. To explain what the word "conceited" means, my teacher used me as an example: "One of you asked me yesterday whether he could skip some of my classes to attend classes in mathematics for the science students. English Literature is already a difficult subject and one needs to attend all classes and spend a lot of time reading and writing essays to do well. Mathematics is even harder. Thinking that he can do both with only partial effort is an example of being conceited." [Laughs] Since his implicit answer was no, I modified my "conceit" by studying a minimal amount of mathematics to pass the subject that I had registered for the Matriculation Examination. Basically, I focused on differentiation and gave up integration in studying for the examination. Despite this weak background, I enjoyed my first-year mathematics course but found the economics course somewhat disappointing.

I Why?

L Because it was too soft.

I Descriptive?

L Yes, it was too descriptive. The instructor Lee Goodstadt, who received his diploma in agricultural economics from Oxford and master's degree in economics from Manchester, came to Hong Kong as a Commonwealth Scholar in 1962 and joined HKU in 1964 when I entered the university. He did not have much teaching experience but had to face a large class of over a hundred freshmen. He had difficulties in explaining indifference curves and the law of marginal returns to many bewildered students and I tried to help him out by suggesting the use of differential calculus and concave functions. He was visibly upset with my unsolicited suggestion. He paid me back by being unfairly critical of my essay in that week's tutorial session. This made me switch to mathematics as my major. I made up for my aforementioned weakness in background by working very hard and benefiting from the excellent tutorial sessions in my mathematics course. I even won the first prize in the Arts Faculty at the end of my first year because of top scores in the examinations of the four papers (including economics). Actually, I began to like Goodstadt's lectures after he finished microeconomics and moved to his areas of expertise – theory of land, which was very relevant to the rising housing prices in Hong Kong, and money and banking, which was very timely because there was a series of bank runs in 1965 following the bankruptcy of Canton Trust and Commercial Bank on February 8, 1965. Goodstadt and I later got along well, and he became the deputy editor of *Far Eastern Economic Review* from 1966 to 1976 and the editorial director of *Asiabanking* from 1981-1986. He left HKU to be head of the newly established

“WHEN I LOOK BACK ON MY CAREER, I FEEL EXTREMELY FORTUNATE IN HAVING SEVERAL GREAT TEACHERS AND MENTORS, AND PROFESSOR [YUNG-CHOW] WONG IS ONE OF THEM.”

Central Policy Unit in 1989 and was later awarded CBE [Commander of the Most Excellent Order of the British Empire] by Queen Elizabeth II and Justice of Peace by the governor of Hong Kong. Winning the first prize in the Arts Faculty first-year examinations boosted my confidence in taking all nine papers in mathematics (including two papers in applied mathematics, for which I chose statistics) for my examination in the final year; we did not have examinations in the second year. I won the top prize in the Faculty of Arts and the Walter Brown Memorial Prize in Mathematics and graduated from HKU with B.A. (First Class Honours), preparing me for my dream job of joining civil service as an Administrative Officer.

I Why did you go overseas to study instead of joining civil service?

L The end of my final-year examinations in May coincided with the beginning of the 1967 leftist riots in Hong Kong, marked by labor disputes in taxi, textile and cement companies, in particular demonstrations against the factory Hong Kong Artificial Flower Works, where pro-communist trade unionists set up picket lines that clashed with management, who called in riot police on May 6 that led to violent clashes, resulting in the arrests of 21 picketing workers and many more injuries. Many large-scale demonstrations erupted on the streets of Hong Kong the following days, and the winds of Cultural Revolution had already blown to Hong Kong. The leftists formed the Hong Kong and Kowloon Committee for Anti-Hong Kong British Persecution Struggle on May 16, and put up posters on walls with slogans such as "Down with British Imperialism", "Stew the White-Skinned Pigs" (referring to the British rulers) and "Fry the Yellow Running Dogs" (referring to the local yellow-skinned civil servants working for the British colonial government). Hence my dream job of joining civil service as an Administrative Officer suddenly became unattractive and even dangerous. Fortunately, switching from economics to mathematics had huge payoffs in those tumultuous times. Professor Yung-Chow Wong, head of the Mathematics Department and one of the most distinguished professors at HKU, called me and asked if I would like to take an opening in the Department as Demonstrator (corresponding to Tutor in British universities) of Mathematics. He also congratulated me on my performance in the examinations and winning the prizes. I expressed my deep gratitude to him and thereupon began my long career in academia instead of joining civil service.

