Britton Chance: Former Olympian and Pioneer in Enzyme Kinetics and Functional Spectroscopy

BY NICK ZAGORSKI

In the heart of historic Philadelphia lies the headquarters of the American Philosophical Society (APS), a learned society that offers a testament to the incredible thinkers, past and present, who have helped shape the United States. Not too far away, on the campus of the University of Pennsylvania, one of the society’s members is busy at work, offering his own testament to longstanding scholarly excellence. For even at 95 years of age, there is no slowing down for Britton Chance, the Eldridge Reeves Johnson University professor emeritus of Biophysics, Physical Chemistry, and Radiologic Physics at Penn.

Born in nearby Wilkes-Barre, PA in 1913, Chance, occasionally referred to as the “father of modern biophysics,” has been making contributions to science, medicine, and engineering ever since producing his first practical invention as a teenager.

From his elucidation of enzyme-substrate compounds, to his insights into mitochondrial physiology, Chance helped bring forth a renaissance in biochemistry research, while his studies into photon migration through tissues and his advances in magnetic resonance spectroscopy have transformed the field of biomedical optics. His countless scientific honors include memberships in the APS, the National Academy of Sciences, and the Royal Society of London. He has also received the Pennsylvania Award for Excellence in Life Sciences, and the APS Benjamin Franklin Medal for Distinguished Achievement in the Sciences.

Yet just think, all of these scientific achievements may never have happened, if not for Chance’s love of a few of nature’s simple gifts: the sun, the sea, the wind, and a sail to catch it.

Sailing for the Stars

For Britton Chance, science and sailing have been intertwined for as long as he can remember, and he may not have achieved greatness in one area if not for the other. His love of the sea dates back to some of the earliest summers of his youth, when he went sailing and fishing with his family throughout the Caribbean and Latin America.

His enthusiasm for sailing grew rapidly, as did a competitive spirit to excel, and in the years since his early sailing adventures, Chance has challenged his sailing skills throughout the world, from the local waters outside Philadelphia to exotic locales such as Indonesia, Tahiti, and the Galapagos Islands. His talents even took him to the pinnacle of the sport; in 1952, Chance was part of the three-man...

Chance has been a pioneer in the field of biomedical optics, including studies combining near-infrared diffuse optical tomography (DOT) and magnetic resonance imaging (MRI) to identify tumors in breast tissue, like the ductal carcinoma above.

crew, along with Edgar and Sumner White, which won the Olympic gold medal in the 5.5-meter class sailing event at the Helsinki games.

That spirit continues to this day, and Chance, who considers life without sailing unendurable, is always just steps away—figuratively—from his boat, ready to set sail. (It’s an infectious spirit as well; Chance’s son, Britton Jr., has followed in his father’s wake. He has become a renowned ship designer and has been an integral part of many America’s Cup yachts.)

Long before his Olympic victory, however, Chance’s passion for sailing proved to be the catalyst for his first major contribution to science. At the tender age of 13, Chance, the son of an engineer, used his burgeoning mechanical skills to design and build an autosteering device that detected deviations in a ship’s course and generated a feedback signal to redirect and correct the ship’s steering—a simple yet elegant invention that would forever shape the course of Chance’s career.

**The Enzyme Enigma**

In 1931, Chance enrolled at Penn to study chemistry and engineering, and after receiving his B.S. in 1935, he stayed on to conduct graduate studies in enzyme kinetics. Enzymes were an elusive beast at this time—there were many theories about how they worked but no experimental data to back any of them up. Chance, who always enjoys a challenge, took on this enzyme mystery. As he points out, “I used elements of engineering, electronics, and mechanics to build my automatic feedback circuit, and studying enzyme kinetics required those exact same skills and more.”

Chance was intrigued with the theory put forth by Leonor Michaelis and his graduate student, Maud Menten, in 1913, which proposed that enzymes actually combined with their substrates to form an intermediate complex. “The trick,” says Chance, “was finding a method to observe this combination within an extremely rapid reaction.” Two separate events would lead him to the solution. First was his own observation that adding hydrogen peroxide to a crude extract of horseradish peroxidase could produce a colored compound; the second was reading about a stop-flow apparatus developed by Cambridge University researcher Glenn Millikan that could measure the rate of formation of oxymyoglobin.

