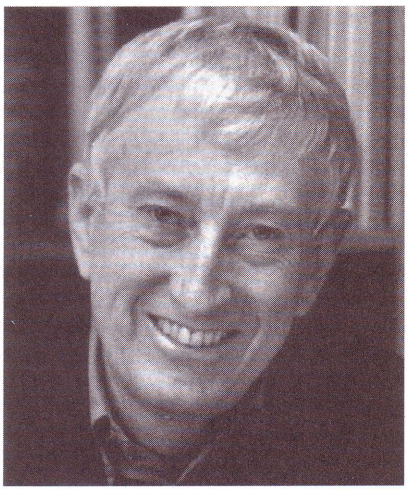
proved untenable for de Klerk when, in May 1996, a new constitution was adopted. The National Party, headed by de Klerk, formally left the coalition, and de Klerk announced that South Africa's "first nonracial democracy was strong enough for a robust opposition party and that he intended to lead it," according to the *New York Times.*

ABOUT: London Observer March 12, 1989; Macleans September 18, 1989; New York Review of Books October 26, 1989, October 20, 1994; New York Times March 23, 1989, December 10, 1993, May 10, 1996; Time January 3, 1994.

DOHERTY, PETER C.

(October 15, 1940–)
Nobel Prize for Physiology or Medicine, 1996 (shared with Rolf M. Zinkernagel)



PETER C. DOHERTY

The immunologist Peter C. Doherty was born in the Australian state of Queensland and raised there in Oxley, a working-class suburb of Brisbane. A dislike of his childhood surroundings led the young Doherty to concentrate on the one sure way of escaping from Oxley—getting an education. He chose to attend the University of Queensland, where, despite his admission in the *Weekend Independent* that his "best subjects were literature and writing," he pursued a career in veterinary science. He received his bachelor's degree in 1962 and his master's degree in 1966. Doherty then traveled to the United Kingdom, where, in 1970, he received his Ph.D. in animal pathology from the University of Edinburgh.

By 1971 Doherty had completed a term as a veterinary officer at Brisbane's Animal Research Institute (1963–1967) and worked as scientific officer at Edinburgh's Moredun Research Institute's department of experimental pathology (1967–1971). In 1972 he received a research fellowship in the microbiology department of the John Curtin School of Medical Research, part of the Australian National University, in Canberra. At the Curtin School Doherty, along with fellow researcher ROLF M. ZINKERNAGEL, probed the inner workings of the human immune system and made a discovery that would one day provide new insight into immune response against a variety of diseases, including cancer and HIV, the virus that causes AIDS.

Prior to the work of Doherty and Zinkernagel, relatively little was known about the signaling and recognition mechanisms of the cellular immune system. It was understood that T lymphocytes, or T cells, were the part of the cellular immune system responsible for recognizing cells infected with various viruses and destroying them. Plaguing immunologists was the question of exactly how these T cells were able to detect and attack only infected cells while leaving healthy cells completely untouched. "There were a number of different people who had been snuffling around this problem, but they couldn't reach a conclusion," Philippa Marrack, an immunologist at the National Jewish Center for Immunology and Respiratory Medicine, told the *New York Times.* She further explained that many of these previous attempts had been hindered by extremely complicated experimentation systems that yielded information that was nearly impossible to interpret.

Doherty and Zinkernagel, who collaborated not out of a strong desire to work with one another, but rather because of a shortage of space at the John Curtin School of Medical Research, decided to conduct experiments on the immune system reactions of mice exposed to the virus that can cause meningitis. After injecting mice with the virus, the pair mixed samples of both the virus-infected cells and T cells from the mice in a test-tube. The results led to a very surprising discovery: the T cells would recognize and kill the infected cells only if they were from the same strain of mice. Infected cells from different strains of mice would simply be ignored. Doherty and Zinkernagel deduced that the T cells would attack an infected cell only after it recognized two key factors: a set of certain molecules known as the major histocompatibility antigens that indicate that the cell is, indeed, part of the self, and not foreign matter; and a fragment of the virus itself, indicating that the cell is infected.

This discovery immediately solved a mystery that had puzzled immunologists for years. The major histocompatibility antigens, which had actually been discovered by scientists studying transplantation biology, differ in each individual and quickly label transplanted organs as foreign, thus provoking the immune system to attack and reject them. But why, since

transplants do not occur in nature, did these major histocompatibility antigens exist? The hypothesis presented by Doherty and Zinkernagel provided a much-needed answer to this question. The major histocompatibility antigens exist because they are an integral part of the body's two-step process in recognizing infected cells. Suddenly, from the pair of scientists whom Dr. Ronald Schwartz, chief of the laboratory of cellular and molecular immunology at the National Institute of Allergy and Infectious Diseases, described in an interview with the *New York Times* as having appeared "out of left field," came an answer to one of immunology's fundamental questions. "Then they took over leadership in the field," Schwartz added.