My job as Demonstrator of Mathematics began in September 1967 and lasted for a year. I was assigned to be the assistant of Professor Wong in his course on calculus on manifolds for third-year B.A. and B.Sc. special students in mathematics. He used a book with the same name by Michael Spivak. I learned a lot on differential geometry from him during that year, which many years later benefited my research that resulted in a series of joint papers on large deviation and saddlepoint approximations for generalized likelihood ratio statistics, Markov random walks, and asymptotically Gaussian random fields, from 2000 – 2006 with my former Ph.D student Hock Peng Chan, who is the current chair of the Department of Statistics and Applied Probability at NUS.

Professor Yung-Chow Wong came from Sun Yat-Sen University to HKU to succeed Professor Walter Brown as Professor of Mathematics in 1948. He received his B.Sc. degree in mathematics from Sun Yat-Sen University [(also known as Zhongshan University)] in 1935 and was selected in 1938 as a Sino-British Boxer Indemnity Scholar to pursue doctoral study in Britain, where he wrote his thesis on generalized helices in Riemannian space under Professor Evan Davis of University of London and received his Ph.D in 1940. He spent several years in the US at the Institute for Advanced Study in Princeton, MIT and University of Pennsylvania before returning to Sun Yat-Sen University as Professor of Mathematics. He built up the Department of Mathematics at HKU with five members on its teaching staff (including demonstrators) into the best department in the Faculties of Arts and Science, with over twenty members, when I entered the university. On his 90th birthday on 31 May 2003, the Vice-Chancellor of HKU mentioned the exceptional contributions of Professor Wong to HKU and to tertiary education in Hong Kong during his “six decades as a mathematician and educator”. I also sent my heartfelt congratulatory note: “When I look back on my career, I feel extremely fortunate in having several great teachers and mentors, and Professor [Yung-Chow] Wong is one of them.”

In October 1967, I was selected for the Commonwealth Scholarship to pursue doctoral study in Britain. I had also applied to Stanford, Toronto and Columbia, which required the applicants for their Ph.D programs to take the Graduate Record Examination (GRE). Now that I already got the Commonwealth Scholarship, I did not have much incentive to take the GRE. After finding out that Columbia did not require the GRE for overseas applicants, I just applied to Columbia where I also had former classmates from HKU Math studying for their Ph.D.s. That was why I left Hong Kong in September 1968 to study at Columbia.

I Why did you apply to the Department of Mathematical Statistics instead of the Department of Mathematics at Columbia, and why did you go to the US instead of the UK?

L To answer this question, I want to follow up with subsequent developments in Hong Kong and at HKU in the year of the leftist riots. The violent clashes

between the leftist rioters and the police peaked in the summer. The British Hong Kong Government imposed emergency measures to quell the unrest. Leftist newspapers and schools were shut down; leftist rioters retaliated by planting bombs throughout the city. On August 24, a popular anti-leftist radio commentator Lam Bun was burned to death in his car when he drove to work with his cousin. There was widespread outcry against the violence, which began to taper off. Therefore, when I reported to work at HKU in September, the leftist riots and demonstrations subsided and normal life gradually returned to Hong Kong. I also got another offer from a former teacher to move to his new Department of Statistics.

The Faculty of Social Sciences at HKU was established in September 1967 and consisted of the Departments of Economics, Geography, Psychology, and Sociology that had belonged to the Faculty of Arts, together with two new Departments – Statistics and Social Work. (The candidate for the next governor of Hong Kong, Carrie Lam ^[1] received her bachelor's degree from the Department of Social Work at HKU about ten years after I received mine from the Department of Mathematics.)

