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Retrospective: Britton Chance (1913 – 2010)

BY ANGELO AZZI AND NICOLE KRESGE

Molecular biologist Britton Chance, whose multifaceted research advanced the understanding of biology, instrumentation and medicine, passed away on Nov. 16. He was 97.

Britton Chance was born in Wilkes-Barre, Penn., in 1913. He spent many summers during his youth sailing, and his love of the sea was the catalyst for his first significant contribution to science and technology. When he was just a teenager, Chance invented an autosteering device that detected deviations in a ship's course and generated a feedback signal to redirect the ship's steering mechanisms. Later in life, his love of sailing and intense competitive spirit landed him a spot on the U.S. yacht Olympic team, where he won a gold medal in the 1952 Olympics.

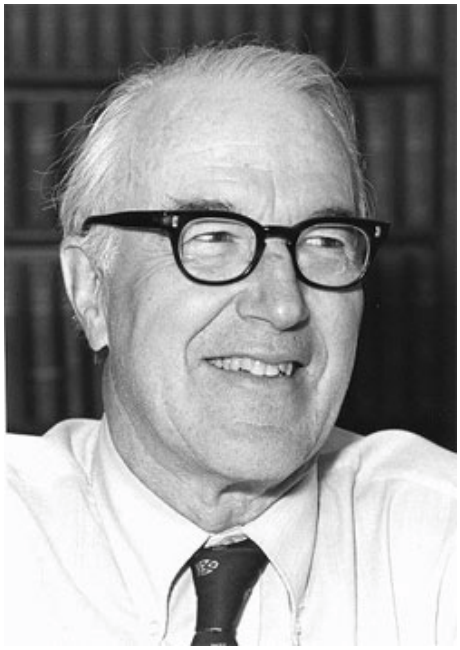

Image courtesy of the University of Pennsylvania Archives.

Chance received his bachelor's degree (1935) and his doctorate in physical chemistry (1941) from the University of Pennsylvania and his doctorate in physiology from Cambridge University (1943).

In 1938, while still a graduate student at the University of Pennsylvania, Chance started constructing a microflow apparatus. He completed the instrument by 1939 and did some initial studies on luciferase-O2 reactions. Several years later, using a new version of his rapid-flow instrument, he elucidated the peroxidase enzyme-substrate reactions, providing the first direct evidence of the correctness of the Michaelis-Menten theory.

During World War II, Chance was recruited to the Massachusetts Institute of Technology Radiation Laboratory to work on radar systems. His first project was developing radar for blimps searching for submarines off the U.S. coast. Later, he worked on radar-guided bombs.

After World War II, Chance went to Stockholm on a two-year Guggenheim Fellowship to work with Hugo Theorell. He and Theorell used another version of the stop-flow apparatus to study the kinetics of NAD in alcohol-aldehyde interconversion and found that product release was rate-determining. This is now called the Theorell-Chance mechanism.

Chance returned to the University of Pennsylvania after his fellowship was over and became a professor of biophysics and physical biochemistry and director of the Johnson Foundation. In the early 1950s, he shifted his focus to biological phenomena and studied the control of oxidative phosphorylation in mitochondria and revealed the role of ADP in respiratory control.

Britton Chance and wife Shoko in Phuket, 2008.

Chance, along with Henry Lardy and later Ron Williams, worked out methods to separate mitochondria from cells and preserve their metabolic activity in vitro and invented the dual wavelength spectrophotometer to analyze mitochondrial electron transport coupled to ATP synthesis. Spurred by this success, Chance later developed methods for using optical spectroscopy to study living tissues. In the late 1970s, he was the first to use magnetic resonance spectroscopy on a whole organ, the excised brain of a hedgehog.

After his retirement in 1983, Chance became director of the Institute for Biophysical and Biomedical Research, part of the University City Science Center, as well as president of the Medical Diagnostic Research Foundation in Philadelphia.

Chance's achievements gave him an international reputation as an encyclopedic scientist. As such, he received 10 honorary degrees, 70 national and international awards – including the National Medal of Science – and 30 memberships in the most exclusive academies, from the U.S. National Academy of Sciences to the Royal Swedish Academy.

