Paul Lauterbur

1929–2007

BIOGRAPHICAL *Memoirs*

A Biographical Memoir by
Joan Dawson

NATIONAL ACADEMY OF SCIENCES

PAUL **LAUTERBUR**

May 6, 1929–March 27, 2007

Elected to the NAS, 1985

Photograph by Corley Photography, Champaign, Illinois. Courtesy Joan Dawson

By Joan Dawson

Paul Lauterbur is best known for his invention, in 1971, of magnetic resonance imaging; its benefits can hardly be overstated. His other great achievements are better known within their specific fields, and may have as much impact, albeit indirect. For his earlier work Paul is sometimes called the "father of heteronuclear NMR," or the "father of 13C NMR," tools he used to show that molecular structure behaves in a regular predictable way, according to a few simple parameters. Late in life he produced a full, integrated, and testable theory of how the physics and chemistry of early Earth may have given rise to basic forms of life, the impact of which remains to be fully evaluated. Some have called the breadth of Paul Lauterbur's achievements heroic, others say almost wild.

The secret of Paul's science was "to look at problems up side down," or "to see the problem as its own solution." The secret to a satisfying personal life is no secret. Paul was engaging and personable, with an easy wit, unfailing intellect, and courageous temperament. He loved life, his family, colleagues, and students. His sense of integrity rivaled that of storied ancient Romans. He balanced on the edge of human knowledge and pursued it steadfastly. A handyman uniquely expressed a common sentiment: "He never made himself up big. He's small because he chose to be. He always stays on the playing field like the rest of us." And again: "He's got his own deck of cards and he plays it his way."

The Father of the Man

Paul was a dignified child, gentle, and a little shy. His interests never quite matched those of his playmates, and they all believed he was thinking about things beyond their ken. He read widely: natural history, anthropology, geology, history, biology, chemistry, physics, and more. In middle school a favorite activity was reading the Encyclopedia Britannica. He didn't read a great deal of fiction, but began his lifelong fantasia with science fiction. Although he could draw well, he wasn't much interested in art. Classical

music, especially opera, and poetry, were lifelong passions. His cousin says he became interested in science while still in his baby cot.

Paul studied the world around him—hunting, fishing, and exploring the farms, forests, lakes, and rivers of the gentle Miami Valley, near Dayton, Ohio. He collected specimens of this and that and caught small creatures to observe and let go. He ordered exotic animals by mail and kept them as pets. He taught himself taxidermy and produced awesome lifelike preservations. By middle school he was allowed a chemistry laboratory in the basement of his home, one with real chemicals that we now consider too dangerous for children. He proved the justice of our concerns by trying to make rocket fuel from what turned out to be components of strike-anywhere matches. The explosion sent him to the hospital. He carried glass shards to his grave, and with his parents' approval carried on his chemical experiments.

But while everyone admired and encouraged young Paul's intellectual pursuits, he was a poor student, getting A's in classes he liked and D's in some classes he didn't. His parents seriously considered that he should pursue the mechanical rather than the academic track while in high school. They were wary of his otherworldliness and thought he should be anchored in a saleable skill. His favorite high school teacher, John McDermott, did Paul the serious favor of dismissing him from all the normal chemistry study and allowing him to pursue college level work on his own. When, in his junior year, Paul came in first in chemistry in the statewide exams of Ohio, parental permission to attend college was assured.

College Daze to Army Daze

At Case Institute of Technology (now a part of Case Western Reserve University) in Cleveland, Ohio, Paul enrolled in the industrial chemistry program where he learned all forms of science (with the exception of biology) and engineering, including civil, electrical, mechanical, and chemical, and all of the related technologies, such as surveying, mechanical drawing, and endless labs of all kinds, for which he attested eternal gratitude. But with one small laboratory class short of a degree, Paul switched to chemistry, his marvelous mystery science. He was still an erratic student. Irvin Krieger, a professor at Case put it this way: "Lauterbur was a bright Case undergrad who refused to let his coursework get in the way of his education."[1] Over 50 years later Krieger could still explain the merits of Paul's audacious junior-year physical chemistry project. Paul entered Case as a bright young man and left it, as he felt, fully prepared to make his mark on the world.