The Department of Statistics basically moved the faculty members (including demonstrators) teaching statistics courses in the Department of Mathematics to the Faculty of Social Sciences. E. R. Chang, Head of the Department of Statistics was a Reader in the Department of Mathematics and had received his master's degree from Yale. Although he was of Chinese ancestry, he could neither speak nor write Chinese. He had only taught me in my first-year statistics course but liked me, and explained to me the advantages of moving to his department as a demonstrator. He would recommend me for a Commonwealth Scholarship to study for a higher degree in statistics in Britain so that I could be promoted to Lecturer upon my return in a couple of years. He told me that Mathematics had so many talented students and junior staff that it would be hard to move up the academic ladder. I took his offer of going overseas to study for a higher degree in statistics and then returning to his department as Lecturer, but still remained in the Department of Mathematics as Professor Wong's assistant. That was why I pursued my doctoral study in statistics instead of mathematics. Although I was definitely interested in statistics and there was a position for me in the Department of Statistics at HKU, I knew much more pure mathematics than statistics in those days.

Concerning why I went to Columbia instead of going to the UK with a Commonwealth Scholarship, a simple answer is to cite the economic principle of hedging with options. Although I didn't know that principle in those days, I was an economist at heart. The position at HKU only required a higher degree in statistics. If I went to Columbia, I had more options to apply for positions in the US besides that of returning to HKU. On the other hand, taking the Commonwealth Scholarship had no other option than returning to Hong Kong. Many years later,

when I had to learn and teach option (pricing) theory in finance, I asked myself the price of taking the Columbia option, but this is irrelevant to your question. ^[2]

I After your Ph.D, you stayed on the faculty at Columbia from 1971 to 1987. Then you moved to Stanford. Please tell us why you stayed at Columbia for 16 years and then joined Stanford, and some highlights of your work at both universities.

L Well, actually these questions were already asked by three former Ph.D students and my answers to them were published in "Conversations with Tze Leung Lai", ICSA (*International Chinese Statistical Association*) Bulletin January 2016, pp. 29-40. ^[3] Therefore let's move on to your next question.

I The late Peter Hall (1951-2016) once said that statistics is not its own master, unlike pure mathematics which is free to choose its own problems to solve. [<https://ims.nus.edu.sg/imprints/imprints-28-2016.pdf#page=12>]

Is there such as a thing as "pure" statistics which is free to chart its own course of development without being overly directed by practical problems and applications?

L Concerning Peter Hall's career, he started to study physics at the University of Sydney to follow the footsteps of his mother, who was a pioneer in radiophysics and solar radio astronomy. However, he did not like the teaching there and switched to mathematics after his first year. He then studied for the M.S. degree in mathematics at the Australian National University (ANU), where he worked in probability under Pat Moran [(1917-1988)], and later Chris Heyde [(1939-2008)]. Then he went to Oxford to pursue his doctoral study and wrote his Ph.D thesis on limit theorems for stochastic processes and sums of random variables under the supervision of Sir John Kingman, who had visited ANU and first met Peter in 1974. After receiving his Ph.D from Oxford, Peter returned to Australia where he spent his academic career at ANU and later at the University of Melbourne, while also holding visiting and fractional appointments at many other universities in different parts of the world. His research exemplifies "charting its own course of development" and being "its own master", yet finding important real-world applications such as his work on fractals and his papers on the bootstrap method in the *Breakthroughs in Statistics* collection. Unlike me, Peter had planned to be an academic mathematician dating back to his undergraduate days at the University of Sydney.

I want to conclude with a related story. Peter's wife Jeannie received her B.A. degree from HKU about five years after mine, joined the civil service as an Administrative Officer and was sent by the British Hong Kong government to study at Oxford, where she met Peter. In one of the parties with Peter who was visiting HKU, I told her that she had taken my dream job in civil service and explained how I got another dream job as an academic like her

husband. In those years, there was the famous movie "The Accidental Tourist" that was nominated for four Academy Awards, and won one, in the 1988 Oscars. Jeannie said: "So you are the accidental mathematician. ^[4]" [Laughs] Her cute remark also addresses your question to the point. Yes, as an accidental statistician, I do not have the luxury to choose my own problems, especially when I am working in a large team with other "masters" charting the course of development of an interdisciplinary project. Instead I try to learn from my collaborators with different backgrounds across different disciplines and also keep a group of talented students from different schools and departments working on the statistical or data analytic aspects of the projects. Examples can be found in the aforementioned ICSA article "Conversations with Tze Leung Lai".

