

THE INSTITUTE LETTER

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THE SIMONS CENTER FOR SYSTEMS BIOLOGY: FINDING SIGNALS IN THE NOISE

Discoveries in biology historically have been the province of experimentalists. But advances during the past decade in sequencing human and other genomes have brought forth a vast amount of data that has led to the nascent but burgeoning field called systems biology in which theoretical approaches to biology play a vital role. "Biology has been predominantly an experimental science," said Arnold J. Levine, Professor in the School of Natural Sciences and head of The Simons Center for Systems Biology at the Institute for Advanced Study. "That is especially true of twentieth-century biology, which really did not have a strong theoretical component, but instead, was based on observations."

Systems biology is a rapidly growing and increasingly important field. Under Professor Levine, The Simons Center is focused on research at the interface of molecular biology and the physical sciences. To move forward the frontiers of understanding of fundamental biological problems, Members and Visitors explore and mine large data sets of genomes of organisms, expression patterns of genes in normal and pathological conditions, the genetic diversity found in species, and clinical and molecular correlations. The Center draws researchers from an array of disciplines, including mathematics, physics, astrophysics, molecular biology, chemistry, and computer science.

"Their training in analytical methods enables our Members to separate the signals in large data sets from the noise of the data, to make statistical associations, to establish probabilities of events occurring, and to predict outcomes that are testable," said Levine. "The theorist now plays a role in biology that did not exist before."

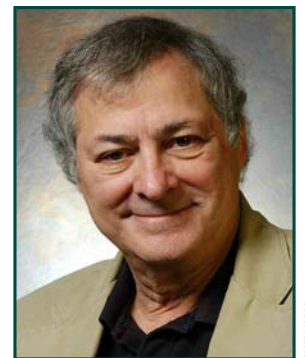
In analyzing these large data sets of information, systems biologists are able to reconstruct virtual genomes based on probability and develop a better understanding of evo-

lution, migration, and the probabilities of the distribution of genes in populations. "We can trace back through time the evolution of humans into different races, into different groups," said Levine.

Current research involves using such data to look at systems at the molecular, cellular, and organismic levels, to understand how they develop and interact and to discern what goes wrong in certain disease states, as well as to address important problems in biology that concern genetics and genomics, polymorphisms and aspects of evolution, signal transduction pathways and networks, stress responses, and pharmacogenomics in cancer biology.

Before Levine arrived at the Institute, a program in theoretical biology had been initiated in 1998 with the five-year appointment of Dr. Martin Nowak. Nowak, now Professor of Mathematics and Biology at Harvard University and director of its Program for Evolutionary Dynamics, had, with Oxford University professor Sir Robert May, a former Member in the School of Natural Sciences (1971–72), developed a wide variety of mathematical models to address a broad range of problems in evolutionary biology and infectious diseases, from how infectious agents spread within individuals and the dynamics of viral resistance, to

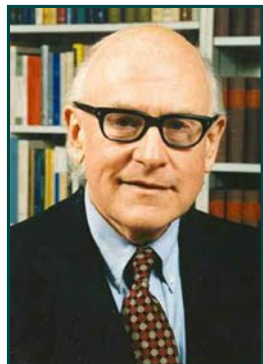
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Professor Arnold J. Levine

CLIFF MOORE

GLEN BOWERSOCK, LEADING AUTHORITY ON ANCIENT HISTORY, RETIRES AFTER TWENTY-SIX YEARS AT THE INSTITUTE



Glen Bowersock

After twenty-six years at the Institute for Advanced Study, Glen Bowersock, a preeminent authority on Greek, Roman, and Near Eastern history, retired in July as a Professor in the School of Historical Studies and became Professor Emeritus. He intends to remain at the Institute and to continue his research here.

Over the past four-and-a-half decades, Professor Bowersock has applied an innovative and multi-disciplinary approach to the study of ancient history, using his exceptional knowledge of classical texts in many languages, together with inscriptions, coins, mosaics, and archaeological remains, to illuminate the mingling of different cultures and to draw unexpected and revelatory conclusions. He has worked particularly on the history of Roman Greece and Asia Minor, and of pre-Islamic Arabia.

More than a dozen books have been written or edited by Professor Bowersock and he has published some three hundred articles on Greek, Roman, and Near Eastern history and culture, as well as the classical tradition in modern literature. His books include *Greek Sophists in the Roman Empire* (1969); *Julian the Apostate* (1978); *Roman Arabia* (1983); *Fiction as History, from Nero to Julian* (1994); *Martyrdom and Rome* (1995); and *Late Antiquity: A Guide to the Post-classical World*, edited with Peter Brown and Oleg Grabar (1999). His *Mosaics as History: The Near East from Late Antiquity to Islam* will be published by Harvard in November, and

a volume of studies on the classical tradition will be published in Italian next year by Einaudi. He has also recently completed an annotated translation of Lorenzo Valla's fifteenth-century oration on the Donation of Constantine for publication next year.

Professor Bowersock has received wide recognition for his contributions to the field, including being named a Chevalier of the Légion d'honneur in 2004. Instituted by Emperor Napoleon I in 1802, it is one of France's most prestigious awards and the country's highest civilian honor. In 1992, the American Historical Association presented Professor Bowersock with the James Breasted Prize for his book *Hellenism in Late Antiquity* (1990).

In addition to having been awarded honorary degrees from the University of Strasbourg, l'Ecole Pratique des Hautes Etudes, and the University of Athens, Professor Bowersock was named an Honorary Fellow of Balliol College, Oxford University, in 2004. He is also a Fellow of the American Academy of Arts and Sciences, Foreign Fellow of the Accademia Nazionale dei Lincei, Member of the American Philosophical Society, Member of the Académie des Inscriptions et Belles-Lettres, and a Foreign Member of the Russian Academy of Sciences. He is in charge of the Fonds Louis Robert in Paris, and he also serves on the Board of Directors of the Metropolitan Opera.

Professor Bowersock earned his A.B. from Harvard University in 1957, and after receiving a B.A. and M.A. at Oxford University, he was awarded a D.Phil. from Oxford in 1962. He taught at Oxford in Balliol, Magdalen, and New Colleges from 1960 to 1962, when he joined the faculty of Harvard. There, he was Professor of Classics and History, as well as Chairman of the Department of Classics from 1972 to 1977, and Associate Dean of the Faculty of Arts and Sciences from 1977 to 1980, at which time he joined the Faculty at the Institute. ■

RANDALL HAGGARDEN

NEWS OF THE INSTITUTE COMMUNITY

In June, PETER GOLDREICH, Professor in the School of Natural Sciences, was the recipient of the Grand Medal of the Academy of Science of the Institute of France. Since its creation in 1997, the Grand Medal is awarded annually to a scholar, French or otherwise, having made significant contributions to the development of science. Professor Goldreich was recognized for his many contributions to the field of astrophysics.