The implications of the pair's discovery are extremely broad. Already, their work has been vital in helping to avoid rejection in organ transplants. Further, Doherty and Zinkernagel have provided a strong foundation upon which scientists may be able to expand the knowledge and, one day, treat such diseases as rheumatoid arthritis and non-insulin-dependent diabetes, illnesses in which the body loses the ability to differentiate between self and nonself and the immune system attacks the body's own tissues. As T cells are one of the body's foremost defenses against HIV, there is much hope that the work of Doherty and Zinkernagel may lead to better treatments for AIDS. Additionally, their work is being applied to the development of new vaccines for a variety of illnesses. "Already it has led to successful vaccines for animals, and if one has such a vaccine for animals, then it must not be far away before you can do the same with humans," said Sten Grillner, chairman of the Nobel medicine committee.

After the conclusion of the pair's work at the John Curtin School of Medical Research, Doherty, the man who had once harbored aspirations of becoming a "country vet," now found that he was one of the world's premier immunologists. "It's not really what I expected to do with my life, but that's just the way it turns out," he said in a 1996 interview with Reuters.

In 1975 he left Australia to become an associate professor and later a professor at Philadelphia's Wistar Institute, where he remained until 1982. He then returned to Australia to head the experimental pathology department in the very place where he had conducted his research with Zinkernagel, the John Curtin School of Medical Research. In 1988 Doherty accepted a position as chairman of the Department of Immunology at St. Jude Children's Research Hospital in Memphis, Tennessee. Four years later he became an adjunct professor in both the pathology and pediatrics departments of the University of Tennessee's College of Medicine.

In 1996, more than 20 years after shedding new light on the responses of the body's immune system, Peter C. Doherty was awarded the Nobel Prize. He shared his award, along with the $1.12 million prize, with the codiscoverer of the body's two-pronged recognition of infected cells, Rolf Zinkernagel. The academy praised the pair for work that has "fundamentally changed our understanding of the development and normal function of the immune system." Fellow immunologists were very pleased with the announcement. "Most of us in the field felt this was an award that was coming, and it was only a question of when they would get it," said Dr. Philip Greenberg, an immunologist and cancer specialist at the University of Washington School of Medicine. "It's all very exciting and gratifying," Doherty said upon receiving the news of his award. "It's very satisfying to have had some responsibility for triggering an enormous area of research."

Doherty has been the recipient of numerous other awards, including the Paul Ehrlich Prize (1983), the Gairdner Foundation International Award (1986), and the Albert Lasker Medical Research Award (1995). Also, Doherty has been a fellow of the Australian Academy of Science (1983) and the Royal Society of London (1987).

SELECTED WORKS: Restriction of In Vitro T Cell–Mediated Cytotoxicity in Lymphocytic Choriomeningitis Within a Syngenic and Semiallogeneic System (with R. M. Zinkernagel), Nature 248, 1974; Immunological Surveillance Against Altered Self Components by Sensitized T Lymphocytes in Lymphocytic Choriomeningitis (with R. M. Zinkernagel), Nature 251, 1974; A Biological Role for the Major Histocompatibility Antigens (with R. M. Zinkernagel), Lancet, 1975; MHC Restricted Cytotoxic T Cells: Studies on the Biological Role of Polymorphic Major Transplantation Antigens Determining T Cell Restriction Specificity (with R. M. Zinkernagel), Advances in Immunology, 1979.

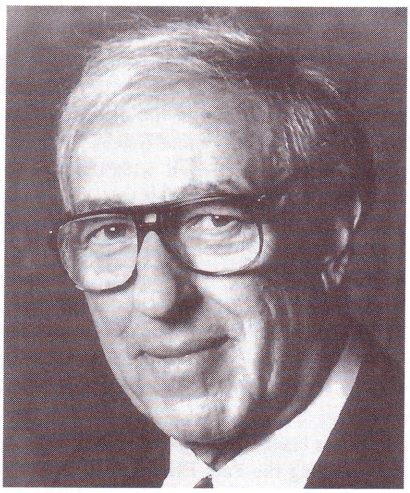
ABOUT: Los Angeles Times October 8, 1996; New York Times October 8, 1996; Newsday October 8, 1996; Reuters October 8, 1996; Royal Swedish Academy of Sciences 1996 Nobel Prize Announcement; Weekend Independent November 1996.

FISCHER, EDMOND H.

(April 6, 1920–)

Prize for Physiology or Medicine, 1992 (shared Nobel with Edwin G. Krebs)

The American biochemist Edmond Fischer was born in Shanghai, China, in 1920, the third son of Oscar and Renée (Tapernoux) Fischer. Fischer's father had come to Shanghai from Vienna, Austria, after studying law and business. His mother had come by way of Hanoi with her parents from France. His grandfather, a prominent figure in Shanghai, helped to established the first French newspaper in China, *Courrier de Chine*, and established the first school that



EDMOND H. FISCHER

Fischer attended. At the age of seven, Fischer, along with his two older brothers, Raoul and Georges, moved to Switzerland to attend the Swiss Federal Polytechnical Institute, in Zürich. He began his study of chemistry at the University of Geneva in 1939, and he was awarded his Ph.D. in 1947, after completing his doctoral thesis, entitled "Purification and Crystallization of Hog Pancreas ∝ Amylase." From 1948–1950 he was a fellow of the Swiss National Foundation, and from 1950–1953 he was a fellow of the Rockefeller Foundation.