Part II. The Interdisciplinary Statistician in Academia

I Your faculty appointments at Stanford University are in statistics, biomedical data science, and computational & mathematical engineering, and you are also the Director of the Financial and Risk Modeling Institute, Co-director of the Center for Innovative Study Design, and also a core member of several centers and institutes at the Stanford University Medical School. How do your inter-disciplinary appointments work at Stanford, particularly in terms of your teaching and research?

L First I want to point out that these interdisciplinary appointments expanded in stages over the years during the past 32 years that I had spent at Stanford. When I first moved to Stanford, my appointment was in the Department of Statistics, one of the 23 departments of the School of Humanities and Sciences. My teaching load was exclusively in statistics, ranging from undergraduate service courses to advanced Ph.D-level courses. In a Ph.D-level course that I taught in the fall quarter of 1988, I chose the topic of multi-armed bandits and stochastic control to organize my past research at Columbia into an advanced course and to attract potential Ph.D advisees. In the audience was Lewis Sheiner, a visiting professor in the School of Medicine who was spending his sabbatical leave from the University of California in San Francisco (UCSF), one of the premier medical schools of the University of California (UC) system. Lewis introduced himself after the first class and told me about his work in population PK/PD (pharmacokinetics/pharmacodynamics) and his intuition about how stochastic control ideas could be used in this work and in other areas that he was working with the Department of Medical Informatics (now renamed Biomedical Informatics). Also in the audience was Ray Zhu, a Ph.D student in Statistics who later became my first Ph.D student from Stanford and with whom I have been collaborating intermittently to this day. Lewis, a distinguished clinical pharmacologist, later introduced me to the chair Edward Shortliffe of Medical Informatics

and to Mark Musen, an assistant professor who was Shortliffe's former student, about an automatic ventilator for emergency hospital care of patients with severe respiratory diseases. Although I did not know it at that time, this was a precursor of today's AI (artificial intelligence) in medicine. I brought Ray Zhu, who expressed interest in working with me on research related to my course, to meetings concerning the development of the automatic ventilator, and Ray began to know Lewis well through those meetings.

Lewis returned to UCSF after his sabbatical, Shortliffe subsequently left Stanford for Columbia and Musen succeeded him and quickly rose to prominence, while Ray joined the pharmaceutical company Schering-Plough as biostatistician after receiving his Ph.D degree. Lewis and his colleague Stuart Beal, who had his Ph.D in biostatistics from UCLA before joining UCSF, had developed the NONMEM (Nonlinear Mixed Effects Models) software package which Lewis began to promote to pharmaceutical companies by giving professional courses in different cities. Ray took such a course in Piscataway, New Jersey and got reconnected with Lewis. He then "fell in love" with population PK/PD to such an extent that he left Schering-Plough to join FDA [Food and Drug Administration] and later the company Globomax in Maryland, where he worked with Lewis's collaborator Tom Ludden. He also got me interested in the subject, which eventually led to my work and related projects beyond PK/PD. Some of these applications can be found in my book *Sequential Experimentation in Clinical Trials: Design and Analysis* with Bartroff and Shih (Springer, 2013), and in the forthcoming book *Data Analytics and Risk Management in Finance and Insurance* with Xing (Chapman & Hall/CRC). Ray later moved back to the pharmaceutical industry, beginning as associate director of biostatistics at Aventis, subsequently as Vice President (VP) at Eisai and currently as VP at Allergan. He consulted me on several occasions about the efficient design of confirmatory clinical trials for regulatory approval of new treatments developed at these companies. My discussions with him first rekindled my interest in efficient group sequential designs of clinical trials that began when I was at Columbia following the early termination of the Beta Blocker Heart Attack Trial in 1981, which led to consultations with pharmaceutical companies and also an NSF [National Science Foundation] university-industry grant, as described in "Conversations with Tze Leung Lai" (*JCSA Bulletin* Jan 2016, p.32). They also led to new research projects in the area of adaptive designs that are summarized in the aforementioned Bartroff-Lai-Shih book. Even more importantly, they led to my work, described below, at Stanford Cancer Center (now Comprehensive Cancer Institute) and at the Center for Innovative Study Design (CISD). ^[5]