In March, ROBERT P. LANGLANDS, Hermann Weyl Professor in the School of Mathematics, was awarded the Frederic Esser Nemmers Prize in Mathematics by Northwestern University. Professor Langlands was recognized for his "fundamental vision connecting representation theory, automorphic forms, and number theory."

EDWARD WITTEN, Charles Simonyi Professor in the School of Natural Sciences, received an honorary doctorate in science from the University of Cambridge in June for his research in string theory and quantum field theory.

GLEN W. BOWERSOCK, Professor Emeritus in the School of Historical Studies, was honored on April 7 at "East and West: A Conference in Honor of Glen W. Bowersock on the Occasion of his Retirement from the Faculty of the School of Historical Studies, Institute for Advanced Study." Sponsored by the Princeton University Departments of Classics and History, the Humanities Council, the Program in the Ancient World, and the Program in Hellenic Studies, the conference was held at Princeton University and featured scholars from Italy, France, Germany, England, and the United States, discussing various areas in which Professor Bowersock has worked and produced scholarship.

Many-colored Glass: Reflections on the Place of Life in the Universe, by FREEMAN J. DYSON, Professor Emeritus in the School of Natural Sciences, is due to be published by University of Virginia Press later this year or early next year.

In March, OLEG GRABAR, Professor Emeritus in the School of Historical Studies, co-chaired a scholarly meeting in Jerusalem with BENI KEDAR, former Member (1981-82) and Visitor (1997-98) in the School of Historical Studies. The meeting centered around the collective publication of a book on the Haram al-Sharif, or Temple Mount, written together by Palestinian, Israeli, European, and American scholars. The last two of Professor Grabar's four volumes, containing some 83 articles written over a period of nearly half a century, were published under the title *Constructing the Study of Islamic Art* (Ashgate, London, 2005 and 2006).

CHRISTIAN HABICHT, Professor Emeritus in the School of Historical Studies, had a second, revised, and enlarged edition of *Athènes hellénistique*, originally published in 2000, published earlier this year by Les Belles Lettres, Paris. His book *The Hellenistic Monarchies: Selected Papers*, was published in May by the University of Michigan Press. Two international symposia were held to mark the eightieth birthday of Professor Habicht: "On Attic Epigraphy," from April 3rd to 5th in Athens, and "The Epigraphy of Thessaly," from April 7th to 9th in Volvos, Greece.

IRVING LAVIN, Professor Emeritus in the School of Historical Studies, delivered the following lectures: "Caravaggio's Flight into Egypt," in Barcelona, Spain, on the occasion of the exhibition *Caravaggio y la pintura realista europea*, and "The Baldachino in St. Peter's: Did Borromini Forget Himself?" in Bonn, Germany, on the occasion of an exhibition and colloquium, *Sankt Peter in*

Rom 1506-2006. The lecture he delivered when he received Italy's *Premio Internazionale Galileo Galilei* in October 2005 is soon to be published in Spanish.

"The Analytic and the Synthetic: An Untenable Dualism," by MORTON WHITE, Professor Emeritus in the School of Historical Studies, which was originally published in 1950, has been reprinted in a volume entitled *Pragmatism, Old and New*, edited by Susan Haack (Prometheus Books, 2006). This essay was first published in a volume honoring John Dewey on his ninetieth birthday and has been reprinted several times. A French translation of Professor White's *A Philosophy of Culture* was published by Vrin, Paris.

SIR MICHAEL ATIYAH, former Faculty member (1969-72) and former Member (1955-57, 1959-60, 1967-68, 1975-76, 1987-88) in the School of Mathematics, received an honorary Doctor of Science degree from Harvard University at the school's 335th Commencement ceremony in June.

DAM ASHFORTH, former Visiting Associate Professor (1999-2006) and former Member (1997-98) in the School of Social Science, has been named Associate Director of the Program for African Studies and a full professor at Northwestern University, effective in September.

Former Institute Trustee (1994-99) and former Member in the School of Social Science (1981-82) JEAN BETHKE ELSHTAIN, the Laura Spelman Rockefeller Professor of Social and Political Ethics at the University of Chicago, was recently confirmed by the U.S. Senate to serve as a member of the National Council on the Humanities.

MATIAS ZALDARRIAGA, former W.M. Keck Visiting Associate in Cosmology (2001-2002), and former Member (1998-2000, 2002-2003) and short-term Visitor (2004 and 2005) in the School of Natural Sciences, has been named a 2006 MacArthur Fellow, as has TERENCE TAO, former short-term Visitor in the School of Mathematics (2005). The MacArthur Fellows Program awards unrestricted fellowships to talented individuals who have shown extraordinary originality and dedication in their creative pursuits and a marked capacity for self-direction.

WOLF LEPENIES, former Director's Visitor and Visitor (2002, 2003, 2004) in the School of Social Science and former Member (1979-80, 1982-84) in the School, has been awarded the 2006 Friedenspreis des Deutschen Buchhandels (the Peace Prize of the German Book Trade). Lepenies is a sociologist and former director of the Wissenschaftskolleg in Berlin, where he remains a permanent fellow.

VINCENT CARRETTA, former Member in the School of Historical Studies (2003-04), was awarded the biennial Annibel Jenkins Prize for his book *Equiano, the African: Biography of a Self-Made Man*. The prize is awarded for the best book-length biography of a late seventeenth- or eighteenth-century subject.

In April, CAROL GLUCK, former Member in the School of Historical Studies (2005-06), was honored by the government of Japan with The Order of the Rising Sun, Gold Rays with Neck Ribbon, for her outstanding contributions to the development of Japanese studies and the promotion of cultural and scholarly exchange between Japan and the United States.

DON HARRAN, former Member in the School of Historical Studies (2001-02), was elected as an Honorary Foreign Member of the American Academy of Arts and Sciences (2006). At an official ceremony in conjunction with festivities to mark the sixtieth anniversary of the Italian Republic in June, Harran was made a Knight of the Order of the Star of Italian Solidarity (Cavaliere dell'Ordine della Stella della Solidarietà Italiana). The honor was in recognition of his distinguished contribution to Italian musical scholarship.

Former Member in the School of Mathematics (1954-56) KIYOSI ITÔ is the first laureate of the inaugural Carl Friedrich Gauss Prize for applications of mathematics. Itô was honored for creating a mathematical formalism, beginning in the 1940s, called stochastic analysis, which has evolved into "a rich, important and fruitful branch of mathematics with a formidable impact on technology, business, or simply people's everyday lives."

Neuroscientist P. READ MONTAGUE, former Member (2005-06) and participant in the School of Social Science's 2005-06 theme, "Psychology and Economics," has co-authored an article, "Agent Specific Responses along Cingulate Cortex during Iterated Economic Exchanges," in the May 19 issue of *Science*. The paper employs a new technique in imaging, called hyperscanning, where two interacting brains are imaged simultaneously.

