Statistical Ultrasonics: the Influence of Robert F. Wagner

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ABSTRACT

An important ongoing question for higher education is how to successfully mentor the next generation of scientists and engineers. It has been my privilege to have been mentored by one of the best, Dr Robert F. Wagner and his colleagues at the CDRH/FDA during the mid 1980s. Bob introduced many of us in medical ultrasonics to statistical imaging techniques. These ideas continue to broadly influence studies on adaptive aperture management (beamforming, speckle suppression, compounding), tissue characterization (texture features, Rayleigh/Rician statistics, scatterer size and number density estimators), and fundamental questions about how limitations of the human eye-brain system for extracting information from textured images can motivate image processing. He adapted the classical techniques of signal detection theory to coherent imaging systems that, for the first time in ultrasonics, related common engineering metrics for image quality to task-based clinical performance. This talk summarizes my wonderfully-exciting three years with Bob as I watched him explore topics in statistical image analysis that formed a rational basis for many of the signal processing techniques used in commercial systems today. It is a story of an exciting time in medical ultrasonics, and of how a sparkling personality guided and motivated the development of junior scientists who flocked around him in admiration and amazement.

Keywords: Memorial, mentoring, remembrance

1. INTRODUCTION

This year we gather to celebrate the life of Robert Wagner at his favorite annual scientific conference. He would be thrilled to see all the fuss made about him and grateful that so many felt a real connection to his scientific ideas and outgoing personality. At this year's conference, image scientists will recount Bob's scientific legacy and his warm engaging friendships, which were many, enduring, and far reaching.

This report recounts a few of my memories of working daily with Bob and his colleagues at the Center for Devices and Radiological Health (CDRH) in Rockville, MD during the beginning of my career 25 years ago. His style of mentoring helped complete my education and enabled me to achieve career goals similar to aspiring young scientists today. Today is a very different, perhaps more difficult time for professional scientists as well as the research institutions that employ them. The large startup packages commonly provided to launch science careers today are facing faltering world economies that are reducing corporate research expenditures and the values of private university endowments. Also widening deficits are forcing reductions in government support for state academic institutions and national labs. Young scientists, more than ever, are being pressured to win more extramural support to fund their research enterprise in addition to providing more time to support the base missions of their employer. The increased workload is not lost on students entering the workforce. I often ask promising students as they graduate to pursue industrial positions why they are not considering academic careers. They usually respond that professors all work too long and hard; that it seems difficult to be both successful and have a happy life independent of the lab. Considering that many of us simultaneously teach full time, direct a lab of 5-20 people, and serve on many committees, some as administrators, it is difficult to argue against that observation. How then can we recruit the next generation of professional scientists and academics from the best and brightest on which our country so desperately depends for its future? Outstanding mentoring is at least part of the answer. Inspired mentors leading by example must show the next generation how much fun and personal satisfaction is possible from all the hard work, and that they really can make a difference. I wish to share my experiences with Bob to describe one mentoring template that worked very well.

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2. EARLY MOTIVATION

In December 1983, I completed doctoral work in the Department of Medical Physics at the University of Wisconsin on the topic of bio-acoustic scattering. I wanted an academic career but had the delta-function knowledge bandwidth of the average recent PhD. I specifically felt a need for a broader view of image science, especially statistical methods, to be independently successful. Shopping for postdoctoral positions, I was seeking persons (not institutions) that could guide my continuing education. As an undergraduate student, I liked philosophy and physics classes but settled on science because because of weak writing skills. I formed an early dislike for probability and statistics, which I associated with combinatorics (just how many red balls are there in that darn urn?). Yet, to paraphrase Harry Barrett years ago at Lee Rosen's first NIH grant writing workshop here at SPIE Medical Imaging, the basic skills required of successful image scientists involve mathematics, statistics, computation, and strong communication skills. Here I was avoiding two of the four basic skills for success!

I looked for a mentor skilled in statistical analysis of imaging systems and whose writing spoke clearly and directly to me. By chance, I ran across a paper by Robert F. Wagner and David G. Brown[1] in the first volume of a new journal, IEEE Transactions on Medical Imaging. It offered the bold title "Overview of a unified SNR analysis of medical imaging systems," and its first sentence was "Once a physicist has studied the harmonic oscillator, it is hard to stop him from finding one under every bed." Hmmmm...these guys had promise.