In 2004, Stanford's School of Medicine planned a Cancer Center application to the National Cancer Institute (NCI) and asked me to be interim director of the Biostatistics Shared Resource in the application, based on my publications on innovative clinical trial designs summarized in the preceding paragraph. After receiving

“HE [PHILIP LAVORI] HAD EXTENSIVE EXPERIENCE IN RUNNING LARGE CLINICAL TRIALS IN THE VETERANS ADMINISTRATION COOPERATIVE STUDIES PROGRAM BEFORE CHAIRING HRP, AND WAS A PIONEER IN SEQUENTIAL MULTIPLE ASSIGNMENT RANDOMIZED TRIALS – AN IMPORTANT TOPIC IN THIS IMS PROGRAM.”

the Cancer Center award, Philip Lavori was recruited by the School of Medicine to be Director of the Biostatistics Shared Resource and Chair of the Department of Health Research and Policy (HRP), which consisted of biostatistics, epidemiology, and health policy. Phil asked me to stay on as Co-director and to join HRP as courtesy faculty; "courtesy" appointment at Stanford means that my salary comes from my dean, whereas a "joint appointment" would mean that the salary is split between the two deans. Working with Phil in the past 14 years has greatly advanced my research in clinical trial design and analysis. He had extensive experience in running large clinical trials in the Veterans Administration Cooperative Studies Program before chairing HRP, and was a pioneer in sequential multiple assignment randomized trials – an important topic in this IMS program. Our close collaboration not only resulted in a very favourable review of the Cancer Center by NCI [National Cancer Institute] that granted the "comprehensive" status to the Center in 2016, but also to the establishment of CISD in 2009. In 2016, the Dean of the School of Medicine moved the faculty in Biostatistics out of HRP to form a new Department of Biomedical Data Science (BDS) that also consisted of certain faculty members from Biomedical Informatics and Genetics, hence I became a courtesy faculty member of the new department. Ying Lu, who succeeded Phil in the Veterans Administration Cooperative Studies Program, moved over to BDS as Professor and also joined CISD as Co-director. Since then, CISD has enough manpower to expand its activities and has been growing quickly, especially after FDA established the UCSF-Stanford Center of Excellence in Regulatory Science and Innovation (CERSI). ^[6] My recent book *Medical Product Safety Evaluation: Biological Models and Statistical Methods* with Jie Chen and Joseph Heyse and my forthcoming book *Real World Data and Evidence: An Interdisciplinary Approach and Applications to Precision Medicine and Healthcare* with Richard Baumgartner and Jie Chen represent some of the "priority areas, based on FDA's current unmet regulatory science needs" for CERSIs, and can be used for "regulatory science-related training, workshops, and seminars." Both books are published by Chapman & Hall/CRC. Jie, Joe and Richard are all from Merck, which is an Industry Affiliate of CISD, and I have been collaborating with Jie and Joe since 2009 after their first visit to Stanford. Other pharmaceutical, biotech and healthcare companies have also joined the

Industry Affiliates Program of CISD and collaborated with the core and extended faculty members of the Center. CISD is only one of the centers and institutes in the School of Medicine. I have also joined some centers as a core member, most recently the Center for Precision Mental Health and Wellness, for which “precision” involves brain imaging and genomics. Moreover, besides the School of Medicine, I am also involved in the School of Engineering through ICME (Institute of Computational & Mathematical Engineering) since 2009 and the Mathematical & Computational Finance Program since 2014. I have also been Director of the Financial and Risk Modeling (FARM) Institute since 2012. How this came about has been described in “Conversation with Tze Leung Lai” (*ICSA Bulletin* Jan 2016, pp. 34-35). These interdisciplinary appointments have definitely made my research more interdisciplinary.