ANDREI OKOUNKOV, former Member in the School of Mathematics (1995-96) and TERENCE TAO, former short-term Visitor in the School of Mathematics (2005) have each won the 2006 Fields Medal. Okounkov was cited for his "contributions bridging probability, representation theory and algebraic geometry," and Tao was acknowledged for his contributions in "partial differential equations, combinatorics, harmonic analysis, and additive number theory."

The National Endowment for the Humanities has awarded former School of Social Science Member (2005-06) MICHAEL G. PELETZ a fellowship that will enable him to spend the 2007 calendar year on research leave from Emory University, completing his current book project on gender pluralism in Southeast Asia. His article, "Transgenderism and Gender Pluralism in Southeast Asia since Early Modern Times," appeared in the April issue of *Current Anthropology*.

ADRIANA PETRYNA, former Visitor (2005-06) and Member (2003-04) in the School of Social Science, has co-edited *Global Pharmaceuticals: Ethics, Markets, Practices*, with Andrew Lakoff and Arthur Kleinman. JOÃO BIEHL, former Member in the School of Historical Studies (2005-06), was a contributor. The book was published in March by Duke University Press.

In March, OMER REINGOLD, former Visitor in the School of Mathematics (1999-2004), won the Grace Murray Hopper Award, presented by the Association for Computing Machinery. Reingold was recognized for his proof that resolves a longstanding and central problem in computational complexity. The Hopper Award honors the outstanding young computer professional of the year.

Pursuit of Genius: Flexner, Einstein, and the Early Faculty at the Institute for Advanced Study by STEVE BATTERSON, former Member in the School of Mathematics (1980-81), has been published by A K Peters, Ltd. Members of the Institute community who are interested in purchasing a hardcover copy are entitled to a 15% discount. To place an order, visit www.akpeters.com, e-mail marketing@akpeters.com, or phone 1-781-416-2888 x18, and specify the discount code IAS1006. The discount will be valid through December 31, 2006, and is available only when ordering through A K Peters, Ltd.

ASTROPHYSICIST SCOTT TREMAINE JOINS INSTITUTE FACULTY



Scott Tremaine

Astrophysicist Scott Tremaine has been appointed to succeed the late John Norris Bahcall (1934–2005) as the Richard Black Professor of Astrophysics in the School of Natural Sciences. Bahcall, who joined the Faculty of the Institute in 1971, served as the Richard Black Professor from 1997 until his death in August 2005.

One of the world's leading scientists, Dr. Tremaine has made seminal contributions to the field of astrophysics that have led to a greater understanding of the formation and evolution of planetary systems, comets, black holes, star clusters, galaxies, and galaxy systems. He is presently Charles A. Young Professor of Astronomy at Princeton University, where he has served as Chair of the Department of Astrophysical Sciences since 1998. He will join the Faculty of the Institute on January 1, 2007.

"Scott Tremaine's breadth of understanding of dynamics as applied to natural systems is unmatched among astrophysicists and has enabled him to contribute unique insights to a diverse set of problems," commented Peter Goldreich, Professor in the School of Natural Sciences. "He combines an excellent appreciation for phenomenology with superb instincts for the most efficient tool to apply to any given problem."

His appointment to the Faculty at the Institute, Dr. Tremaine said, would give him "unparalleled opportunities to develop my own research, and, following John Bahcall's

vision, to help exceptional young astrophysical theorists develop their full potential."

Among Dr. Tremaine's major contributions are predicting the Kuiper belt of comets beyond Neptune, and, with Professor Goldreich, the existence of shepherd satellites and density waves in Saturn's ring system, as well as the phenomenon of planetary migration. In addition, he has investigated the evolution of the solar system and other planetary systems over very long times; developed methods for measuring the rotation speed of barred spiral galaxies and the phase-space distribution of the stars in elliptical galaxies; interpreted double-nuclei galaxies, such as the nearby Andromeda galaxy, as eccentric stellar disks; and elucidated the role of dynamical friction in galaxy evolution. He is also a member of a collaborative group of scientists whose investigations into the properties of black holes has found that almost every galaxy contains a massive black hole at its center and that the masses of these black holes are strongly correlated with the dynamics of the surrounding galaxy.

Raised in Toronto, Canada, Dr. Tremaine received his undergraduate education at McMaster University. He was awarded a Ph.D. in physics from Princeton University in 1975, and he held postdoctoral fellowships at Caltech and Cambridge University. In 1981 he joined the faculty of MIT after being a long-term Member at the Institute (1978–81); he subsequently became a professor in the Departments of Physics and Astronomy of the University of Toronto from 1985 to 1997. While at the University of Toronto, he served as founding Director of the Canadian Institute for Theoretical Astrophysics, establishing it as a leading international research center. He revisited the Institute for Advanced Study as a Member on four occasions between 1983 and 2002.

A Fellow of the Royal Societies of London and of Canada and a member of the National Academy of Sciences, Dr. Tremaine is coauthor with James Binney of the influential textbook *Galactic Dynamics* (1987) and has contributed over 150 papers to the *Astrophysical Journal*, *Icarus*, and other journals. He received the Dannie Heine-man Prize for Astrophysics in 1997. ■

Biology at the Institute

On September 14 the Regional Planning Board of Princeton gave approval to the construction plans for an extension to Bloomberg Hall, designed by architects Pelli Clarke Pelli. The extension, which is scheduled to be complete in time for the start of the next academic year, will provide a home for The Simons Center for Systems Biology. With its opening, the Institute's commitment to the study of biology will take a concrete or, rather, bricks-and-mortar form.

Discussion of whether biology should be included within the work of the Institute goes back to its early days. From the beginning, founding Director Abraham Flexner envisioned that fields of study within the Institute should be created "one by one, as men and funds are available—and only then—a series of schools or groups" that might change from time to time with designations "so broad that they may readily cover one group of activities today, quite another as time goes on."

But Flexner's views on biology at the Institute apparently oscillated. In 1937, after he and Oswald Veblen had discussed the possibility of inviting the British biologist J.B.S. Haldane as a Member, Flexner expressed the view that "we have no present or, as far as I can see, future reason for taking chemistry or biology into consideration at all."

However, in his report to the Trustees the next year, he seems to have altered his opinion somewhat, stating, "it is quite possible that biology will never obtain the precise position occupied by physics, but these difficulties are a challenge.... Sciences, whether they be natural sciences or social sciences, are the vanguard of human thinking and human progress.... We are quite comfortable for the time being in the field of mathematics, but it is a mistake to suppose we shall remain permanently comfortable."

Although occasional work was done on biological topics at the Institute in the 1940s and 1950s, it was not until the beginning of the 1960s that Director J. Robert Oppenheimer revisited the question of whether, following the recent dramatic advances in molecular biology, the Institute had a role to play in the area. As before, the absence, and perhaps inappropriateness or infeasibility, of laboratories at the Institute was an obstacle to the development of a subject where experiment is

ubiquitous in research. Francis Crick and Jacques Monod came to discuss possible approaches but no program was established.