When not in his laboratory, in his darkroom or in his workshop, Chance was sailing. One legend suggests that Chance beat out a young Ernest Hemingway in a race to catch a great blue marlin; the mounted marlin hung from the ceiling in Chance's Philadelphia home.

The following are reflections from Britton Chance's friends and colleagues. Please feel free to add your recollections in the comment section below.

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Chance had a remarkable breadth of interest and competence. At scientific meetings it could be expected that Chance would provide pertinent questions and comments.
– Paul Boyer, professor emeritus, University of California, Los Angeles

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About two months ago, Brit was putting the finishing touches on an article that he was writing. I asked where he was going to send it, and he replied, "to the RSI (Review of Scientific Instruments)." I said, "Didn't you send your 1939 paper there?" Brit thought for a second and said, "I guess that I did."

Two papers, the same sole author, 71 years apart! Brit was a true giant of biochemistry; a brilliant innovator who helped to develop the radar that, more than the atomic bomb, won the second world war; one of the electronic engineers that made ENIAC, on the one hand, and amplification of biological signals on the other, possible; one of the founders of biophotonics and

a wonderful, warm human being.
– Brian Salzberg, professor of physiology and neuroscience, The University of Pennsylvania School of Medicine

Britton Chance and Brian Salzberg at Surin Beach on the West Coast of Phuket.

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Without even knowing it, Britton Chance was my biochemistry hero. He attracted me to the field at the late 1960s when I was a medical student. From enzyme kinetics to radar systems, from mitochondrial energy metabolism to compasses, and from spectrometry to how to win in the Olympic games, he was clearly a renaissance man.

I came to know him only in recent years, and all I had imagined until we met was dwarfed when we met in life. We lectured together on several occasions in the Far East, and there was a lot to learn from this giant in his mid-90s. In his lectures, he simply described his history. This history began with his childhood as a son to a ship builder, which brought him to the world of automated navigation, and then in WWII he was part of the team that developed radar, and with it, radar-directed anti-aircraft guns. And biochemistry and the stop-flow technique he developed that helped him prove the Michaelis-Menten kinetic model were mixed into his story as well.

It was a suspension story, with many lessons to learn. He taught me that focusing is one kind of advantage, but a broad interest provides one with an even better advantage. He taught me that whatever one's background – physics, chemistry, biology, medicine or mathematics – one should never be deterred from conquering new terrains, and it is actually simple, as the principles are the same; one just has to realize it and apply them. Lastly, he understood what we all know but somehow most of us fail to apply – that a healthy soul can reside only in a healthy body. At 95 he asked me to join him biking around the campus of NCKU University in Tainan, Taiwan, but I knew I would trail behind and gave up. He promised to bike slowly. For me, meeting him was like walking through a textbook of basic biochemistry with one of the founding fathers of this wonderful discipline.
– Aaron Ciechanover, Technion distinguished university professor and laureate of the 2004 Nobel Prize in Chemistry

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Visiting the Johnson Foundation at Penn for the first time to give a seminar was simultaneously a frightening and exhilarating experience for a young postdoc. Dr. Chance sat at a table, where he was served lunch, while I spoke and wondered whether I was on the menu. His questions were tough and provocative because they got right to the core of the problem I was speaking about and for which I still was in the process of planning experiments. Several years later, during the first week when I came back to join the faculty at Penn, he asked me a question about that same work as though the seminar was still going on.

At Penn I inherited the Britton Chance dual wavelength spectrophotometer, the main component of which was labeled serial #1, from Dave Cooper. Dave and Ron Estabrook had used this instrument, with its built in oscilloscope to balance the beams and pulley operated prisms to change wavelength, to do their seminal work on adrenal cytochrome P450. That instrument was so valuable to me that I transported it to USC and then to UAB, where it was retired to the Alabama Museum of the Health Sciences.
– Henry Jay Forman, professor in the School of Natural Sciences, University of California, Merced

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I was acquainted with Britton Chance from the early 1960s since he was friends with Eraldo Antonini and had visited Rome more than once. However, for me the event that stands out is the two days (or better, the two nights) spent watching Brit in his darkroom at the JF while doing experiments with the low-temperature triple trapping method to detect intermediates in the reaction of cytochrome oxidase with oxygen.