Concerning teaching, I still have to teach three courses every year as I am a full-time faculty member of the Department of Statistics. These courses now are all related to the different programs that I run, and I no longer have the luxury of teaching an advanced Ph.D-level course of the kind that I taught in the fall quarter of 1988 to attract Ph.D advisees such as Ray Zhu. On the other hand, because of my interdisciplinary research projects, I have been able to recruit talented students from different schools and departments (including statistics) to work on these projects, which have eventually led to their Ph.D theses under my supervision.

I You have mentioned about “a precursor of today’s AI in medicine” at Stanford in the late 1980’s. What is today’s AI in medicine (or in finance) that you have been involved in teaching and research for your interdisciplinary appointments at Stanford?

L The major department in AI research and teaching at Stanford is Computer Science (CS), which has AI, CS theory, computer systems, graphics and human-computer interaction, database and network/graph analysis as its five core research areas. CS theory includes complexity theory, cryptography and algorithms, whereas AI includes machine learning, computer vision, robotics, natural language processing and computational biology. AI, also called machine intelligence, is intelligence demonstrated by machines, as opposed to natural intelligence displayed by humans and animals. Other departments and schools are also involved in many of these topics in AI. For example, statistics has introduced many innovations in machine learning. Electrical engineering, mechanical engineering, and aeronautics & astronautics have been involved in robotic navigation and “driverless” cars and spacecrafts; and radiology and biomedical informatics have major advances in computer vision for medical imaging. I have recently developed a new joint course “Deep Learning and AI with Applications to Medical Imaging and Real-World Evidence” with Biomedical Informatics, and another new course “Neural and Statistical Sciences in Artificial Intelligence”. The latter course discusses the interactions between machine intelligence and natural intelligence and describes recent

developments that advance both types of intelligence through such interactions. I also have Ph.D students from statistics, CS and ICME working on related research projects and helping us to develop and teach these courses. AI has become a pillar of FinTech (Financial Technology); the ABCD of FinTech are Artificial intelligence, Blockchain, Cloud computing and big Data. “Blockchain” is another CS topic that is related to cryptography, and so is cloud computing. Big data pertain to Statistics. I have recently been working with some colleagues at FARM and my Ph.D students on FinTech and RegTech (regulatory technology).

Notes by T.L. Lai

^[1] Election for the 4th governor of Hong Kong, SAR, took place on 26 March 2017 and Carrie Lam won the three-way election with 777 of the 1194 votes of the Election Committee. She joined civil service as an Administrative Officer and was sent by the British Hong Kong Government to study at Cambridge University, where she met her husband [Siu-Por Lam] who was working on his Ph.D thesis on algebraic topology under Frank Adams.

^[2] Of greater interest to readers at NUS is that E.R. Chang left HKU in 1968 for the University of Southampton, and the Faculty of Social Sciences advertised the opening for the head of its Department of Statistics. Professor Saw Swee Hock of the University of Malaya in Singapore became the founding Professor of Statistics at HKU in 1969. He received his BA and MA from the University of Malaya in Singapore, and his Ph.D in Statistics from the London School of Economics in 1963. In 1971 he returned to Singapore, which became an independent republic on August 9, 1965, as the first chairman of the National Commission of Statistics. He joined the University of Singapore (formerly University of Malaya in Singapore, and later National University of Singapore since 1980) as Professor of Statistics in 1975. He is also well known for his philanthropy, and was named one of the 48 Heroes of Philanthropy in the Asia-Pacific Region by Forbes Asia Magazine in 2014. His largest donation was in 2011 for the establishment of the Saw Swee Hock School of Public Health at NUS.

^[3] <http://icsaimage.files.wordpress.com/2016/05/icsabulletin16jan1.pdf>

^[4] Actually “statistician”, to be more precise.

^[5] <http://med.stanford.edu/cisd.html>

^[6] There are currently four such centers: University of Maryland, Johns Hopkins, UCSF-Stanford, and Yale-Mayo Clinic. They are “collaborations between FDA and academic institutions to advance regulatory science through innovative research, training, and scientific exchanges” because “evolving areas of science are promising new approaches to improving our health while demanding new ways to evaluate the safety and effectiveness of the products FDA regulates.”