Chance believed he could modify Millikan’s apparatus to study more rapid reactions by measuring colorimetric output; so, in 1937, he started building a “rapid-flow” apparatus, incorporating some features from his own photoelectric autosteering device. Not long after, the British General Electric Company offered Chance a contract to test out his autosteering on a ship sailing from London to New Zealand and Australia. Chance took this opportunity to introduce himself to Millikan and ask if he could study with him. Millikan agreed, and after Chance returned from his seafaring...
science focus continued

...these scientific achievements may never have happened, if not for Chance’s love of a few of nature’s simple gifts: the sun, the sea, the wind, and a sail to catch it.

adventure, he and Millikan constructed a second rapid-flow apparatus and tested it with preliminary studies on luciferase reactions.

In 1940, Chance returned home to visit his parents, but this temporary trip became permanent following the continued escalation of World War II. Unable to continue his work with Millikan, Chance resumed his studies at Penn and began building a third version of the rapid-flow apparatus. The design involved emptying two syringes, one filled with peroxide and a chemical reagent called leuco-malachite green (MG) and the other filled with peroxidase, into a narrow tube that flowed towards a photocell. Inside the cell, peroxidase would convert leuco-MG to malachite green, which could be measured with a spectrometer.

By varying the peroxide or leuco-MG concentrations, Chance could determine any changes in reaction rate or equilibrium and thus assay the kinetics of the reaction. “And, by comparing my results with Michaelis and Menten’s predicted results on a point by point basis, I was able to provide the proof to their theory,” he says. In 1950, Chance received the Paul Lewis Award in Enzyme Chemistry for these groundbreaking studies, the first of many scientific honors he would receive.

Helping the War Effort

While Chance’s development of the stop-flow method for measuring enzyme kinetics would usher in a new era of biochemistry, he hardly had time to celebrate. In 1941, with war continuing to rage and with U.S. involvement drawing ever nearer, Chance left Penn—and his newly appointed assistant professor position in the Department of Biophysics and Physical Biochemistry—to participate in secret government research at the MIT Radiation Laboratory. Here, Chance became part of an international team focused on improving nascent radar technology for defense efforts.

Chance recalls those eventful years at MIT: “I was working 80-hour weeks, trying to oversee a 300-person lab, with the Army, Navy, and Air Force constantly breathing down my neck.”

Still, the efforts were for a great cause, and they ultimately proved successful: Chance notes that over 5,000 planes in both the Pacific and European theaters employed the technology his lab helped develop, including the aircraft involved at the beaches of Normandy.

After the war concluded, Chance went to the Karolinska Institute in Stockholm to work alongside the renowned Hugo Theorell, one of the greatest contributors to our knowledge of oxidative enzymes like peroxidases.

Renewed Energy

Following his sailing success at the 1952 Olympics—“that was the one year where sailing took complete priority over science,” Chance notes, “but it also helped invigorate my research. Having conquered the waters, I was ready for an even bigger challenge, tackling the great unknowns of biochemistry.”—Chance decided to shift the focus of his enzyme studies to look at oxidative phosphorylation and electron transfer in mitochondria.

For someone with a lifelong interest in athletics and staying fit, the study of bioenergetics seemed a natural choice. Using his inventive mind yet again, Chance worked out a method to separate mitochondria from cells while preserving their metabolic activity and also designed a dual wavelength spectrophotometer (a machine still often used today) that could measure ATP synthesis in the isolated mitochondria. With these techniques, Chance carried out a long series of experiments that revealed previously unknown details about the nature of various electron transport coenzymes, the localization of respiratory chain components, the effects of altering oxygen concentra-
tion, and the role of molecules like calcium and manganese.

These studies also led to one of the most surprising moments of Chance’s career: the discovery of electron tunneling in biological systems. “This idea had never even been hypothesized, let alone tested,” he says. “Yet, we were studying photosynthesis in bacteria, and we observed electron transfer at liquid nitrogen temperatures, which meant the transfer couldn’t be a thermal process; it had to be physical. It really shook the hell out of me.”

**Medical Miracles**

In the 1970s, Chance began wondering if he could broaden his bioenergetic spectroscopy studies to look at whole tissues or even organs. His idea stemmed from a research group at Oxford who had found that phosphorous NMR (which measures the chemical shifts of the phosphorous isotope \(^{31}\)P) could track metabolites in living tissue. Chance then set out to improve the use of NMR technology in living systems, and soon his lab produced groundbreaking observations of active metabolism and cellular respiration in whole animal organs such as brain, heart, and liver, as well as in living leg muscle of a human subject. (In an interesting coincidence, Edward Purcell, who discovered NMR in 1946, also worked on radar development at the MIT Radiation Lab.)