The introduction to the TMI paper describes Bob and Dave's development of a "grand unified theory" of medical imaging, which appealed to the physicist in me. They proposed the self-deprecating yet stimulating title *Grand Unified ANalysis Of (GUANO) Medical Imaging* for their theory. It was published three years later in Physics in Medicine and Biology[2] with a modified title; the editors apparently did not appreciate the humor. Nevertheless, here was a group of scientists who thought big and were having fun.

Reading the paper further, I found the appealing idea that all medical imaging systems could be divided into a detection stage, where a system transforms properties of objects into data, and a display stage, where raw data is arranged for presentation to a decision maker.* They go on in the paper to define the importance of task-dependent evaluation of systems – that the system ideal for one clinical exam can perform poorly for others. They further suggest that the engineering measures of "image quality" that I just learned about in school – SNR, NEQ, DQE – could not by themselves determine the quality of an imaging system. They could, however, be related to objective task-dependent performance metrics obtained via signal detection theory, and that somehow human observer performance was related to all of this. The paper hinted that the foundation for these ideas begins with the information theory of Fisher and Cramer, and it was built upon by television pioneer Otto Schade from RCA and later Rodney Shaw from Xerox to ultimately point Bob and Dave to a definitive treatment applicable to all of imaging (hence the Grand Unified adjectives). I was blown away by the possibility that ideas from many fields could be assembled to achieve grand challenges. Here was a place to learn *imaging*. You also need to understand that all of the ideas listed above appeared on the first page of this TMI paper!

My campaign to find some way to work for Bob and Dave began.

3. CDRH IN THE 1980'S

I worked directly for Bob at the CDRH from July 1984 until July 1987; David Brown was division director and our boss. I started my adventure by reading about coherent and square-law detectors, circular Gaussian statistics, and laser speckle. We met many times each week to discuss what I was learning. Bob let me stay at his house for the first two weeks until I landed on my feet and, since Bob lived alone, I was able to talk about this stuff with him day and night. He didn't seem to mind and I was happily immersed.

From Bob's classic 1983 papers with his CDRH colleagues, John Sandrik, Hector Lopez, and Steve Smith,[3,4] I saw that the statistical properties of ultrasonic image speckle were determined entirely by the point spread function of the transducer (except for the spatially averaged intensity), provided that all of the scattering was from a "random medium" with "many scatterers." *Random* meant a Poisson distribution of point scatterers in

*Bob told me a story of his investigations early in his career at challenging claims by newly-minted CT manufacturers promoting "low dose reconstruction algorithms." He often used this story as an example of errors that occur when one confuses the two stages.

a volume; but the scatterer number density necessary to meet the fully-developed speckle condition was not easily defined. Goodman's work on laser speckle,[5] which was derived from the pioneering work of Middleton and Rice in communications, showed that at least 5-10 scatterers per pulse volume were required to ensure that the in-phase/quadrature phasor was described by a circular Gaussian probability density function (pdf). Fully-developed image speckle is obtained by taking the envelope of the demodulated analytic signal. The signal envelope follows a Rayleigh pdf (not to be confused with Rayleigh scattering). William Strutt (Lord Rayleigh) was first to derive the echo statistics named after him.[6] Because I had time to study, I went to the Library of Congress (a subway ride away from Rockville) and read the original papers associated with my work. I highly recommend that students and postdocs read the original papers of their field, many are now available electronically. You will find that the assumptions on which many analyses are based can be forgotten or "softened" over time and thus may affect your work in both subtle and profound ways.

Bob and Dave would often say that, in the world of coherently detected signals, we count scatterers 1, 2, 3, 4, 5, ∞. The consequences of a signal from 5 scatterers per pulse being statistically equivalent to a signal from 20 per pulse[†] meant that the inverse problem was not well posed, and the variance for estimates of scatterer number density N increased uncontrollably once $N >\sim 5$.[7] These details were poorly understood in the ultrasonic research community at the time, so imposing the appropriate bounds on the solution space was of great interest to those developing ultrasonic tissue characterization. I was learning that important insights are often buried in tiny details of the analysis and assumptions.

