Watt W. Webb

Samuel B. Eckert Professor in Engineering; Professor of Applied Physics

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B.S. 1947, Sc.D. 1955 (Massachusetts Institute of Technology)

Watt W. Webb is a Professor of Applied Physics and the S.B. Eckert Professor in Engineering. He joined the Cornell faculty in 1961 as Associate Professor of Engineering Physics and was named Professor of Applied Physics in 1965 and S.B. Eckert Professor in Engineering in 1998. He served as the Director of Cornell's School of Applied and Engineering Physics from 1983 to 1988. He began his career at Union Carbide Research Laboratories as a Research Engineer in 1947-1952. After receiving his Ph.D. in 1955, he returned to Union Carbide in successive positions as a Research Scientist (1955-1959), Coordinator of Fundamental Research (1959-1960), and Assistant Director of Research (1960-1961). As a Cornell faculty member, he has supervised over 60 Ph.D. theses.

Webb's recent awards include the National Lectureship of the Biophysical Society (2002), Rank Prize in Opto-electronics (2000), the Jablonski Prize of the Biophysical Society (2000), the Michelson-Morley Award of Case-Western Reserve University (1999), and the Biological Physics Prize of the American Physical Society (1991). He is an elected Fellow of the American Physical Society, the Biophysical Society, the American Association for the Advancement of Science, and Founding Fellow of the American Institute of Biological and Medical Engineers. He is an elected member of the National Academy of Engineering, the National Academy of Science, and the American Academy of Arts and Science. He lectures broadly and is active as a consultant and advisor.

Research Group website.

Research Interests

The solution of seeming impossible experimental problems drives our creation of new experimental technologies, which during the past thirty years have focused primarily on observing the dynamics of the biomolecular processes of life. This challenge requires benign, effectively non-invasive methods that frequently push the physical limits of resolution in space, time and sensitivity. The first of them we invented is Fluorescence Correlation Spectroscopy to observe the dynamics of molecular binding of regulatory proteins to DNA. Most recently, we have extended these methods to observations of gene transduction *in vivo*.

Seeming Impossible Biological Problems

Several of these innovations: Multiphoton Microscopy (MPM), Fluorescence Correlation Spectroscopy (FCS), nanoscopic molecular tracking and most recently, nanostructured molecular dynamic probes are being applied to some of these seeming impossible biological problems. Over the years, about 35 of our publications have focused on the challenges of neuroscience, including: molecular mechanisms and physics of auditory transduction, the first successful single channel recording of reconstituted natural ion channels and on their structural fluctuations and mechano-sensitivity, signal delays along neural processes in neural networks, detection and imaging of serotonin and its secretion, imaging the development of the lesions of Alzheimer's Disease in transgenic mice, and recently successful optical imaging of the propagation of action potentials along in live neural networks.

Clinical Medicine

As our biophysical research has evolved, we have come closer to realizing direct applications of our techniques in clinical medicine. Thus, our current multiphoton imaging research focuses on *in vivo* imaging, particularly on disease states generated in transgenic animal models of human diseases and on development of potential medical tools such as Medical Multiphoton Microscopic-Endoscopy (M-MPM-E) for successful optical diagnostics, now demonstrated in urological cancer. This strategy now impinges on the realm of biomedical engineering.

Membrane Heterogeneity

Our early emphasis on optical measurement of molecular mobility in cell membranes led to the engineering of Fluorescence Photobleaching Recovery, also called FRAP and later to the first nanoscopic tracking of the individual cell surface receptor molecules in the complete population on living cells, which led eventually to evidence for the membrane heterogeneity now known as "membrane rafts" in the form of our discovery of anomalous subdiffusion and diversity of characteristics of tracking trajectories on the living cell surfaces. We have recently resumed research on the fundamentals of membrane heterogeneity, motivated by the chronic violations of the elementary paradigms of chemical physics in its current biological discussions. We have recently analyzed the behavior of