The subject remained on the agenda. In the late 1980s, Director Murph Goldberger brought John Maynard Smith, who had been a student of Haldane, to give a series of lectures. Steve Adler and others in the School of Natural Sciences had become actively interested in areas of biology, and, following a conference jointly organized in 1995 by Director Phillip Griffiths and Arnold Levine, then Chair of the Department of Molecular Biology at Princeton University, Frank Wilczek undertook a study of the fields within biology that might be appropriate for development at the Institute, given the constraints and potential synergies.

This led to the appointment in 1998 of Martin Nowak, then Professor at Oxford University, to lead a program in theoretical biology concentrating in the areas of ecology and evolution dynamics. When he left in 2003 to establish a program in evolution dynamics at Harvard, Arnold Levine, former President of The Rockefeller University, came to the Institute to create a center for systems biology, first as a Visiting Professor and then, from 2004, as the Institute's first Faculty member in biology. As the article in this issue shows, he has established a group that both maintains essential contact with experiment and also brings in highly talented young scientists from physics and mathematics, effectively addressing the concerns that inhibited earlier development.

As Flexner noted, expansion of activity requires additional funding if the health and strength of the Institute is to be maintained. It is through the generous support of The Simons Foundation, The Leon Levy Foundation, and others that the establishment of biology is being made possible. Further support is needed and is being sought, but when the new wing on Bloomberg Hall opens next fall, biology will be firmly established at the Institute at last.

Peter Goddard
Director

Institute Hosts Kurt Gödel Centenary Program

On Friday, November 17, the Institute will host a special program from 2:00 to 6:30 p.m. in Wolfensohn Hall to mark the centenary year of the birth of Kurt Gödel (1906–1978), the foremost mathematical logician of the twentieth century. The program will consist of talks aimed at a general audience

on the life and work of Gödel and his impact on mathematics, philosophy, and computer science. Gödel was among the Institute's first Members in 1933–34, returning for further periods in the 1930s and 1940s before joining the Faculty in 1953. He remained at the Institute until his death in 1978. Scheduled speakers

include John Burgess, Princeton University; John W. Dawson, Jr., The Pennsylvania State University; Solomon Feferman, Stanford University; Juliette Kennedy, University of Helsinki; Karl Sigmund, University of Vienna; and Avi Wigderson, Institute for Advanced Study. ■

THE SIMONS CENTER *(Continued from page 1)*

the mechanism of disease progression. At the Institute, Nowak led a small group of postdoctoral scholars and visiting senior scientists whose theoretical research interests included the dynamics of infectious diseases, evolutionary genomics, genetic instability, tumor progression, the evolution of language, and evolutionary theory in general.

Professor Levine, a molecular biologist, joined the Institute as Visiting Professor in the School of Natural Sciences in 2002, assumed leadership of the Institute's biology initiative in July 2003, and subsequently established the Center for Systems Biology. Levine is a former President of The Rockefeller University (1998–2002) and professor (1984–98) and chair of the Department of Molecular Biology at Princeton University (1984–96). A widely acclaimed leader in cancer research, Professor Levine discovered in 1979 the p53 tumor suppressor protein, a molecule that inhibits tumor development and whose disruption is associated with an estimated 50 percent of human cancer. For this discovery, he has won numerous awards, including the Keio Medical Science Prize, from the Keio University Medical Science Fund, Japan, in 2000; the Alfred Knudson Award in Cancer Genetics from the National Cancer Institute in 2001; the Albany Medical Center Prize in Medicine and Biomedical Research in 2001; and a 2006 *Freedom to Discover* grant from Bristol-Myers Squibb.

When Professor Levine was appointed to the Faculty in July 2004, systems biology was formally made a program of the School of Natural Sciences. Last year the Center was renamed The Simons Center for Systems Biology to reflect the generosity of Trustee James H. Simons, a former Member in the School of Mathematics, and his wife Marilyn Hawrys Simons, who have endorsed the Center's work with a \$10 million challenge grant from their foundation, The Simons Foundation. The Institute will expand the systems biology program demonstrably this fall when it begins construction of an extension to Bloomberg Hall, which will house the Center and unite the School of Natural Sciences in one building (see below).

Because of the Institute's long history in mathematics, physics, and astrophysics, the program has attracted exceptionally talented physicists, chemists, mathematicians, computer scientists, and statisticians who see the potential of an interdisciplinary approach to biology.

Harlan Robins, now an assistant professor in computational biology at the Fred Hutchinson Cancer Research Center in Seattle, was a trained physicist specializing in string theory when he arrived at the Institute as a Member in systems biology (2002–2006). "I didn't know any biology when I got here, so I would say my

entire career as a biologist developed here," said Robins. "The first two years, I put a considerable effort into developing a background in biology."

Raúl Rabadán, who spent the last three years as a particle physics Member in the School of Natural Sciences, has moved to systems biology for a three-year membership, beginning this term. Nils Baas, who twice has been a Member in the School of Mathematics, will spend a six-month sabbatical as a joint mathematics and systems biology Member, beginning in January.

Although there are no laboratories at the Institute, the Center enjoys close interactions with the Cancer Institute of New Jersey; the Robert Wood Johnson Medical School; Lewis-Sigler Center for Integrative Genomics at Princeton University; Bio-MaPS Institute at Rutgers, The State University of New Jersey; IBM; Merck & Co.; and Bristol-Myers Squibb. "Many of the things done here are tested in laboratories," said Levine. "We try to make it a rule that everything we work on has a testable outcome."

Professor Levine has made it a priority to position the Center in the middle of the biological community, rather than to operate in isolation. "We hold symposia here to introduce the Institute to experimentalists," said Levine. The program also benefits from close collaborations with leading laboratory scientists who "jump right in and do experiments that either verify or contradict the theoretical work we do," Levine said. "In this sense then, biology is adopting the paradigm that physics starts with. The theorist can actually lead the experimentalist rather than the experimentalist leading the theorist."

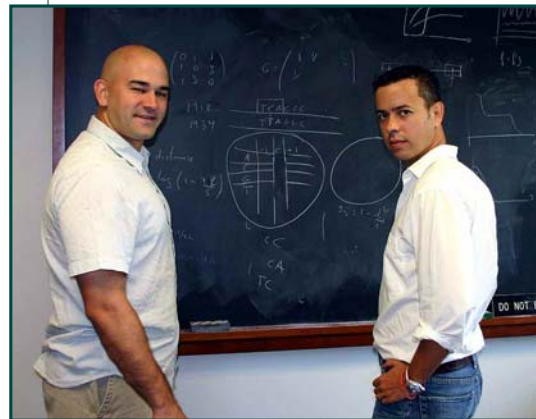
During his time at the Center, Robins developed algorithms to identify various genome sequences and their implications. With fellow Member Michael Krasnitz, Robins designed an algorithm that uncovered hidden sequences that are underrepresented in the human genome but are prominent in the HIV genome. "The idea is that these particular sequences cause HIV to be underexpressed in the human cell and, therefore, when people try to do things like make a DNA vaccine for HIV, they don't get any product," said Robins. "You may need to change these sequences in order to make a DNA vaccine."