Fischer came to the United States in 1953, first spending a year at the California Institute of Technology as a research associate in the division of biology. He then joined the faculty of the University of Washington in 1954. It was there that he met his research partner, the American physiologist EDWIN G. KREBS. In the autobiography Fischer wrote for *Les Prix Nobel*, he recollected his first days at the University of Washington: "Within six months of my arrival, Ed Krebs and I started to work together on glycogen phosphorylase. He had been a student of [CARL F. CORI and GERTY T. CORI] in St. Louis. They believed that AMP [adenosine monophosphate] had to serve some kind of cofactor function for that enzyme. In Geneva, on the other hand, we had purified potato phosphorylase, for which there was no AMP requirement. Even though essentially no information existed at that time on the evolutionary relationship of proteins, we knew that enzymes, whatever their origin, used the same coenzymes to catalyze identical reactions. It seemed unlikely, therefore, that muscle phosphorylase would require AMP as a cofactor but not potato phosphorylase. We decided to try to elucidate the role of this nucleotide in the phosphorylase reaction. Of course, we never found out what AMP was doing: that problem was solved 6–7 years later when Jacques Monod proposed his allosteric model for the regulation of enzymes. But what we stumbled on was another quite unexpected reaction: i.e. that muscle phosphorylase was regulated by phosphorylation-dephosphorylation. This is yet another example of what makes fundamental research so attractive: one knows where one takes off but one never knows where one will end up.

"These were very exciting years, when just about every experiment revealed something new and unexpected. At first we worked alone in a small, single laboratory with stone sinks. Experiments were planned the night before and carried out the next day. We worked so closely together that whenever one of us had to leave the laboratory in the middle of an experiment, the other would carry on without a word of explanation. Ed Krebs had a small group that continued his original work: determining the structure and function of DPNH-X, a derivative of NADH. I was still studying the ∝ amylases with Eric Stein. In collaboration with Bert Vallee, we were able to demonstrate that these enzymes were in reality calcium-containing metalloproteins."

In 1992, more than 40 years later, Fischer and Krebs were awarded the Nobel Prize for this work, which led to the accidental discovery of a basic process in human cells that regulates most of the biochemical processes of life. The process of reversible protein phosphorylation controls how chemical reactions within cells are turned on and off. It is now known to be a prominent player in most, if not all, normal cellular phenomena. It also may play a major role in the treatment of most diseases, including cancer and AIDS.

Fischer and Krebs began this work with a grant from the National Institutes of Health to study the problem of how adrenalin causes the breakdown of glycogen, giving muscles the energy to contract in the "fight or flight" response. They were concentrating on an enzyme called phosphorylase, which Fischer had previously worked with in plant studies at the University of Geneva. It was known that both active and inactive forms of the enzyme were present in muscle cells, but how the two forms differed was not understood.

Proteins have a defined three-dimensional structure that dictates molecular interactions. An enzyme's ability to act on other proteins depends on an elaborate "lock and key" mechanism by which the enzyme and the protein upon which it acts fit together perfectly; thus each has the ability to act only on specific molecules. Fischer and Krebs's research proved that a phosphate molecule attached to the inactive form of phosphorylase at a key location activated the enzyme. The removal of the phosphate group rendered the enzyme inactive. The scientists thus discovered that proteins could be regulated by having their structure modified in a reversible way.

The process by which a phosphate group is added to an enzyme is called phosphorylation. The enzymes that carry it out are called protein kinases. The reverse process, called dephosphorylation, is carried out by enzymes called phosphatases. The overall process is referred to as reversible protein phosphorylation.

"We stumbled on it," said Fischer. "We had no idea how widespread this reaction would be." The process turned out to be responsible for regulating a huge variety of metabolic processes, including the action of hormones in the body, muscle contraction, immune responses, cell growth and division, blood pressure, inflammatory reactions, and signals in the brain. The Nobel Academy's statement on the prize states that an estimated 1 percent of the genes in human DNA are devoted to blueprints for the production of phosphorylating enzymes. Fischer was modest on the subject of the prize. "So much superb work has been carried out by so many investigators . . . you wonder why we were selected," he said. "You can think of literally dozens of other people who would deserve it."

One of the most important applications for the study of phosphorylation is oncology. More than half of the cancer-causing cells are known to encode protein kinases. Some biologists have theorized that blocking phosphorylation in cancer cells could halt tumor growth. Continued study of the phosphorylation process in cancer cells may lead to the development of new and different types of anticancer drugs.