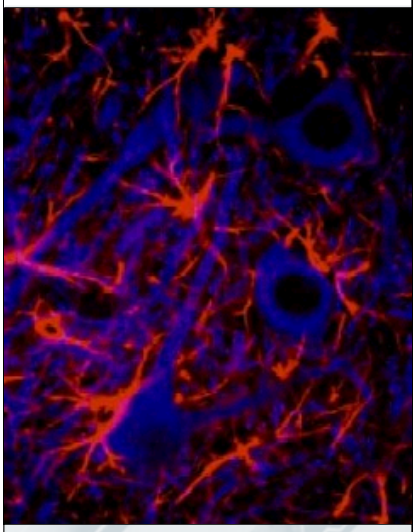
People

Developmental Resource for Biophysical Imaging Opto-Electronics

Biophysics

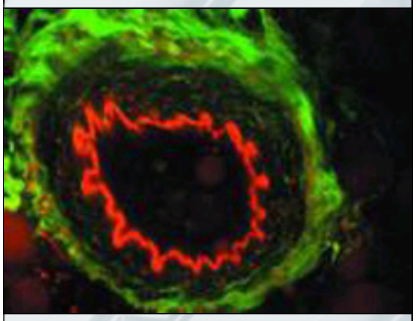
Nanoscience and Nanotechnology

Optical Physics, Quantum Electronics, and Photonics



Astrocytes (red cells) and neurons (blue cells) were labeled with specific antibodies in this fixed rat brain section. Because NADH, the coenzyme involved in brain metabolism, fluoresces differently in astrocytes and neurons in living brain tissue, biophysicists at Cornell could determine precisely when astrocytes were providing extra lactate "fuel" to neurons, confirming the controversial astrocyte-neuron lactate shuttle hypothesis.

(K. Kasischke, P. Fisher, Applied and Engineering Physics, DRBIO, Cornell University)



Cornell patented multi-photon excitation autofluorescence imaging of cardiac muscle tissue, studied for use in medical diagnostics.

(Webb Research Group, DRBIO, Applied and Engineering Physics, Cornell University)

large multiphase bilayer vesicles to measure the interphase energies (line tension) for the first time, detect the effects of the Gaussian curvature energy of membranes and discover the facilitation of vesicle budding by interphase tensions. This research also demonstrated the onset of critical fluctuations in these two-dimensional fluids as the temperature approached the line of critical points where the two phases merge and the energy cost of fluctuations and the interphase tension vanish. It is ironical that the three-dimensional analog of precisely this problem was first observed and studied in our laboratory nearly 40 years ago.

Enzyme Kinetics

We have also recently developed methods for detection and measurements of enzyme kinetics with single molecule sensitivity to measure enzyme kinetics fluctuations, individual particle detection sensitivity and molecular size scaling even to attomolar concentrations, and convenient small volume chemical kinetics with fast enough mixing for one microsecond time resolution (presently we reach about 30 microseconds).

Research Grants

- NIH-NIBIB, Development of Medical Multiphoton Microscopy Endoscopy
- NIH-NIA, Nascent Dynamic Intermediates in Amyloid Aggregation
- NSF, Regulatory Protein-DNA Interactions *in vivo* Analyzed by Ultrafast Photochemical Crosslinking

Selected Publications:

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Full Publication List

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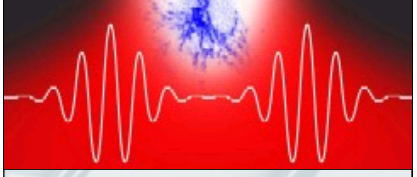

"Multiphoton Imaging the Molecular Dynamics of Living" The intrinsic fluorescence of NADH (nicotinamide adenine dinucleotide in its reduced form) in mitochondria is imaged by multiphoton microscopy to measure metabolic state of living systems. Here, a few living cells in a primary culture from the hippocampus of mouse brain are shown imaged by two-photon excitation at 737 nm with 100 fs pulse trains at 80 MHz. The NADH fluorescence (blue) primarily in the cellular mitochondria are presented in a schematic background illustrating the 0.5 µm diameter focal volume (white) of the focused (red) laser. The dynamics of the changes of metabolic state throughout living brain preparations during anoxia and recovery on re-oxygenation can be imaged by a time series of images of the organ to show the rapid oxygen depletion in active layers of the hippocampus and faster recovery in quiescent regions on re-oxygenation.

(Karl Kasischke, Sam Hess, Harsh Vishwasrao and Kevin Hodgson, Webb Group, Applied and Engineering Physics, DRBIO, Cornell University)