In my first project in the lab, we asked: What are the statistical properties of image data when the random scatterers in the body also contain periodic scatterers? Linda Fellingham and Graham Sommers[8] from Stanford found that the bandwidth of ultrasonic pulses was sensitive to the spacing of a narrow-band set of liver tissue scatterers, and that scatterer spacing was sensitive to disease processes. Bob led the group in the analysis of Rician statistics,[9] which described the echo data from a combination of random and diffuse specular (quasi-periodic) scatterers.[10] We hypothesized that hepatocytes and microvasculature served as random scatterers, and that a grouping of three vessels, the portal triads at the apexes of each 1 mm hepatic lobule, served as nearly-regularly-spaced (non-random, anyway) scatterers. Simulations showed that we could sense the average distance between 1-mm-spaced scatterers using statistical moments of the echo signal provided the variance of the structure periodicity was small. Bob called it *diffuse specular scattering* from *thermalized* quasi-periodic liver structures buried in weak random scatterers.[11] To test these ideas in patients, we teamed up with Brian Garra,[12] an army radiologist working in Building 10 at NIH and who had a Diasonics ultrasonic scanner that provided radio-frequency (RF) data. This instrument was a real rarity in the 1980's. Later, we worked with Murray Loew at George Washington University and his graduate student, Reza Momenan,[13] as we learned to select statistical features and combine them to maximize our ability to classify tissues based on microstructural features.[14] We were able to classify the sizes and spacings of tissues scatterers smaller than the resolution limit of the ultrasonic imaging system by analyzing statistical moments of the echo signals – a type of super-resolution method that worked as long as tissue regions provided weak-sense stationary random scattering from which the moments were estimated.

Our group then wondered if there were indeed regularly spaced scatterers, why couldn't radiologists see them directly from the B-mode images? In addressing this question, Bob introduced me to visual observer performance studies.[15,16] According to the conjectures of Bela Julesz from Bell Labs, the limitations of human observers at visual discrimination were directly related to the statistical order of the image texture. Perhaps classifying tissue structures placed in an acoustic speckle field was a high-order visual task inaccessible to humans. I learned directly from Bob Wagner and Bob Jennings about two-alternative forces choice (2AFC) experiments and how to measure human visual performance and efficiency via the ideal observer response. More fundamentally, I learned that the second stage of the imaging system, the display stage, could be a bottleneck in visual detection, and that removing this kind of bottleneck was the domain of image processing. Not only must the detector stage transfer information from the object to the raw data, but the display must be "impedance matched" to the eye-brain system of the observer if information in the data is to be transferred with high efficiency. Analogously, I

[†]It was shown independently by Victor Twerski, Kirk Shung, and others that once the volume fraction of scattering particle material exceeds 50%, waves are scattered from holes where there are no particles. So the statistical generalizations above break down and thus require careful interpretation for biological applications.

knew from ultrasonic imaging that flowing blood signals are present in tissue echoes but often cannot be reliably detected from B-mode images. Color-flow imaging uses signal processing to extract these sub-threshold signals and remap them into another form of signal that humans are very efficient at discriminating – bright colors. The generally idea of impedance matching information impressed me for its ability to help classify imaging problems into the two stages of imaging systems.

The CDRH was and is charged with the role of reviewing medical devices, including imaging systems, to be sure that they are safe and effective. As a public servant my job was to help discover principles determining safety and efficacy of medical imaging devices. Observer performance studies clarified for me the task-dependent nature of evaluations. I also saw that the role of Bob's group at the FDA was to be sure that others understood the principles his group was discovering because of the implication for public policy on commercial products and for funding agencies and companies making tough decision about where to invest scarce resources. I also learned something that later influenced my teaching style. It was absolutely essential that the mathematical studies undertaken be matched with a computational or laboratory experiment to truly understand the problem. Each of the engineering courses that I teach now combine analysis with computation, since it is clear to me that the two are complimentary learning devices.