Some immunosuppressant drugs, such as cyclosporine, utilize the reverse process of dephosphorylation to block the activation of white blood cells that would attack transplanted organs. Researchers are currently working on a possible role for dephosphorylation in the fight against diabetes. Since the original discovery, further research has shown that many phosphorylation reactions are considerably more complicated than they first appeared. Some kinases phosphorylate other kinases, which in turn phosphorylate still other kinases, producing a biochemical cascade. A corresponding number of phosphatases work against the cascade, creating a regulatory mechanism that is more like a dimmer than a mere on/off switch. Each time enzymes act upon each other in sequence, their effect is amplified one millionfold to 20 millionfold. The cascade effect in hormone reactions, for instance, allows a tiny amount of hormone to exert an enormous influence and yet still be very closely regulated.

Initially, the discovery of reversible protein phosphorylation by Fischer and Krebs gathered little attention in the scientific community. It was not until the mid-1970s that the wide application of the process was appreciated and research in the area blossomed. A whole new field of research has been initiated concerning the signaling processes that control cellular events; a particularly large area in recent years is the role of kinases and phosphatases in growth control. Unofficial estimates have suggested that up to 10 percent of articles published in the field of biochemistry deal with this topic.

As of 1996, Fischer was a senior researcher and professor emeritus at the University of Washington, where he continued to carry out research in the field he helped to found almost 40 years earlier. Around the time he was awarded the Nobel Prize, his research involved studying the process of cell transformation in cancer.

Fischer has two sons, FranDcois and Henri, from his first wife, Nelly Gagnaux, who died in 1961. He married Beverley Bullock in 1963. Fischer also has two grandsons.

In addition to the Nobel Prize, Fischer has received numerous awards from various institutions including the Swiss Chemical Society, the Guggenheim Foundation, the University of Geneva, and the University of Washington. He is the recipient of honorary doctorates from both the University of Montpellier in France and Switzerland's University of Basel. Additionally, he is a member of the American Academy of Arts and Sciences, the National Academy of Sciences, and the Venice Academy of Sciences, Arts and Letters, and a foreign associate of the Spanish Royal Academy of Sciences.

ABOUT: Los Angeles Times October 13, 1992; New York Times October 13, 1992; Science October 23, 1992; Seattle Post-Intelligencer October 13, 1992; Wall Street Journal October 13, 1992; Washington Post October 13, 1992; Who's Who in America, 1992.

FOGEL, ROBERT W.

(July 1, 1926–)
Nobel Memorial Prize in Economic Sciences, 1993 (shared with Douglass C. North)

The American economist Robert William Fogel was born in New York City to Harry G. and Elizabeth Fogel, both Russian immigrants. He received his bachelor's degree from Cornell University in 1948. When he entered Columbia University in the 1950s to study statistics, as Sylvia Nasar reported in the *New York Times*, he had already established himself as being "both brilliant and something of a bomb thrower." "By the time he arrived at Columbia University," Nasar wrote, he "had spent several years as a Communist youth organizer."

He served as an instructor at Johns Hopkins University (where he received his Ph.D. in 1963) in 1958 and 1959 and as an assistant professor at the University of Rochester from 1960 to 1964. In the latter year he joined the faculty of the University of Chicago and remained there until 1975, when he became professor of economics and history at Harvard. In 1981 he returned to the University of Chicago, where he has remained since.

nent parts," decided to challenge it. Believing that nature rarely operates in such an orderly and compact manner, MARTIN RODBELL thought that Sutherland's model of cellular communication lacked a vital step. Through his research, he eventually concluded that after a receptor grabs the adrenaline or other chemical messenger, it changes shape. This shape change causes the molecule next to the receptor to change shape as well. This second molecule then acts as a transducer, a chemical messenger that is powered by the receptor and, in turn, stimulates another molecule. In the case of an unexpected scare, the molecule stimulated by the transducer then causes the liver to produce glucose. The existence of this transducer molecule was neither mentioned nor suspected in the Sutherland model. Unfortunately, few scientists took much notice of Rodbell's theory. He became the victim of a scientific community unwilling to accept a more complicated version of Sutherland's well-accepted theory. "I would go to meetings and people would say, 'Oh Marty, not again,'" Rodbell recalled in an interview with *Newsweek*. For Rodbell's theory to be accepted by the scientific community, he needed the one thing he could not find—solid proof of the existence of a transducer molecule.

In 1980, while working completely independently of Rodbell, Gilman discovered the much-needed proof. Gilman, who, ironically, had once been a student of Sutherland, was conducting experiments on leukemic cells with mutated genes. He found that cells with normal receptors that generated acceptable levels of cyclic adenosine monophosphate, or AMP, a messenger chemical found in all humans, did nothing when exposed to outside stimuli. Realizing that the mutated cells lacked a transducer, he tried injecting the cells with various proteins found in normal cells. Eventually, he found a protein that, when injected into the mutated cells, restores the normal transduction function. This protein, called the G protein because it binds with a nucleotide known as guanosine triphosphate (GTP), acts as a "biological traffic light" that processes a variety of external signals such as neurotransmitters, light, and smell and converts them into specific cellular responses, all in about four or five seconds.

