



Biophysicist in Profile

Watt Webb

Professor of Applied Physics and the S.B. Eckert Professor in Engineering at Cornell University, Watt W. Webb approaches his 82nd birthday with few signs of decelerating. He and his wife did reluctantly stop yacht racing recently, but he's still determined to follow through with research projects that he thinks will make a positive impact on people's lives.

A late start to formal education due to illness did little to slow him down. At three years of age, Webb developed empyema, a pleural cavity inflammation. By the time he was well enough to start school, he was nine—but motivated. Not only did he make up for lost time, he entered MIT at age sixteen in Business and Engineering Administration since his father wanted him to run the family's "country bank," where he had worked through high school.

Webb's banking experience exempted many business courses. Instead, he focused on science, engineering and philosophy and joined MIT's successful sailing and rifle teams. He merged these interests and completed his BS in 1947. He then joined Union Carbide Corp to engineer the metallurgy of automatic submerged arc welding processes. "I learned more about engineering science there than at MIT," Webb admits. The most stimulating project was to measure the plasma temperature of the submerged arc: he applied his interest in astrophysics to measure the plasma temperature (~ 6500°K) by its atomic emission spectra, just as is applied for stars. This motivated graduate school!

After returning to MIT in 1952 for his ScD in metallurgy with minors in physics and

mathematics, Webb returned in 1955 to Union Carbide for fundamental research group, and later research administration. His research in solid-state and chemical physics stimulated his future interdisciplinary academic research at Cornell University as an Associate Professor of Engineering Physics in 1961.

"I've changed my directions in science many times," Webb says. "Gliding from one challenge to another, they all seem to flow from each other. Each discovery raised another question. Frequently, being the only experimentalist with theorists all around was exciting!" Quantum superconductivity led to analysis of quantum fluctuations measurements as well as engineering and construction of the first stable superconducting magnet of the type still used for Magnetic Resonance Imaging (MRI).

New theoretical challenges—coupled with practical experience and opportunities for collaboration with other disciplines—ultimately led to a variety of discoveries and inventions. In 1969, Webb and Elliot Elson, now professor of biochemistry and molecular biophysics at Washington University, conceived Fluorescence Correlation Spectroscopy (FCS). Joined by Douglas Magde, now an experimental physical chemist at UC San Diego, they published their findings in 1972. The motivating challenge was exploring partition of the DNA double helix of Watson and Crick for its transcription. That focused Webb on biophysical dynamics and ultimately to imaging transcription processes in living cells with John Lis, professor of molecular biology and genetics at Cornell, and to the conception of Zero-Mode Waveguides for efficient DNA sequencing.

Webb is best known for co-creating, with Winfried Denk, Multiphoton Microscopy (MPM) in 1990. Denk is now a professor and researcher at the Max Planck Institute for Medical Research at the University of Heidelberg.

"How did we arrive at MPM?" Webb reflects, "All of the tools we needed for first experiments happened to exist." Computers and

scanning microscopy had become standard, and faculty colleague Frank Wise had built a colliding pulse mode-locked laser. With MPM, cellular DNA could be imaged with 3D resolution for long times, while conventional confocal imaging destroyed the cells in seconds.

Webb sees beneficial prospects for future medical applications of MPM. For example, by capitalizing on the body's natural fluorescence, MPM excitation can provide diagnostic images in living tissue *in situ* in real time without dyes. Resulting MPM images, comparable with pathologists' delayed fixed and stained biopsy images, can help surgeons recognize cancerous tissue while operating. The ability to observe bio-molecules *in vivo*—including observation of gene transduction—brings researchers much closer to solving the “impossible biological problems” that keep Webb from taking life at a more relaxed pace.

“Obviously, he has had a long and highly productive career,” observes Webb's collaborator Lis. “What may be less clear is the high level of energy and love of science that he brings to collaborations and his willingness to tackle both new technologies and new areas in biology as he helps open new vistas of research. He continues to be a treasure for Cornell and the broader scientific community.”

About a year ago, Webb parted with his beloved “Wavetrain,” the last of his sailboats of that name. Last summer he and his wife, Page, who has sailed and raced with him since they met, cruised in Alaska. Interesting, he acknowledges, yet not an exciting substitute for racing. They also enjoy bird watching, and Page is an avid painter.

The Webbs have three sons. Watt Webb III is senior director of portfolio management for The Bank of New York Mellon and father of grandson Watt IV—who is called Wiley. Bucknell Webb is a researcher for IBM, working on micro- and nano-electronics. His twin, Spahr Webb, is an oceanography research scientist at

Columbia University's Lamont Doherty Earth Observatory.

Watt Webb continues to have a sense of purpose: “There are still numerous challenges for biophysical science. We need to recognize the challenges whose resolutions maximize human benefits.” Collaborator Bradley Hyman, Professor of Neurology at Harvard University, said: “He has the unique ability to see the big picture at the same time he sorts out the details of the details. And he is fearless in terms of tackling difficult, even impossible, problems



(Above) Webb in the driver's seat of his boat. Yacht racing is one of his favorite hobbies.

(Right) Webb's “Wave-train,” one of the last of his sailboats bearing that name.



and relentless once he thinks he sees a way to tackle them.”

This motivation now focuses Webb on developing Medical Multiphoton Microscopic Endoscopy. He also watches the commercial development at Pacific Biosciences, Inc., of the “Zero-Mode Waveguide” based DNA sequencing that he and his students and collaborators developed for Genomic Sequencing, hoping to realize the “\$1,000 Genome” in a few years.