As described in this issue's cover, Rabadán, Robins, and Professor Levine also analyzed a large quantity of genomic sequence data for human and avian versions of the Type A influenza virus. In studying this data, which spanned almost ninety years, the team was able to identify genomic features that differed between the human and avian viruses and observe their

evolution. In particular, they were able to discern significant differences in sequence changes that occurred over time, suggesting the possible existence of a previously unknown, innate immune response in humans that has no counterpart in birds. They were also able to provide evidence supporting the hypothesis that the avian version of the virus entered the human population just prior to the 1918 pandemic, probably no earlier than 1910. "Now, one of the questions is: Is it possible for the virus to jump directly from birds into humans?" said Rabadán. "And the other is: If this is possible, how is it possible?"

The potential impact of systems biology on the future of biological research is enormous, and should affect everything from population genetics, where it can impart a tremendous amount of information about selection and the process of evolution, to environmental biology, where it can identify, for example, previously unknown organisms in the air and unidentified viruses in ocean water.

In the field of medicine, it may be possible to draw conclusions from genetic material that will guide treatment of diseases such as breast cancer, where genetic markers may be able to indicate which patients will and will not benefit from certain therapies. Levine proposes that advances in systems biology could eventually lead doctors to conduct routine genetic testing that would identify which diseases a patient is predisposed to—information a patient could then use to make lifestyle decisions to avoid developing those diseases. The pioneering research that will make such advances possible, said Levine, "has very important societal and economic value." ■



Harlan Robins (left) and Raúl Rabadán, authors with Professor Arnold J. Levine of the paper on Type A influenza viruses described on this issue's cover.



The Bloomberg Hall extension, to be built at the east end of the existing building, will house The Simons Center for Systems Biology and unite the School of Natural Sciences in one building. The extension, as depicted at left, has been designed by Pelli Clarke Pelli Architects.

The three-story, 13,750-square-foot addition has been conceived to be distinct but highly compatible with the existing building. Particular attention has been paid to seamlessly incorporating the Center into Bloomberg Hall with an emphasis on maintaining natural circulation patterns to encourage communication within the School as a whole.

The extension has also been designed to accommodate the Center's anticipated future growth. The upper two floors will provide office and meeting space for Faculty, Members and Visitors, and staff. The ground floor will house the Institute's central computing staff as well as a computer equipment room.

In addition, the design features an extensive green roof, the first to be built in Mercer County. Ninety percent of the 4,300-square-foot roof addition will be planted with a mixture of three variants of sedum, a low-to-no maintenance plant that can survive on shallow soil depths and withstand harsh growing environments. The design includes a water retention layer that allows the soil and plants to soak up storm water for prolonged periods of time, which will mitigate storm water runoff.

PETRONIO FELLOWSHIP FUND CREATED AT THE INSTITUTE

Elena Petronio, longtime Friend of the Institute for Advanced Study, has made a gift of her Princeton residence to establish The Giorgio and Elena Petronio Fellowship Fund. A forty-five percent interest in the proceeds from the sale of the home has created the Fund, which will support scholars in the School of Mathematics. The balance of the value of the home will fund a charitable trust benefiting Mrs. Petronio during her lifetime, and the remaining principal will eventually revert to the Institute and the Petronio Fellowship Fund.

Giorgio Petronio, who passed away in 2004, was a group chairman of Johnson & Johnson. In this position, he had frequent dealings with Asia. According to his wife, there is an Eastern philosophy that when a person reaches maturity at age 60, that is when he or she should begin to give back to society. As Mr. Petronio neared this age, the couple started to consider making a serious gift to the Institute, and provided major funding for the Albert O. Hirschman Chair in Economics, as well as establishing a second unrestricted trust. The Petronio Fellowship Fund is the most recent demonstration of their generosity.

"IAS is a home-based institution that we could relate to," said Mrs. Petronio in explaining her decision to donate her home. The couple had met Enrico Bombieri, IBM von Neumann Professor in the School of Mathematics, many years ago and had become quite friendly with him, socializing and conversing in Italian and learning about the Institute. Mr. Petronio admired Professor Bombieri and his work, and through him, the couple became involved in the Institute as Friends.

The Giorgio and Elena Petronio Fellowship Fund will support a Member in the School of Mathematics in a preferential order, first coming from Trieste, the city in Italy where Mr. Petronio spent much of his childhood and where he attended university, then from Italy, then from Europe, and finally from anywhere else in the world. The first Petronio Member is Valentina Riva, whose field of study is low-dimensional quantum-field



Elena Petronio (left) and Professor Enrico Bombieri join Valentina Riva, the first Member to be supported by the Giorgio and Elena Petronio Fellowship Fund in the School of Mathematics.

theories and their applications to statistical mathematics and condensed matter physics. Riva, who is currently affiliated with the University of Oxford, is a native of Como, Italy.

Gifts such as this are particularly important for the School of Mathematics and the Institute in general, helping the Institute to continue its mission of fostering intellectual pursuits that have an impact on scholarship worldwide. ■

Making a Gift of Real Estate to the Institute

By making a gift of real estate to the Institute for Advanced Study you may receive substantial financial benefits. In some cases, you may wish to give the property outright to support the purposes of the Institute and qualify for an income tax deduction on the fair market value of the property. In other cases, you may use a home or land you no longer want or need to fund a life income arrangement.

If you are contemplating leaving your home to the Institute through your will, you may wish to consider giving it now but retaining the right to live in it for your lifetime and that of a second beneficiary if you wish. You will continue to pay taxes, insurance, and maintenance costs. But, by giving now, you receive a substantial charitable income tax deduction in the year the gift is made and may carry any excess deduction over for five more years.

Through the years, several gifts of real estate have been made to the Institute. Former Faculty Member Albert Einstein left his charming 19th century house to the Institute through his will; that house is now the home of a Faculty member in the School of Social Science. The generosity of Harold K. and Mary Marquand Hochschild has provided the Institute with Marquand House, a gracious guest house and a site for important gatherings.

Several donors have chosen to make a partial gift of a house through a bargain sale. In those instances, the donors chose to sell the house to the Institute at a greatly reduced cost, thus making it possible for the Institute to buy the house and ensuring a substantial charitable income tax deduction for the donors.