Gilman's work with G proteins has led to numerous advances in the understanding of cellular signalizing in the human body. Each of the nearly 20 known varieties of G proteins is activated by certain receptors and, in turn, sets in motion specific responses. For example, a specific G protein in the eye reacts when the retina is exposed to light. The G protein then stimulates an enzyme, which, in turn, starts a flurry of activity that results in sight. Similarly, certain G proteins located in the nose and tongue activate enzymes that transmit the sensations of smell and taste to the brain.

Gilman's work with G proteins has also increased understanding of certain diseases. It is now known that an upset in the normal functioning of G proteins can be disastrous. Scientists have found in a variety of cancerous tumors G proteins that have mutated or have suddenly become overactive. The extreme loss of salt and water suffered by cholera victims is a direct result of a toxin secreted by the bacteria that attaches itself to a G protein and forces the protein to remain in an "on" position. This, in turn, prevents the intestines' normal absorption of salt and water, causing often-fatal dehydration and diarrhea. Further, some symptoms of diseases such as diabetes and alcoholism have their roots in a faulty transduction of signals through G proteins.

The increased understanding of the connection between certain diseases and G proteins has also opened up a new realm of possibilities for the treatments of these diseases. Currently, scientists are trying to dissect the complex wiring of cells and discover which receptors activate which G proteins. As there are more than 300 receptors that communicate with the nearly 20 known G proteins, the extremely time-consuming task of sorting them all out has been likened to untangling the wires of an old-fashioned telephone switchboard. Upon completion, however, the understanding of cells' inner wiring would enable scientists to develop drugs that are extremely efficient. "You'll be able to design a drug that works only on the molecule you want and no other molecule in the body," Gilman said in an interview with the *New York Times*. "It will happen. I just can't tell you when."

In 1994 Gilman, who had been working as a professor of pharmacology and chairman of the pharmacology department at the University of Texas Southwestern Medical Center since 1981, was awarded the Nobel Prize for Physiology or Medicine. He shared the award, along with the $930,000 prize, with Martin Rodbell. When asked about his reaction to the news that he had received the Nobel Prize, Gilman responded in terms appropriate to his research. "First, I activated my receptor, then my G protein," he said. "I was obviously extremely excited. I think I secreted all the adrenaline I had."

Gilman lives in Dallas with Kathryn (Hedlund) Gilman, his wife since 1963. They have three children.

In addition to the Nobel Prize, Gilman has received numerous other awards, including the Norwegian Pharmacology Society's Poul Edvard Poulsson Award (1982), the Albert Lasker Basic Medical Research Award (1989), the American Heart Association's Basic Scientific Research Prize (1990), and the Durham, North Carolina City of Medicine Award (1991). Also, Gilman is a member of organizations that include the American Society of Pharmacology and Experimental Therapeutics, the American Society of Biological Chemistry, the National Academy of Sciences, and the American Academy of Arts and Sciences.

ROBERT W. FOGEL

Fogel and DOUGLASS C. NORTH, with whom he shared the 1993 Nobel Prize, are credited with founding the science of cliometrics, which applies rigid statistical methodology to the study and interpretation of history. In 1964 Fogel published his groundbreaking work, *Railroads and American Growth: Essays in Econometric History*, in which he disputed the common notion that railroads were largely responsible for the growth of the American economy in the late 19th century. He began by examining the raw materials that were used to create railroads: iron, coal, machinery, and other commodities. By devising a mathematical model to account for the materials that went into railroad construction, Fogel showed that only 10 percent of American production involved the use of crude iron. Because American railroad manufacturing relied primarily on the recycling of scrap metals and on British imports, Fogel asserted, the impact of railroad-building on the economy was not as great as had been previously believed. Fogel also documented the importance of other means of transport, such as waterways, further downplaying railroads' economic importance.

Fogel's next major work, written with Stanley L. Engerman, was his most controversial: *Time on the Cross: The Economics of American Negro Slavery*, published in 1974. Written both for academics and for educated lay readers, *Time on the Cross* was read widely and touched off heated debates about the role of slavery in the American economy before the Civil War. By meticulously examining records of all sorts, from plantation medical documents to crop outputs to slave auction reports, Fogel challenged the accepted belief that slavery as a system was economically ruinous. Asserting that the antebellum North's free-labor system was less productive than that of the South's slave-based economy, Fogel presented, as Stephen D. Engle wrote in the *Historian*, "loads of statistics" to corroborate his thesis. Fogel wrote, "There is no evidence that economic forces alone would have soon brought slavery to an end without the necessity of a war or some other form of political intervention. Quite the contrary; as the Civil War approached, slavery as an economic system was never stronger and the trend was toward even further entrenchment." Fogel also dispelled the notion that slaves were lazy, unmotivated, and unproductive. Instead, he says, the average slave was "harder working and more efficient than his white counterpart." The final sentence of the work reads, "It's time to reveal, not only to blacks but to whites as well, that part of American history which has been kept from them—the record of black achievement under adversity."