Britton Chance and Eraldo Antonini (and son Giovanni) in Piazza Navona in Rome, around 1967-68.

It was very exciting indeed to stand behind Brit's shoulders, watching him fire the flash, look at the recorder and interpret the spectra of the intermediates, their buildup and decay. But equally exciting was to talk about sailing, as I dreamed at the time of buying a faster, more advanced yacht. Brit immediately suggested that since on my way back to Europe I was going through Cambridge to see Max Perutz, I should visit Mr. Richardson of the Elephant Boatyard at Old Bursledon, near Plymouth; the man was the builder of the quarter tonner Chance 24, designed by Britton Chance Jr. I went, saw Gretel II and fell in love; she was a very original and beautifully built sailboat, though quite spartan. In the spring of 1974 she was floating in the Mediterranean, and later Brit came twice for a sail near Rome. I deeply appreciated his suggestion. Brit has been my mentor for sailing, and I still have in my room an elegant picture of him at the helm of Complex II.

I never worked for Brit, though we discussed pulsed-oxidase quite frequently; we always got along very well, possibly because I never signed a scientific paper with him. Together, we only wrote the preface to a volume of the N.Y. Acad. Sci. (1988) containing the papers presented at a meeting organized by the two of us and held in Rome and in the Convent of Santa Teresa (Caprarola) where the structure-function relationships and the physiopathology of cytochrome oxidase were discussed in depth. The meeting was also an occasion to honour Brit, who had just been elected foreign member of the Accademia Nazionale dei Lincei, the oldest Academy in the world (it was founded in 1603). Since then, he frequently visited the Lincei Academy for meetings and talks. He was always excited by the latest experiments; he will be missed.
– Maurizio Brunori, biochemistry department, Sapienza University of Rome

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With the departure of Britton Chance the life of a protagonist of scientific research in the second half of the last century came to an end.

At the beginning of the seventies, I was one of the many young investigators from Europe spending research visits at Britton Chance's Johnson Foundation in Philadelphia. We were attracted by his fame due to the first spectrophotometric determination of the Michaelis-Menten enzyme-substrate complex and the characterization of the functional states of the respiratory chain by advanced rapid kinetics and spectrophotometric original approaches.

I was introduced by Brit to the excitement and commitment of the biochemical and biophysical study of cellular respiration. My introduction to the field by a vigorous man like Brit was an immediate, full immersion in the intensive research activity he carried out day and night at his laboratory.

I cannot forget the way in which I was received upon my arrivals at the Philadelphia airport after long overseas flights by Tom, a very kind character delegated by Brit to help his guests, including the preparation of fabulous sandwiches for the lunchtime seminars held regularly at JF. Tom met me with a wide smile, put me in a huge but rather old car and drove me directly to JF. There, I reached Brit in his open-door office – there were, in fact, no doors. There followed a detailed discussion about the experiments that I was going to start the same evening. It was around 5 p.m. local time, a little late in the evening for somebody arriving from Europe. I was then literally pushed into the huge darkroom, a

continuous extension of Brit's office. There, in full darkness, reinforced by my jet-lag, I was introduced to people fully busy carrying out their experiments in a jungle of double-triple wavelength spectrophotometers, laser-beam generators and stopped flow cells, all devices being continuously assembled and disassembled according to personal needs and wishes. In half an hour, I was facing the spectrophotometer assembled by Brit to run my experiments. One of these was the analysis of the impact of inorganic phosphate on the steady-state redox levels and rapid kinetics of respiratory chain carriers. In two to three days I was "helped" by Brit to run experiments in the darkness of the darkroom without any interruption for the whole week, discussing the results with him in real time, while he moved between the darkroom and his office, where he tape recorded what was discussed.