For further information, please contact Kamala Brush at 609-734-8031 or kbrush@ias.edu. ■

THREE NEW TRUSTEES APPOINTED TO INSTITUTE BOARD

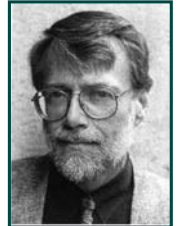
The Institute for Advanced Study has appointed Dr. Victoria B. Bjorklund, Dr. David Hollinger, and Dr. Florian Langenscheidt to its Board of Trustees. Dr. Bjorklund is a Partner at Simpson Thacher & Bartlett LLP, where she heads the Firm's Exempt Organizations Group. Dr. Hollinger, who will serve as Academic Trustee for the School of Historical Studies, is Preston Hotchkis Professor of History at the University of California, Berkeley, and Chair of the Department of History. Dr. Langenscheidt, a leading author and publisher, is a partner of Langenscheidt Publishing Group, a company that produces a diverse range of bilingual dictionaries, and map, travel, and language publications used throughout the world.



Dr. Victoria B. Bjorklund advises public charities, private foundations, boards, and donors in her role at Simpson Thacher & Bartlett LLP, an international law firm headquartered in New York City. In 2001, she was appointed by the U.S. Secretary of the Treasury to serve on the IRS's Tax Exempt/Government Entities Advisory Committee, which she chaired in 2004-2005. From 1989 through 2001, she was director and secretary of Doctors Without Borders, and continues to provide *pro bono* legal counsel to the organization, as well as to the Robin Hood Foundation. In 1997-1998, Dr. Bjorklund was named a David Rockefeller Fellow in recognition of her role as a rising civic leader, and she has received many awards and honors for her work, including the IRS's Commissioner's Award in 2003. She writes and speaks extensively on exempt-organization subjects and is co-author (with Jim Fishman and Dan Kurtz) of *New York Nonprofit Law and Practice* (Lexis Publications, 1997). She earned her J.D. at Columbia University School of Law, her Ph.D. in Medieval Studies from Yale University, and her B.A. *magna cum laude* from Princeton University.

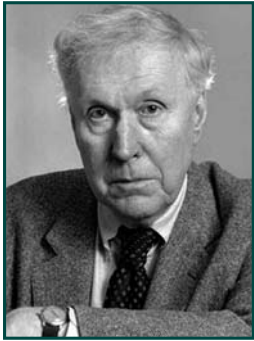
Dr. David Hollinger is a leading scholar who has written extensively on American intellectual history and academe. He was twice a Member in the School of Historical Studies at the Institute, in 1977-78 and 2000, and will serve as the Academic Trustee for the School. Dr. Hollinger has written and co-edited numerous books and articles relating to

educational institutions and history, including *Cosmopolitanism and Solidarity: Studies in Ethnorracial, Religious, and Professional Affiliation in the United States* (2006); *Postethnic America: Beyond Multiculturalism* (10th anniversary edition, 2006); *Science, Jews, and Secular Culture* (1996); and, co-edited with Cathryn Carson, *Reappraising Oppenheimer* (2005). He currently serves on the editorial boards of *Modern Intellectual History*, *Comparative Studies in Society and History*, and the *Journal of the History of Ideas*. Dr. Hollinger, who is a Council Member of the History of Science Society, received his Ph.D. in History and his M.A. from the University of California, Berkeley, and earned his B.A. at La Verne College.



Dr. Florian Langenscheidt is recognized for his innovative approach and expertise in the field of publishing, including the future of new media and e-business. Dr. Langenscheidt headed the esteemed 150-year-old Langenscheidt family of publishers from 1986 until 1994, during which time he diversified operations and expanded the company's reach into and across the Internet. He has authored and edited numerous publications and children's books, including *Bei uns zu Hause-Prominente erzählen von ihrer Kindheit* (1995); *Hundertmal Mut* (1999); *Brands of the Century* (2004); and *The Best of Germany* (2006), and is a columnist for the periodicals *Capital*, *Forbes*, and *Max*. Dr. Langenscheidt founded the global organization Children for a Better World and is a partner of the German Children and Youth Foundation. He is also a trustee of the World-Wide Fund for Nature, Stiftung Lesen, Deutsche Olympische Gesellschaft, and the Deutsches Museum, and is a founding chairman of the Electronic Publishers Working Party, which represents the German book industry in multimedia and the Internet. Dr. Langenscheidt received his Ph.D. in Advertising at Ludwig Maximilians Universität (LMU) in Munich and earned a Masters in Business Administration at INSEAD in Fontainebleau, France. As an undergraduate at LMU, he studied German Literature, Journalism, and Philosophy. ■

MAJOR BEQUEST FROM FORMER MEMBER WILLIS DONEY (1925–2005)



Willis Doney

Just how influential a Membership at the Institute for Advanced Study might be in the life of an individual can be difficult to predict. But in the case of Dr. Willis Doney, former Member in the School of Historical Studies (1972–73), the experience must have been profound. More than thirty years after his last stay at the Institute, the depth of his gratitude became evident. Dr. Doney, who passed away on July 2, 2005, left a major bequest to the Institute, valued at \$3 million.

Born in Pittsburgh in 1925, Dr. Doney was educated at Princeton and Dartmouth. An internationally recognized scholar of seventeenth- and eighteenth-century philosophy, he joined the faculty of Dartmouth in 1958 and was Professor Emeritus there at the time of his death, some forty-seven years later.

Dr. Doney was the first philosopher to come to the Institute under the aegis of Professor Emeritus Morton White in the School of Historical Studies, who remembers him as a scholar of Descartes and a loyal friend of the Institute.

“He was a charming man who organized a group of philosophers interested in seventeenth-century European philosophy that met for five years or so at the Institute during the summers,” Professor White recalled. “Willis was very grateful to IAS for bringing him here, and for allowing him to host this group.”

This informal group, organized jointly by Dr. Doney and Margaret Wilson, former Visitor in the School of Historical Studies (1973), was called the Seventeenth Century Study Group, according to Robert C. Sleight, Jr., Professor Emeritus of Philosophy at the University of Massachusetts, Amherst.

“The idea was to have some of the leading scholars of seventeenth-century philosophy in the United States meet for approximately ten days each June to present the research material each had developed during the prior academic year,” Sleight recounted. “The group met at the Institute from 1975 through 1980, with the exception of 1976, when we met at Rockefeller University. Both Margaret Wilson and Willis had previously spent time at the Institute, working on their research projects with Professor White, who was instrumental in paving the way for Institute approval of these June meetings.

“Willis kept the group on track both with respect to working hard and with respect to enjoying the amenities of the Institute,” he continued. “It was a very successful venture; I believe that Willis’s regard for the Institute reached a tipping point during these June meetings, leading to his generous bequest.”

The Institute will receive the bulk of Dr. Doney’s estate, which, in addition to cash, stocks, bonds, and retirement accounts, consists of an apartment in Paris, his home in Vermont (including furnishings, fine china, stemware, silver flatware, and artwork), and an extensive library.