"Seldom has the advent of a historical study been greeted with such publicity and ballyhoo," the critic Nathan Irvan Huggins declared in *Commonweal*. "Despite its argumentative style," Naomi Bliven wrote in the *New Yorker*, *Time on the Cross* "is continually interesting, even absorbing. And still more important for any contribution to historical understanding, it is productive of reflection." Still, some critics saw the work as a justification for slavery and assailed it as racist.

Continuing on the same theme, *Without Consent or Contract: The Rise and Fall of American Slavery* appeared in four volumes from 1989 to 1992. William N. Parker wrote in *Business History Review* about *Without Consent or Contract*, "As the tumult and shouting died, Fogel surveyed the flooded scene and placed a rainbow in the sky in the form of a final work." In the second volume, Fogel and coeditors Ralph A. Galantine and Richard L. Manning compiled 74 pieces by 18 scholars discussing their interpretations of slavery and the emancipation movement as well as the methodologies that led the scholars to their respective conclusions. This volume, Winifred B. Rothenberg wrote in *Reviews in American History*, is "a window on the state of the art of quantitative social science history." In the third and fourth installments, Fogel (with Engerman again as coeditor) included papers that revisited some of the controversial assertions of *Time on the Cross*, employing new data sets and new methods of historical demography to probe further into the institution of slavery, which is denounced in the volumes. Rothenberg wrote that Fogel's work contained "the finest statement of the moral problem of slavery that I have ever seen."

Fogel and Douglass C. North were credited by the Royal Swedish Academy of Sciences for "applying economic theory and quantitative methods" to historical questions and for their pioneering work in cliometrics.

According to Claudia Rosen, a Harvard University economic historian, "Fogel leans more in the direction of the empirical. . . . He tries to find a fact, prove it's a fact, and then prove it is a fact a hundred times over."

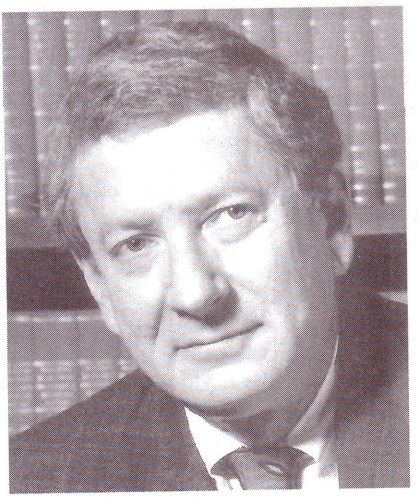
Fogel is currently investigating the phenomena of hunger and extended life spans in both America and Europe. He has found, for example, that France had a lower rate of food consumption during the French Revolution than India did more than 100 years later, and he asserts that large-scale starvation became a significant problem more recently than is generally believed.

As a winner of the Nobel Memorial Prize in Economic Sciences, Fogel became one of the 21 American winners in that category and one of the seven from the University of Chicago. He has been named a fellow by numerous groups, including the American Academy of Arts and Sciences, the Econometric Society, the American Association for the Advancement of Science, and the Royal Historical Society. Other awards and honors include many National Science Foundation grants, a Fulbright grant, and the Bancroft Prize in American History from Columbia University. He was the honorary vice-president of the Economic History Society of Glasgow in 1967 and president of the Economic History Association in 1977 and 1978. His other books include *The Union Pacific Enterprise*, published in 1960, and *The Dimensions of Quantitative Research in History*, published in 1972. He has also written numerous essays and articles for various publications. Fogel has lectured all over the world, and his works have been published in Italy, Spain, the United Kingdom, and Japan. He and his wife since 1949, the former Enid Morgan, have two sons, Steven Dennis and Michael Paul.

ABOUT: Business History Review Winter 1993; Contemporary Authors, 1979, 1984; Historian Winter 1994; NBER Reporter Fall 1993; New York Times October 13, 1993, November 7, 1993; Reviews in American History December 1993; Wall Street Journal October 13, 1993; Washington Post October 13, 1993.

GILMAN, ALFRED G.

(July 1, 1941–)
Nobel Prize for Physiology or Medicine, 1994 (shared with Martin Rodbell)



ALFRED G. GILMAN

The American pharmacologist Alfred Goodman Gilman was born in New Haven, Connecticut, the son of Alfred and Mabel (Schmidt) Gilman. Gilman's father was the founding head of pharmacology at New York's Albert Einstein School of Medicine and a member of a Yale Medical School research team that developed nitrogen mustard as a treatment for cancer. Gilman credits his father with igniting his interest in science and medicine by taking the then 10-year-old boy to visit his laboratory. The son's love of medicine would continue into his adulthood and eventually take him to the apex of the field.

Gilman was educated at Yale University, where he received his bachelor's degree in 1962. He then left the East Coast for Cleveland, Ohio, where he received both his M.D. and his Ph.D. in pharmacology from Case Western Reserve University in 1969. Upon graduation, Gilman accepted a position as a research associate at the National Institutes of Health in Bethesda, Maryland. In 1971, Gilman left the NIH to embark on a teaching career at the University of Virginia in Charlottesville, where he would eventually serve as director of the university's Medical Science Training Program. It was during his years at the University of Virginia that Gilman immersed himself in the work that would one day earn him the Nobel Prize, the study of how cells within the human body receive and communicate outside stimuli.