Forthcoming

Mathematics of Shapes and Applications

EDITED BY:

- **Sergey Kushnarev** (*Singapore University of Technology and Design, Singapore*)
- **Anqi Qiu** (*National University of Singapore, Singapore*)
- **Laurent Younes** (*Johns Hopkins University, USA*)

The volume illustrates this wealth of subjects by providing new contributions on the metric structure of diffeomorphism groups and shape spaces, recent developments on deterministic and stochastic models of shape evolution, new computational methods manipulating shapes, and new statistical tools to analyze shape datasets. In addition to these contributions, applications of shape analysis to medical imaging and computational anatomy are discussed, leading, in particular, to improved understanding of the impact of cognitive diseases on the geometry of the brain.

Genealogies of Interacting Particle Systems

EDITED BY:

- **Matthias Birkner** (*Johannes Gutenberg-Universität Mainz, Germany*)
- **Rongfeng Sun** (*National University of Singapore, Singapore*)
- **Jan M Swart** (*The Czech Academy of Sciences, Czech Republic*)

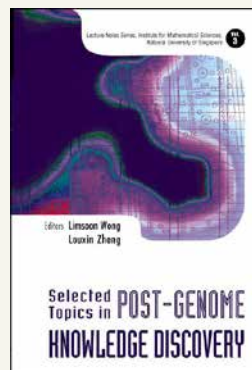
The program on Genealogies of Interacting Particle Systems, held at the Institute for Mathematical Sciences in 2017, brought together experts and young researchers interested in this modern topic. Central to the program were learning sessions where lecturers presented work outside of their own research, as well as a normal workshop. This volume contains two types of articles:

- Lecture notes of the learning sessions, which provide valuable introductions to topics of active interest
- Original contributions by participants, which include both survey articles and original research.

Past Volumes

VOLUME 3

Selected Topics in Post-Genome Knowledge Discovery



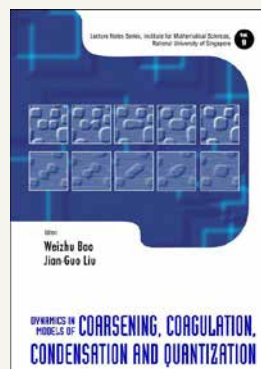
EDITED BY:

- **Limsoon Wong** (*National University of Singapore, Singapore*)
- **Louxin Zhang** (*National University of Singapore, Singapore*)

Topics include comparison and alignment of biological sequences, modeling and analysis of biological pathways, data mining and knowledge discovery from biological and clinical data.

VOLUME 9

Dynamics in Models of Coarsening, Coagulation, Condensation and Quantization



EDITED BY:

- **Weizhu Bao** (*National University of Singapore, Singapore*)
- **Jian-Guo Liu** (*University of Maryland, USA*)

Topics covered include dynamics in different models of domain coarsening and coagulation and their mathematical analysis in material sciences; a mathematical and computational study for quantized vortices in the celebrated Ginzburg–Landau models of superconductivity and the mean field Gross–Pitaevskii equations of superfluidity; the nonlinear Schrödinger equation and applications in Bose–Einstein condensation and plasma physics as well as their efficient and accurate computation; and finally, an introduction to constitutive modeling of macromolecular fluids within the framework of the kinetic theory.



For more information on the other volumes under this series, visit ims.nus.edu.sg/resource/lns.php

Research in Industrial Projects for Students (RIPS) 2019 – Singapore

17 JUNE–9 AUGUST 2019

In collaboration with the Institute for Pure and Applied Mathematics (IPAM), IMS is organising an eight-week summer program for undergraduate students to work on projects proposed by the industry. This program provides students an opportunity to explore potential careers in mathematics, science and technology, while they also learn specifically about a company based in the region.