Although this bequest was the more significant, it was not Dr. Doney’s first gift to the Institute. In 1987, he made a gift of \$18,000 in securities. ■

HELLENIZATION AND ISLAMIZATION: CULTURAL STRATEGIES IN THE WAKE OF IMPERIAL EXPANSION

Some thirty national and international scholars gathered at the Institute for Advanced Study from May 1st to the 3rd to attend a colloquium organized by Patricia Crone, Andrew W. Mellon Professor in the School of Historical Studies, titled “Natives as Members of Imperial and Post-Imperial Elites: Apologetics and ‘Shu’ubiyya’ in Hellenism and Islam.”

Unique in its exploration of the reaction to foreign conquest and the adoption by the natives of the culture of the conquerors, the colloquium focused on cultural strategies seen in the wake of great imperial expansions of the type leading to the erosion of the prestige, and eventually also the substance, of the native cultures. While rare, there are three famous examples of such conquests that have affected the Near Eastern-Mediterranean region: the expansion of the Greeks was followed by Hellenization, that of the Arabs by Islamization, and that of the Europeans by Westernization. This conference concentrated on the first two.

The colloquium was not meant to produce new research (though in practice, it actually did), but rather to enable classicists and Islamicists to compare notes, to get a sense of what texts were available on the two sides, to examine how the texts have and could or should be handled, and how researchers might go about engaging in comparative work.

The three-day colloquium compared the Hellenization of culture with Islamization, something Professor Crone said has never been spoken of in the same context before. “We hoped to open people’s minds to a phenomenon that has occurred repeatedly in history but has not been closely examined. The conference was unusual because we didn’t call for written papers,” she noted. “Participants were asked to prepare dossiers of original texts that showed how people thought and the language that they used in this context.”

This novel approach provided participants with a compilation of historical texts that will be useful tools as they return to their home institutions, which ranged from Pomona College, Berkeley, and Harvard, to Hebrew University, the University of Freiberg, and Spain’s High Council for Scientific Research. ■

IMMANUEL KOHN RETIRES FROM BOARD

Immanuel Kohn retired from the Institute’s Board of Trustees in May 2006. While he served on the Board for nearly a decade, Ike Kohn’s connections with the Institute stretch back more than half a century, to 1948 and 1955 when his father, Hans Kohn, was a Member in the School of Historical Studies. Ike and Vera Kohn have been extraordinarily generous to the Institute, creating a Membership in the School of Historical Studies to honor Hans Kohn’s legacy as an educator and intellectual historian noted for his work on nationalism. In addition to endowing the Hans Kohn Membership, Ike Kohn has fostered fruitful relationships with foundations that have strengthened the Institute’s endowment, East Asian Studies, its program in systems biology, and the IAS/Park City Mathematics Institute. ■



Immanuel Kohn

PROGRAM FOR WOMEN AND MATHEMATICS



Fifty-three women mathematicians from throughout the United States participated in the Women and Mathematics program this year. The sessions, which focused on zeta functions, were held in Simonyi Hall between May 15th and the 26th. The program, sponsored by the Institute and Princeton University, celebrated its 13th year at the Institute.

FRIENDS NEWS

Friends of the Institute for Advanced Study are privileged to receive regular opportunities to participate in the intellectual life of the Institute. This November at a Friends Forum, School of Historical Studies Professor Jonathan Israel, whose recent work focuses on, among other things, the nature and influence of radical thought, will consider Spinoza’s impact on the world through philosophy. Friends with an interest in planetary science and astrophysics can look forward to a lecture by Professor Peter Goldreich, School of Natural Sciences, which will take place during the Institute’s spring 2007 term. For information on becoming a Friend, please contact Pamela Hughes, 609-734-8204 or phughes@ias.edu.

A new charitable giving provision just signed into law makes it possible, for the first time, for donors to make tax efficient charitable gifts from IRAs and Roth IRAs during their lifetimes. During the 2006 and 2007 tax years, owners of IRAs who are already required to take distributions from their retirement accounts can transfer up to \$100,000 to the Institute each year. This contribution does not create a charitable deduction, but it does allow the donor to exclude the IRA distribution from gross income. There are some restrictions on this “charitable rollover.” For more information, please contact Kamala Brush at 609-734-8031 or kbrush@ias.edu.

ON MUSIC AND ECONOMICS: A Conversation between Jon Magnussen and Eric Maskin

In June, Artist-in-Residence Jon Magnussen and Eric Maskin, Alfred O. Hirschman Professor in the School of Social Science, sat down to discuss their mutual interest in music and performance. Highlights of the conversation follow.

MAGNUSSEN: As the Alfred O. Hirschman Professor of Social Science at the Institute for Advanced Study, you've done groundbreaking work in implementation theory and game theory. Yet, you also played your clarinet in a beautiful chamber music concert this spring at the Institute, with a program of works by Mozart, Schumann and Reincke. How long has music been a part of your life?

MASKIN: Oh, it's always been there. I come from a musical family. My mother was a concert pianist. My father wanted to be a violin soloist but was told at some point that he wouldn't be the next Jascha Heifetz, and so went into medicine instead. My brother is a professional oboist and English horn player. He plays in the Charlotte Symphony.

So it was inevitable that music would be important for me. I was exposed to it from the beginning and I've always made it a big part of my life.

MAGNUSSEN: Did you have any ideas about being a professional musician while you were growing up?

MASKIN: Well, when I was growing up, I was quite conscientious about practicing and actually got to be pretty proficient. So I toyed with the idea. But my teachers didn't seem to think that that was such a good idea. First, because they weren't sure I was cut out for it, but also because they knew how tough the music business is. Of course my parents knew this too. So I can't say I got a great deal of encouragement about going into music professionally. But I got a lot of encouragement to develop it as a serious avocation. So, I've tried to play music whenever I can. At this point, I don't have the time to get to it every day. And I'm afraid that that shows. But one way of building it into my schedule is by being involved in chamber music. If I have a rehearsal or concert coming up, then I'm forced to make sure that I put in the practice time, although it's not always easy to juggle with everything else.

MAGNUSSEN: Of course. It seems to me that the Institute community is like many other academic communities in that it is home to a fair amount of scholars who enjoy playing music for the love of it. It's not what they do professionally, but they derive great satisfaction from it.

How has music influenced the way you approach other aspects of your life—particularly your work as an economist? And has this influence evolved since those days when you were pondering what you might do with your music?

MASKIN: Well, as a kid I was interested in technical perfection. And a lot of the time I put in was just for developing my technique. So I would play loads of exercises, which I don't think had much resonance for the rest of my life at all. But now I spend no time on exercises. I just try to play music. The music, I think, is important for my life in a couple of ways. First, it provides a great break from work. Not that it doesn't require effort, too. It does, but a more physical sort of effort than academic work calls for.