In the early 1970s, much of what was known about the process of cellular signaling was based on work conducted by EARL W. SUTHERLAND JR. According to the Sutherland model, when a person is startled or suddenly frightened, the individual's body produces adrenaline that quickly arrives at the liver. Receptors, which are dotted across the liver's outside lining, were believed to capture the adrenaline and somehow convey the message of the adrenaline's presence to the enzyme inside the cell. Thus notified, the enzyme would signal the liver cell to release glucose, allowing the body to respond to the adrenaline surge.

Despite the wide acceptance of this theory, one man, sparked by a Sutherland lecture that encouraged researchers to "tear apart a cell and isolate its compo-

SELECTED WORKS: The Pharmacological Basis of Therapeutics (ed.), 1975, 1980, 1985, 1990; more than 150 articles in professional journals.

ABOUT: Boston Globe October 11, 1994; Newsweek October 24, 1994; New York Times October 11, 1994; Royal Swedish Academy of Sciences 1994 Nobel Prize Announcement; Science June 23, 1995; Science News October 15, 1994; Who's Who in America, 1997.

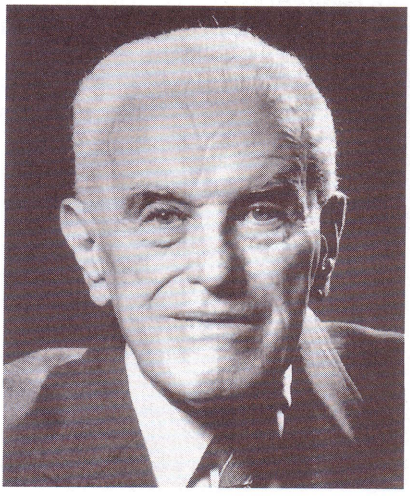
HARSANYI, JOHN C.

(May 20, 1920–)

Nobel Memorial Prize in Economic Sciences, 1994 (shared with John F. Nash and Reinhard Selten)

The Hungarian economist John Charles Harsanyi was born in Budapest, the only son of pharmacists Charles and Alice Harsanyi. His early life was spent comfortably in Hungary. He graduated in 1937 from the Lutheran Gymnasium, one of the best high schools in the country. While in high school, Harsanyi developed a fondness for mathematics, a subject that would become the basis for his life's work. In an autobiographical essay in the *American Economic Review*, he proudly recalled winning "the First Prize in Mathematics at the Hungary-wide annual competition for high school students." Though he preferred mathematics and philosophy, Harsanyi chose to study to be a pharmacist to please his parents—and also to gain a military deferment just as Europe was entering World War II. Being of Jewish origin, his family was particularly fearful of Adolf Hitler's murderous campaign, which was spreading from Germany throughout Europe. When the German army occupied Hungary in March 1944, Harsanyi lost his military deferment and had to serve in a labor unit. From November 1944 to January 1945, he was in hiding from the Nazis in a Jesuit monastery. These good priests, Harsanyi wrote, "probably saved my life."

After the war, he studied philosophy at the University of Budapest, and in 1947 he received his Ph.D. For the next year he was a faculty member at the University Institute of Sociology. It was there that he met his future wife, Anne Klauber, with whom he would have a son, Tom. In 1948 he had to resign from the Institute when it became commonly known that he strongly opposed Marxist doctrine, which had become the norm since Hungary had become a Communist state. Harsanyi and his wife decided to leave their native land, believing that this was the only way he could have an academic career. They traveled to Australia in 1950. There Harsanyi found that his degrees were not recognized by the Australian academic community, and that his English was too poor to enable him to teach. The couple struggled for three years as Harsanyi worked in factories. In the evenings he studied economics at Sydney University, where he received his



JOHN C. HARSANYI

M.A. in 1953. For the next two years he stayed in Australia, as lecturer in economics for the University of Queensland in Brisbane.

Harsanyi first became interested in game theory economics in the 1950s, describing it in his autobiographical essay as "a theory of strategic interaction . . . of rational behavior in social situations in which each player has to choose his moves on the basis of what he thinks the other players' counter moves are likely to be." Game theory analyzes the different interactions among economic players—whether they be individuals, corporations, banks, or governments—and accounts for the entire range of possible options. The ultimate goal of game theory economics is to help to understand why, according to *Business Week*, "existing economic and social arrangements are stable, and what the alternatives might be." In 1944 the mathematician John von Neumann and the economist Oskar Morgenstern put forth the first ideas on game-theoretic tools as applied to a varied group of economic systems. Though Harsanyi wrote several articles on the use of the von Neumann–Morgenstern utilities in welfare economics and in ethics, it was JOHN F. NASH'S work, published later, that piqued his interest. Harsanyi explained: "My interest in game-theoretic problems in a narrower sense was first aroused by John Nash's four brilliant papers . . . on cooperative and noncooperative games, on two-person bargaining games, [and] on mutually optimal threat strategies in such games." By 1950, John Nash had developed the formal mathematical principles of the game theory, but his work was limited by one major assumption—that each side would have perfect knowledge of rivals' motives and resources. Seeing this as a major flaw,

Harsanyi elaborated on Nash's original theory and set out to prove that "nothing need be known for certain so long as it is predictable in terms of chance." An example of this new aspect of game theory might be that if two rival companies were figuring out pricing strategies, each would need only to figure out the *probability* of the rival's responses and counter responses.