The statistical framework we worked on was summarized in 1987[17] and quickly found many applications. At the time, there was great interest in spatial and frequency compounding, whereby the envelope signals from multiple looks at the same scatterers are combined to reduce speckle contrast. Bob worked with Steve Smith and Gregg Trahey from Duke University to expand the ideal observer formalism and include compounding.[19] Their analysis was able to predict quantitatively the potential gains in lesion detection via compounding, which is now used in commercial systems. Bob also described how echo signals of various flavors (RF, IQ, envelope) are correlated in space and time. His paper is still frequently cited because of its wide applicability to virtually any parametric analysis of variance using echo signals.[18] Bob also collaborated with Han Thijssen from Radboud University, Nijmegen Medical Center, to show that lesion SNR can be essentially unaffected by nonlinear amplitude compression despite large changes in the speckle SNR. The myriad applications of distinct SNR concepts was of great interest to Bob.

From our brief time together, we coauthored 14 peer-reviewed journal articles and many abstracts and proceedings papers. Through Bob, I first met many of the leaders in medical imaging research. Also he arranged it so I was able to participate in an NIH grant review session before I wrote my first grant application. Bob was invited to many places. During one European Union-sponsored conference in northern Italy, he paid to bring me along; it was my first trip to Europe. Having a wife, three kids, new mortgage, and student loans, there was no way I was going to travel without help. The trip was memorable. At the time, he suffered terribly from allergies and lower-back pain, but we visited amazing sites anyway and he remained in good humor throughout.

True story. As we boarded the plane back to the states exhausted from our tour of northern Italy, Bob noticed a passenger about to light a cigarette. The wisdom of the day on airplanes was that the last row of first-class passenger seating was a smoking row, as if magically there was an invisible shield keeping the smoke from bother others. Bob was very cautious about his environment, and quickly learned the phrase *non fumare* (no smoking) since it seemed everyone in Italy smoked on trains regardless of the person's age, posted signs, or wagging of a conductor's fingers. We were both really tired after 8 days of conference and touring, so Bob lost some of his usual animation that I came to expect when someone near him was smoking. As we walked to our coach seats, Bob calmly leaned over the person in that smoking row poised to light up and quietly said "If you light that cigarette, I'll throw up on you." The look on that gentlemen's face was priceless.

4. MOVING ON

At the end of three years I left the CDRH for an academic job, and yet those lessons of 20+ years ago have never been forgotten. Bob Wagner created a vibrant work environment at CDRH during the 1980s that shielded budding scientists lucky enough to work with him from bureaucratic activities while they immersed themselves in science, engineering, and applied statistics. Bob had the time to work directly with his charges on a daily basis. Only a few of us have had the joy of working closely for and with Bob, and I would venture to guess that all of us have been profoundly affected.

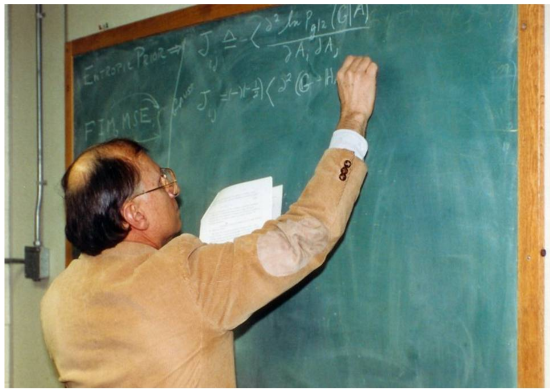

Figure 1. Bob Wagner at the chalkboard. From Ken Hanson's collection.

I was always struck by Bob's ability to intuit the fundamental nature of important scientific problems and their solutions long before solving problems mathematically. He was able to vividly describe essential aspects of problems to small groups in his office as well as large audiences at international conferences, often with the effect of recruiting his audience in the crusade toward discovering solutions. I always figured it was Bob's strong sense of the scientific literature that allowed him to frame difficult problems in their historical context. Even today, when I occasionally attend conferences outside of my field, I cannot help but hear how solutions to seemingly disjoint problems all seem to converge at some level. One of Bob's greatest talents was his ability to translate insights from one set of problems to another. I always felt there was another Grand Unified Theory just around the corner if only I was able to read and synthesize the ideas a little more. Such thoughts add greatly to the excitement of the pursuit, and make putting up with the nonsense of other parts of our job a little easier. This same spirit of team-oriented, interdisciplinary problem solving is a principal factor driving the evolution of engineering education today. It was fun working hard with Bob and with each other, which I try to remember and pass along to those I mentor.

REFERENCES

[1] R.F. Wagner, D.G. Brown, "Overview of a unified SNR analysis of medical imaging systems," *IEEE Trans Med Imaging*, 1:210-213, 1982.