Also music gives me a way to express myself. I guess my writing on economics is a form of expression too, but a pretty impersonal form. It's all in the third person, while music is very much a first-person activity.

Also, there are some parallels between what I do as an economist and as a musician. There are aesthetic principles in economics as well as in music. And some principles are common to both. For example, symmetry is a concept that obviously plays a big role in music. Interestingly it's quite important in economics also.

MAGNUSSEN: Do you use the word "beauty" in economics, as mathematicians do?

MASKIN: Yes. I think it's fair to say that the most important economic ideas are also the most beautiful. They're at the same time simple and deep. Just as the profoundest music is often the simplest, pared down to the essentials with no extra notes. People think of music as the most abstract of the arts and of economics as something quite concrete and practical. But economists, at least theoretical economists like me, don't typically deal directly with reality. Instead they work with models, which are mathe-



Jon Magnussen (left) and Eric Maskin in front of Wolfensohn Hall

tical abstractions of reality. If you'll forgive me, I think that the art of constructing an economic model shares a lot with the art of composing.

MAGNUSSEN: Yes, I think about this in my own work. I've always felt that my highest attainment as a composer would be to create a model which balances that specificity which I desire, on one hand, with the freedom which the performers desire in the moment of performance. The hyper-complex music of British composer Brian Ferneyhough, for instance, is so incredibly specific—and very difficult—that it demands a superhuman concentration in practice and performance and months and months of hard work on the part of the performer. This model has the capacity to achieve a strikingly similar result to a free improvisation, if the performers are invested in it. In both models, the ideal performance can bring the performer to a transcendent state.

Have you thought about the model of chamber music-making and the decision-making process that a group must go through in order to arrive at a satisfactory performance? Are you interested in social interactions involving musical contexts?

MASKIN: Sure, but in my experience those interactions depend a lot on the particular personalities involved. There've been times when my chamber group has almost come to blows over how a particular passage should be played. People felt so strongly and so differently that it wasn't clear we could come to a reasonable compromise. And on other occasions it's been a breeze, either because we all had more-or-less the same idea or because people were willing to be a bit flexible.

MAGNUSSEN: It certainly sounds familiar in my own chamber music experiences. I understand that your work on voting procedures has involved arriving at an optimal set of rules for decision making. I've often wondered if an optimal set of rules exists for the choices people make in their music. How do people decide which kind of music to play—or not to play?

MASKIN: Hmm, I'm not sure whether my work says anything useful about choosing music. But Stephen Sondheim, the Broadway composer, gave a partial answer when he said that most people—musicians or listeners—gravitate to the familiar in music. Appreciating a particular piece is mainly a matter of whether the ear is used to hearing that kind of music. If so, then the music becomes comprehensible. One problem for recent music is that people just don't have enough exposure to it to get comfortable with it. Music isn't taught in schools anymore. There aren't that many classical music stations left on the radio. And the ones that remain play almost exclusively music that was written before, say, 1940. As for concerts, most of them consist of old chestnuts.

I think your concerts here serve a useful pedagogical purpose because they are unapologetically contemporary. And the great thing is that over time, people have been getting more and more out of them.

MAGNUSSEN: Thank you—I appreciate that. The Institute is a special place, and I enjoy it immensely because it offers something extraordinary to the world in each of the many disciplines it encompasses.

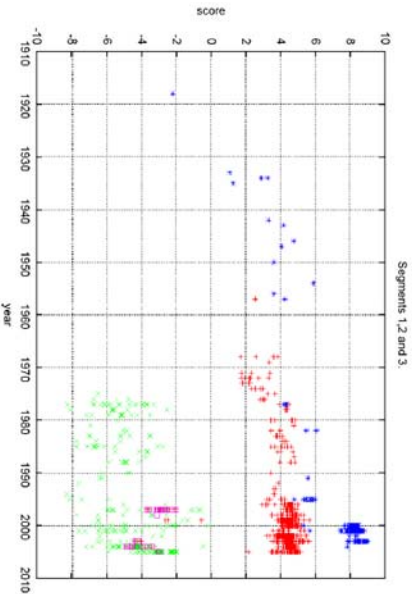
It's wonderful to have you as part of this community—and also that you're interested in music. Do you find that most people in your field are music players?

MASKIN: Maybe not most, but a good many are. The chamber ensembles I've been in have included quite a number of academics.



The 2006–07 concert season at the Institute, curated by Magnussen, begins in October. This also marks Magnussen's last season at the Institute, completing his seven-year term. The season includes *A Gate into Infinity: Music from a Modern Japan*, with the Flux Quartet and pianist Steven Gosling on October 20 and 21, 2006; *A 21st Century Virtuosity*, with the New York New Music Ensemble on February 16 and 17, 2007; and *The Lyric Impulse*, with Trio Solisti and clarinetist Alan Kay on March 30 and 31, 2007. All concerts are held in Wolfensohn Hall. Visit www.ias.edu/air for more information. ■

THE INSTITUTE LETTER



Analyzing Type A Influenza Viruses

Type A influenza viruses are the only influenza viruses known to have caused human pandemics. The steady advance of one such virus, influenza A(H5N1), commonly known as avian flu, has brought with it fears of a new pandemic. To date, no confirmed human-to-human transmissions have been reported in A(H5N1), but it has become increasingly important to understand the possible host-virus interactions.

In a paper that will be published in a forthcoming issue of the *Journal of Virology*, Member Rauli Rabadan and former Member (2002-2006) Harlan Robins together with Arnold J. Levine, Professor in the School of Natural Sciences and head of The Simons Center for Systems Biology at the Institute, present the results of their research comparing genomic sequence data for human and avian versions of the Type A influenza virus.

According to the authors, the genome of the influenza virus contains eight single-stranded negative RNA segments coding for ten or eleven proteins. When two or more different influenza viruses infect the same host cell, the new viral particles can incorporate replicas of segments from different original viruses. The graph above represents the added scores of the three longest RNA segments (1, 2 and 3). The x-axis shows the year when the influenza viruses were found: blue represents human H1N1 viruses; red shows human strains H2N2 (1957) and H3N2 (1968) as well as a few cases of H1N2 (US 2002) and H9N2 (Hong Kong 1999 of avian origin); green represents avian flu; and purple shows avian strains that jumped to humans but were not able to spread from human to human, including the present H5N1 strains. On the y-axis, viruses charted below zero are classified as avian and those charted above zero are classified as human.

As the graph demonstrates, the team was able to identify genomic features that distinguish the human and avian viruses and to observe their evolution. In studying the data, which spanned almost ninety years, they were able to discern significant differences in sequence changes that occurred over time, suggesting the possible existence of a previously unknown, innate immune response in humans that has no counterpart in birds. They were also able to provide evidence supporting the hypothesis that the avian version of the virus entered the human population (possibly after evolving in another organism for a period of time) just prior to the 1918 outbreak, probably no earlier than 1910.

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