In 1956 Harsanyi received a Rockefeller Scholarship and also accepted a position as visiting assistant professor at Stanford University, in California, where he completed work on his Ph.D. in 1959. Harsanyi's dissertation supervisor was KENNETH ARROW, an economist who would have a great influence on his economic work. As Harsanyi wrote: "I benefited very much from discussing many finer points of economic theory with [Arrow]. But I also benefited substantially by following his advice to spend a sizable part of my Stanford time studying mathematics and statistics. These studies proved very useful in my later work in game theory."

Harsanyi spent several years in a research position in the Australian National University in Canberra. By 1961, however, he had returned to the United States, feeling quite isolated from his peers in the field: "At that time in Australia, there was not much interest in game theory." On the recommendation of his mentors, Arrow and JAMES TOBIN, he became a professor of economics at Wayne State University. Once back in the United States, he continued his work on game theory. In 1963, he published an article that "extended the Shapely value [a game with incomplete information] to games without transferrable utility" and also showed that his new theory "was a direct generalization both of the Shapely value and of Nash's bargaining solution with variable threats."

In 1964 Harsanyi became a professor of business administration at the University of California at Berkeley. Around the same time, the German economist REINHARD SELTEN helped the Nash model of game theory by suggesting that game outcomes could be either reasonable or unreasonable—and that one could mathematically distinguish between the two catagories. In 1967-68, Harsanyi published a three-part paper entitled "Games with Incomplete Information Played by 'Bayesian' Players." The paper outlined the way in which to convert a game with incomplete information into one with complete, but imperfect, information. He found that there is a mathematical technique for deciding when the outcome of an economic interaction is in equilibrium. This technique, though first ridiculed by the economic community, has in recent years become the standard tool in many areas of economic theory—from deciding the fluctuation of banks' interest rates to tracking the spending patterns of the largest corporations. By 1973 Harsanyi had proved that nearly every one of the "mixed-strategy Nash equilibria can be reinterpreted as pure-strategy equilibria of a suitably chosen game with randomly fluctuating payoff functions."

In 1976 Harsanyi gathered the numerous journal articles he had written over the years in the volume *Essays on Ethics, Social Behavior and Scientific Explanation.* The next year he published *Rational Behavior and Bargaining Equilibrium in Games and Social Situations,* which unified game theory by extending the use of bargaining models from cooperative games to noncooperative games. In 1982 he and Reinhard Selten brought their work together for the book *Papers in Game Theory.* In 1988 they coauthored *A General Theory of Equilibrium Selection in Games.* These latter two books are often used as the blueprint for game theory today.

In 1990 Harsanyi retired from the staff at Berkeley as professor emeritus. In 1993 and 1994 he wrote two papers in which he proposed a new theory on equilibrium selection. This theory is grounded in the thesis of his 1988 book with Selten, yet it is, according to Harsanyi, "a simpler theory and is in my view an intuitively more attractive one." In 1994 Harsanyi, Selten and Nash were jointly awarded the Nobel Memorial Prize in Economic Sciences for their work through the years in game theory, and they shared the $930,000 award equally. In the October 1994 issue of *Science,* Robert Pool suggested that the work of Nash, Harsanyi, and Selten goes beyond economic theory into the realm of evolutionary biology: "Many of the ideas and mathematical techniques they pioneered are at the cutting edge in understanding competition within and among biological species." Reporting on the announcement of the 1994 Economics Nobel Prize, the *New York Times* quoted Barry Nalebluff of the School of Organization and Management at Yale: "Harsanyi gave shape to the fog in real-world games." The *American Economic Review* praised him in these terms: "In all his work, John Harsanyi exhibits a true scholar's care and temper. He probes deeply and incisively into problems that others see as hopeless muddles, and he pulls out brilliant structures that help us see through the muddle."

In addition to being the author of four books and of numerous journal articles dating back to the 1950s, Harsanyi has received many fellowships and awards, including a fellowship of the Center of Advanced Study in Behavioral Sciences in Stanford, California. He is also a fellow of the Econometrics Society and the American Academy of Arts and Sciences and a member of the American Economic Association.

SELECTED WORKS: Essays on Ethics, Social Behavior and Scientific Explanation, 1976; Rational Behavior and Bargaining Equilibrium in Games and Social Situations, 1977; Papers in Game Theory (with Reinhard Selten), 1982; A General Theory of Equilibrium Selection in Games (with Reinhard Selten), 1988.