[2] R.F. Wagner, D.G. Brown, "Unified SNR analysis of medical imaging systems," *Phys Med Biol*, 30:489-518, 1985.

[3] R.F. Wagner, S.W. Smith, J.M. Sandrik, H. Lopez,"Statistics of speckle in ultrasound B-scans," *IEEE Trans Son Ultrason*, SU-30:156-163, 1983.

[4] S.W. Smith, R.F. Wagner, J.M. Sandrik, H. Lopez,"Low-contrast detectability and contrast/detail analysis in medical ultrasound," *IEEE Trans Son Ultrason*, SU-30:164-173, 1983.

[5] J.W. Goodman, "Statistical properties of laser speckle patterns," in *Laser Speckle and Related Phenomena*, J.C. Dainty, ed., Berlin: Springer 1975, pp. 9-75.

[6] W. Strutt, "On the problem of random variations, and of random flights in one, two, or three dimensions," *Phil Mag*, XXXI:321-347, 1919.

[7] K.A. Wear, R.F. Wagner, D.G. Brown, M.F. Insana, "Statistical properties of estimates of signal-to-noise ratio and number of scatterers per resolution cell," *J Acoust Soc Am* 102:635-641, 1997.

[8] L.L. Fellingham, F.G. Sommers, "Ultrasonic characterization of tissue structure in the in vivo human liver and spleen," *IEEE Trans Son Ultrason*, SU-31,418-428, 1984.

[9] S.O. Rice, "Mathematical analysis of random noise," *Bell Syst Tech J*, 23:282-332, 1944; 24:46-156,1945.

[10] R.F. Wagner, M.F. Insana, D.G. Brown, "Unified approach to the detection and classificiation of speckle texture in diagnostic ultrasound," *Proc SPIE*, 556:146-152, 1985.

[11] M.F. Insana, R.F. Wagner, B.S. Garra, D.G. Brown, T.H. Shawker, "Analysis of ultrasound image texture via generalized Rician statistics," *Proc SPIE*, 556:153-159, 1985.

[12] B.S. Garra, M.F. Insana, T.H. Shawker, R.F. Wagner, M. Bradford, M.A. Russell, "Quantitative ultrasonic detection and classification for diffuse liver disease: comparison with human observer performance," *Invest Radiol* 24:196-203, 1989.

[13] R. Momenan, M.F. Insana, R.F. Wagner, B.S. Garra, M.H. Loew, "Application of cluster analysis and unsupervised learning to multivariate tissue characterization," *J Clin Eng*, 13:455-461, 1988.

[14] M.F. Insana, R.F. Wagner, B.S. Garra, R. Momenan, T.H. Shawker, "Pattern recognition methods for optimizing multivariant tissue signatures in diagnostic ultrasound," *Ultrason Imaging*, 8:165-180, 1986.

[15] R.F. Wagner, M.F. Insana, D.G. Brown, "Progress in signal and texture discrimination in medical imaging," *Proc SPIE*, 535:57-64, 1985.

[16] R.F. Wagner, M.F. Insana, D.G. Brown, B.S. Garra, R.J. Jennings, "Texture discrimination: radiologist, machine and man," In: *Vision: Coding and Efficiency*, C Blakemore, ed. Cambridge University Press, New York, pp. 310-318, 1990.

[17] R.F. Wagner, M.F. Insana, D.G. Brown, "Statistical properties of radiofrequency and envelope-detected signals with applications to medical ultrasound," *J Opt Soc Am A*, 4:910-922, 1987.

[18] R.F. Wagner, M.F. Insana, S.W. Smith, "Fundamental correlation lengths of coherent speckle in medical ultrasonic images," *IEEE Trans Ultrason Ferro Freq Control*, UFFC-35:34-44, 1988.

[19] S.W. Smith, G.E. Trahey, S.M. Hubbard, R.F. Wagner, "Properties of acoustical speckle in the presence of phase aberration. II. Correlation lengths, *Ultrason Imaging*, 10:29-51, 1988.

[20] J.M. Thijssen, B.J. Oosterveld, R.F. Wagner, "Gray level transforms and lesion detectability in echographic images," *Ultrason Imaging*, 10:171-195, 1988.