Those were really hectic, fantastic days whose excitement I could not find in my own or any other laboratory all over the world. On weekends, Brit used to transfer some of us on Saturdays by an open-air truck to his family house on the Atlantic Ocean shore in Mantoloking. There, we were accommodated in the guest rooms and, after a quick chat with Brit's family members, we were taken to the place where he had sailing boats. Brit was an expert in building boats, and a competitive sailing man. We were first asked to help him in repairing and painting one boat or another and then were taken out sailing all day, until late evening when the day closed with an open-air barbecue with giant steaks and plenty of beer.

After the time spent in the seventies visiting JF, I met Brit at conferences all over the world, where he was always giving remarkable lectures. On these occasions he embraced me with affection, something unexpected for a man who otherwise could have appeared rather cold, and gave me support and suggestions for my research and academic activities.

The sadness for his departure is alleviated by the thought that he had a successful, long life as a man and a scientist up until the last days when, I was told, he died serenely with his affectionate wife, Shoko, close to him.
– Sergio Papa, professor of biological chemistry, University of Bari

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Britton Chance was a scientist of Nobel class, a pioneer in many fields of research, full of curiosity and dedication and full also of follow-through. Those of us fortunate enough to have joined him for a few steps on his long journey of scientific endeavor will miss him dearly.

The world has lost a unique personality fruitful in many disciplines ranging from engineering to basic biochemistry and biophysics to medical electronics and diagnosis and therapy.

Brit, as he was called, radiated with energy and dedication, lighting up energies in those around him: His place, the Johnson Research Foundation at U-Penn in Philadelphia, was a bustling universe of young coworkers and visitors from all over the globe. I was fortunate first to meet Brit in 1969 when he visited the laboratory of my doctoral thesis mentor, Theodor Bücher, at Munich, Germany. From that moment, an enduring relationship developed, leading to numerous joint activities and visits across the Atlantic. Transatlantic phone calls were also standard, even during experiments. Once, during such a call, a brief intermission in the

Complex II
Trainig Sandhamn, June 1952
Britton Chance at helm

conversation led to a change of opinion: Brit had put the receiver to the side and had crawled under the bench in his jam-packed laboratory and inverted the polarity of the recording instrument so that there was instant clarification that the deflection indeed was up, not down!

In addition to joint original work carried out with Brit and Nozomu Oshino, with Alberto Boveris we wrote a review on our mutual interests that appeared in Physiological Reviews (1979). It is gratifying to see that this review has received attention, having been cited over 3,500 times, and it is the most-cited publication of Brit's more than 1,500 entries in PubMed.

Our lifelong friendship extended until the very last, and even in 2009 Brit and Shoko took me out for a sail off the New Jersey coast.

Brit has imprinted a whole generation of scientists and formed an international circle of friends, indebted to him forever.
– Helmut Sies, professor of biology and biochemistry, Heinrich-Heine-Universitat

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A less known aspect of Dr. Chance's life is that he was a very caring human being who was concerned about the welfare of women and minority scientists. He appointed the late Mildred Cohn to a tenured faculty position in his department at the University of Pennsylvania School of Medicine in early 1960, when she had been struggling to earn a faculty position for several decades because of well-entrenched gender discrimination in U.S. academia, despite her sustained, brilliant research accomplishments. Both Mildred and Brit were born in 1913 and passed away in succession in 2009 and 2010, respectively. We miss these two great Philadelphians.

Dr. Chance groomed his students and junior research associates to their full potential on the basis of scientific talent and capability regardless of their genders and national or racial origins. Dr. Chance was initially responsible for the founding of the American Association of Women (Bio-) Scientists and was involved actively in the society's activities and promotion in the 1970s. Even after the then-mandatory retirement from his faculty position, Dr. Chance was very active in scientific endeavors, education, and national and international science policies. During the summer months, it was customary to see his laboratories filled with enthusiastic high school students who were participating in science projects for minority high school students.
– Takashi Yonetani, professor of biochemistry and biophysics, University of Pennsylvania School of Medicine

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