Chance’s leg muscle subject also became the first human patient diagnosed with the aid of NMR technology. “That particular individual happened to have a genetic deficiency in phosphofructokinase, which prevents skeletal muscle from properly metabolizing carbohydrates,” says Chance, “and we were able to describe it and eventually remedy it. That patient has lived a happy and healthy life ever since.”

“Now, clinical studies have always been of interest to me,” says Chance, who was director of the Elridge Reeves Johnson Foundation at the Penn School of Medicine from 1949 to 1983, “but the success of treating that bioenergetic defect certainly spurred me on to look at other biomedical applications for optical spectroscopy.”

Over the years, Chance has done exactly that, first with NMR and later moving on to near infrared (NIR) spectroscopy. Through his group’s efforts, physicians now have access to non-invasive diagnostic equipment that can analyze cancer progression, brain oxygenation, internal bleeding,
and even changes in muscle activity during strenuous exercise. In recognition of these efforts, Chance was appointed president of the Medical Diagnostic Research Foundation (MDRF) in Philadelphia in 1995.

A Journey East

Britton Chance has observed, frequently firsthand, some of the great advances in scientific knowledge in the 20th century. So what does he think the next century holds in store in the areas of biophysics and spectroscopy? “I certainly think microelectronics, or more specifically, microoptics, will invade all parts of the body.”

Just recently, Chance himself, along with collaborator Ata Akin at Drexel University, invented a hand-held device—not much bigger than a cell phone—that can detect breast cancer by measuring the differences in blood oxygen ratios of normal breast tissue and angiogenesis-rich tumors. Considering the improvement over the bulky devices employed just a generation ago, one can understand how micro-sized devices may indeed be a part of our near future.

With scientists in Asia taking a prominent role in the field of microoptics, Chance has now added “diplomat” to his repertoire of titles that includes scientist, educator, inventor, and sailor. He has helped set up labs and collaborations in Taiwan (National Cheng Kung University in Tainan), China (the Britton Chance Center for Biophotonics in Hunan), and Singapore (Biopolis Biomedical Research Center) to advance these efforts and has just embarked on a several-month-long trip to these sites to share his expertise. (though officially an emeritus professor since 1983, Chance has remained very active in both his lab and at the University level.)

Out of Focus: Speaking of Medals

While the IUBMB Medal will be the newest addition to Chance’s long and deserved list of honors, it may surprise some to learn what Chance considers one of his favorite awards. “I think receiving the Gold Medal of the American Roentgen Ray Society [in 2006], which I received for my work on non-invasive breast cancer imaging, was the most pleasantly surprising,” he says. As to why recognition by the oldest radiological society (founded in 1900) in the U.S. is so noteworthy, Chance notes that “they’re a pretty closed shop, so being honored as a non-radiologist was exciting.”

Still Going Strong: Chance Wins 2009 IUBMB Medal

Les Dutton, a former Chance postdoc and his successor as director of Penn’s Johnson Foundation, notes that his former mentor “has an international view on life.” This view can be seen in Chance’s own endeavors in spreading and advancing science in China and Singapore, the geographically diverse scientists who have come to study with him over the years, and even the highly multidisciplinary nature of his studies. When taking all three measures into account, it is perhaps fitting that at the 21st International Union of Biochemistry and Molecular Biology (IUBMB)/12th Federation of Asian and Oceania Biochemists and Molecular Biologists (FAOBMB) Congress this August in Shanghai, Britton Chance will be presented with the IUBMB Medal (IUBMB President Angelo Azzi, who will present the medal, is a former Chance postdoc).

In honor of this event, the IUBMB Congress will feature a symposium in tribute to Chance’s legacy and accomplishments that will include noted speakers George Radda and Aaron Ciechanover, among others. Dutton stresses, however, “this symposium is not a retrospective; Brit does not like that term.” Rather, the Britton Chance symposium will encompass the themes of Chance’s many scientific discoveries—from myoglobin/hemoglobin oxygenation to optical diagnostics—in a contemporary framework, highlighting where Chance’s discoveries have led researchers today, and where they’re going in the future. Much like Britton Chance, this will be a forward-looking affair.

Of course, it’s not going to be all business. The waters of South Asia—Singapore, Malaysia, Indonesia—happen to be some of Chance’s favorites, so he’ll definitely find some time to take in a peaceful sunset sail and reflect upon his outstanding career.

Nick Zagorski is a science writer for ASBMB. He can be reached at nzagorski@asbmb.org.

REFERENCES