Symposium in Memory of Charles Stein [1920–2016]

17–28 JUNE 2019

CO-CHAIRS:

Louis Chen | National University of Singapore

Wei-Liem Loh | National University of Singapore

IMS Graduate Summer School in Logic

1–19 JUL 2019

LECTURERS:

Angus MacIntyre | Queen Mary University of London

Theodore A. Slaman | University of California, Berkeley

W. Hugh Woodin | Harvard University

Quantitative Finance II

22 JULY–31 AUGUST 2019

Jointly organized with Risk Management Institute, NUS

CO-CHAIRS:

Min Dai | National University of Singapore

Steven Kou | Boston University

Statistical Data Integration

5–16 AUGUST 2019

CHAIR:

Sanjay Chaudhuri | National University of Singapore

Density Functionals for Many Particle Systems: Mathematical Theory and Physical Applications of Effective Equations

2–27 SEPTEMBER 2019

PROGRAMME COORDINATOR:

Berthold-Georg Englert | National University of Singapore

CO-CHAIRS:

Yuan Ping Feng | National University of Singapore

Heinz Siedentop | Ludwig-Maximilians-University of Munich

Quantum and Kinetic Problems: Modeling, Analysis, Numerics and Applications

30 SEPTEMBER 2019–31 MARCH 2020

CO-CHAIRS:

Bao Weizhu | National University of Singapore

Peter A. Markowich | University of Cambridge and University of Vienna

Benoit Perthame | Sorbonne Université

Eitan Tadmor | University of Maryland

Computational Approaches to the Analysis of Biomolecular Sequences, Structures and Their Functions and Applications to Biotechnology and Clinical Data Studies

23–27 MARCH 2020

CO-CHAIRS:

Igor N. Berezovsky | Bioinformatics Institute, A*STAR

Frank Eisenhaber | Bioinformatics Institute, A*STAR

Lars Nordenskiöld | Nanyang Technological University



Combinatorial Problems for String and Graph and Their Applications in Bioinformatics

30 MARCH–24 APRIL 2020

ORGANIZING COMMITTEE:

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Sohel Rahman | Bangladesh University of Engineering & Technology
Vaibhav Rajan | National University of Singapore
Kunihiko Sadakane | The University of Tokyo
Wing-Kin Sung, Ken | National University of Singapore

Random Matrix EurAsia 2020

4–29 MAY 2020

ORGANIZING COMMITTEE:

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Van Vu | Yale University
Dong Wang | National University of Singapore

Index Theory and Complex Geometry

1–26 JUNE 2020

ORGANIZING COMMITTEE:

Tien Cuong Dinh | National University of Singapore
Fei Han | National University of Singapore
Xiaonan Ma | Université Paris Diderot - Paris 7
Mathai Varghese | University of Adelaide

Causal Inference with Big Data

29 JUNE–10 JULY 2020

CO-CHAIRS:

Hyunseung Kang | University of Wisconsin-Madison
Wei-Yin Loh | University of Wisconsin-Madison

IMS Graduate Summer School in Logic

6–24 JULY 2020

Data Stream Algorithms

13–21 JULY 2020

ORGANIZING COMMITTEE:

Yi Li | Nanyang Technological University
David P. Woodruff | Carnegie Mellon University



For more information on these and other upcoming events, visit the Events section on our website at

ims.nus.edu.sg

IMS in Numbers

December 2018 — June 2019

NUMBER OF
PARTICIPANTS

430

7
EVENTS

208
TALKS

**OVER
7 MONTHS**

67
STUDENTS

CALL FOR PROPOSALS

The Institute for Mathematical Sciences (IMS) of the National University of Singapore (NUS) invites submissions of proposals from researchers in academia and industry. The proposals are for organizing thematic programs or workshops to be held at IMS.

The IMS is particularly interested in receiving proposals of programs/workshops that focus on exciting new developments in the mathematical sciences. Proposals of interdisciplinary nature in areas that interface mathematics with science, social science or engineering are welcome.

A soft copy of the proposal, for the period of funding from June 2021 to March 2022, should be sent to the Director of the Institute at imsdir@nus.edu.sg by 31 May 2019.

The exposition of a proposal should be aimed at the non-specialist and will be evaluated by a scientific panel. Proposals of interdisciplinary programs/workshops should describe how the activity would benefit the intended audience with diverse backgrounds and facilitate research collaboration.

Information on the Institute and its activities, as well as a detailed format for the proposal are available on the IMS website ims.nus.edu.sg. Enquiries may be directed to imssec@nus.edu.sg.



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