

## RETROSPECTIVE

# Britton Chance (1913–2010)

P. Leslie Dutton

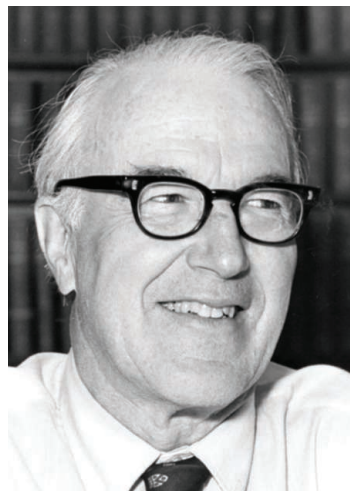
**B**ritton Chance was the Eldridge Reeves Johnson emeritus professor of biophysics, physical chemistry, and radiologic physics at the University of Pennsylvania. In a remarkable life, he was both a renowned biophysicist and a world-class yachtsman. Recognized for his pioneering research on how living organisms capture, manage, and produce cellular energy, he leaves a rich legacy of laboratory and clinical instrumentation and a wide range of discoveries and principles fundamental to biological catalysis and energetics, and biomedical application. Among his many honors was the National Medal of Science (1974). His parallel, lifelong love affair with sailing, mainly enjoyed in Barnegat Bay, New Jersey, culminated in his gold medal in the 1952 summer Olympics. Britton Chance pursued his research and sailing until his death on 16 November at age 97.

Chance graduated from the University of Pennsylvania with bachelor's and master's degrees in the 1930s, and a Ph.D. in physical chemistry and engineering in 1940. Apart from short periods at Cambridge University, England, where he earned a second Ph.D. in biology and physiology (1943), at the Massachusetts Institute of Technology (MIT) during World War II (1941 to 1945) where he worked on radar, and at Stockholm as a Guggenheim Fellow (1946 to 1948), his career was at Penn. He joined the Johnson Research Foundation in the School of Medicine in 1943 and became its director in 1949.

Chance's time at Penn from student to emeritus (1983) was marked by a succession of outstanding achievements, from novel instrumentation to biophysical research strategies. His capacity for innovation with mechanics, electronics, and optics was evident from an early age. During extended family sailing trips he became the qualified radio operator; at age 13, he built his first powerful radio transmitter and became a ham radio enthusiast. By age 17 he had built and patented an automatic ships-steering device incorporating a novel servomechanism. Interest in the device took him to England in 1938, and to Cambridge, where he extended his Ph.D. research in rapid flow/

mixing techniques. Under contract from the British General Electric Company, he installed his automatic steering device in a 20,000-ton refrigerator ship and sailed with it from England to Australia. Back in Cambridge and supervised by Glenn Millikan, he moved from chemistry to enzyme mechanisms. In 1940, at the beginning of World War II in Europe, he returned to the United States and was admitted to the Johnson Research Foundation at Penn. But as the United States entry into the war loomed, Chance's reputation for imaginative and effective use of electricity, electronics, and light prompted his recruitment to the Radiation Laboratory at MIT. Early success there in developing submicrosecond circuits for radar directing guns and bombing elevated him to group leader and then the Steering Committee of the "Rad Lab," and by the end of the war he was in charge of a research team of 300. In looking back on this period, Chance reflected that he was happy to have played a part in the war effort.

The ensuing three decades at Penn saw Chance's many discoveries in biological energetics. His 1930s miniaturized stopped-flow device demonstrated the long-predicted enzyme-substrate complex. In the 1950s, using the dual-wavelength spectrophotometer that he invented, Chance revealed many of the cellular redox cofactors of respiratory electron transfer that remain fundamental textbook knowledge. Moreover, in seminal work, he defined the energetic states and the reversibility of mitochondrial oxidative phosphorylation (state 3, state 4, etc.) that are essential descriptors for assessing health, damage, or disease in mitochondria. In the 1960s, using a ruby laser to activate photosynthetic bacteria at cryogenic temperatures, he discovered that biological electron transfer is governed by quantum-mechanical tunneling, a mechanism that underpins photosynthesis, respiration, and many of the most conspicuous oxidoreductase enzymes. In the



A pioneering scientist and gold medal Olympian had unflagging energy and broad interests that fueled his research.

1970s, he discovered that superoxide and peroxide are generated by respiratory complex III (cytochrome bc<sub>1</sub>) during normal energy-coupled respiratory electron transfer. Now recognized more widely and called reactive oxygen species, this phenomenon is the subject of intensive biomedical research on cellular regulation and in age-related diseases. In the late 1970s, Chance turned to pioneering magnetic resonance spectroscopy to track cellular energetics deep in

live tissue through phosphorous compounds of oxidative phosphorylation. Magnets of ever-increasing bore size saw his research scale from mice to men en route to the now widely used magnetic resonance imaging, but in the 1990s he returned to his forte of small, inexpensive electro-optical instruments designed to analyze living tissue.

In his mid-70s, Chance (then emeritus) launched a new field of optical diagnostics that rests on the physics of light diffusion through scattering materials such as living tissue. He showed that scattered near-infrared light pulses could not only measure the dynamics of oxy- and deoxyhemoglobin levels in performing muscles, but also reveal and locate tumors and cancerous tissue in muscles and breast as well as injury in the brain. Because changing patterns of oxy- and deoxyhemoglobin in the brain reflect cognitive activity, the applications of his diagnostic approach widened to include assessing neuronal connectivity in premature babies.

In recent times, Chance's research focused on the possibility of analyzing the energy status of cells in living tissue in terms of the energy and redox states of mitochondria that he had described over half a century ago. The "metabolometer" that he and colleagues in Taiwan developed is small enough to be inserted into body cavities to make such measurements. Although the application of this device must still be tested, such visions for biomedical optics ensure that his work will be remembered well into the future.

10.1126/science.1200976

CREDIT: BRUCE ROSENBLUM/COURTESY OF PENN MEDICINE

Department of Biochemistry and Biophysics, University of Pennsylvania, Philadelphia, PA 19104, USA. E-mail: dutton@mail.med.upenn.edu