Graduate school never entered Paul's mind. By his senior year, in 1951, Paul explained that he "had had it with classes and lectures and all of that formal learning." He was so very tired of sitting in classes and listening to professors that he could not imagine, and would have been horrified to know, that one day he would become a professor himself. He really didn't like professors; he didn't like to be subjugated to them, to be told what to learn and what to do. He was hired by Dow Corning, early leaders in silicone chemistry and products. Paul already had a strong knowledge of silicon, having worked with it in his home basement laboratory because he wanted to understand why carbon and not silicon is the basis of life. The interviewers may have been impressed with Paul's senior research project, in which he attempted to synthesize triphenylmethyl triphenylsilane. He failed (it was not accomplished for many more years) but redeemed himself by originality and audacity, as well as by a great deal of experimental effort and thought about what went wrong and what further experiments might usefully be done. He was sent to Dow Corning's research laboratories at the Mellon Institute in Pittsburgh, to be supervised by Earl Warrick, the inventor of silicone rubber, and more famously the inventor of Silly Putty. Paul's first research effort, and the subject of his first published paper, was to figure out how fillers, such as carbon black, increase the strength, stiffness, and hardness of natural rubber, and why silica does the same for silicone elastomers.[2]

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The environment at Mellon was more academic than corporate. There was an arrangement between the Mellon Institute and the University of Pittsburgh that fellows of the institute had both student and faculty privileges at the university. This meant access to the library, permission to attend seminars and lectures, use of the faculty lounges, and important for many, faculty football tickets. For Paul the valuable thing was that he could take classes at the University of Pittsburgh for free, and he did so. He thus became an accidental graduate student, accepted as the first in a joint program between the Physics and Chemistry departments at Pitt, having a mentor in physics and completing the chemistry Ph.D. program. Paul's Ph.D. adviser soon left, and the head of the Chemistry Department, Henry Frank, agreed to become the adviser of record. So, Paul advised himself, and led a double life straddling the worlds of industry and academia.

During the 1952-1953 academic year, Herb Gutowsky, sometimes called the "father of NMR in Chemistry" gave a seminar at the Mellon Institute. Herb was one of the originators of molecular studies by nuclear magnetic resonance (NMR) techniques, one of the handful of chemists who took up the field from its physicist founders in the late 1940s and early 1950s. Herb talked about his laboratory's efforts to measure NMR properties of methanes. Paul wanted to know more. "I was very interested in how molecules are put together, and it looked like a much clearer way of solving chemistry problems than anything else I had heard of at that time."[3] Paul, with an audacity startling to himself, suggested to Gutowsky a collaboration in which Paul would synthesize substituted silanes that were not available commercially, and on these Gutowsky's laboratory would do the spectroscopy. Lauterbur and Gutowsky would then try to work out the meaning of the comparative data of the silicon and carbon compounds. Gutowsky agreed, but nothing came of it, because Paul was soon drafted.

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Heteronuclear NMR

America was at war in Korea. An original misassignment to a tank battalion at Fort Knox was soon corrected to the Scientific and Professional Personnel program at the Army Chemical Center in Edgewood, Maryland. There Paul and fellow draftees worked to develop the first chemical weapons of mass destruction, the chemical warfare agents that could kill rapidly and effectively by acting on the nervous system. Before long, Paul learned from another soldier that a nearby laboratory would soon acquire a costly state-of-the-art NMR spectrometer, although no one in that unit knew anything about operating one. Paul was able to wangle a transfer to this unit on the strength of his knowledge of NMR ("I could actually pronounce 'nuclear magnetic resonance' so I became the base expert.")

Paul spent the next three years, installing the system and reading all of the 400 or so papers theretofore published on NMR, and then with other draftees carrying out a series of research projects, four of which were published in public journals. One might predict the direction of the next two decades of Paul's work by what he and his colleagues did while in the Army. Two of the four papers published in that period are studies using nuclei other than hydrogen; the others were an analysis of complex spin-spin coupling

patterns to distinguish among isomeric compounds and one of the earliest NMR studies of an isotopic exchange reaction.

The first of these papers was an early survey of ^{19}F NMR spectra of organofluorine compounds. Fluorine was of interest to the military, but there had been previous publications on ^{19}F NMR and the work was not a technical breakthrough. For Paul and his friends this was a warming-up exercise. The next was ^{31}P, which has very timid signals in comparison. The existence of ^{31}P chemical shifts, which were to become so important to chemists, biologists, and physicians, had only been discovered three years earlier. Herb Gutowsky, working with Charlie Slichter and then student David McCall, had just published the first studies using ^{31}P as a molecular probe.[4] It was thrilling work, and Paul naturally wanted to follow it up. He and his colleagues corrected some errors in this earlier work, and set forward a conceptual framework for interpreting the chemically important ^{31}P signals. But the really exciting stuff was launched when Paul was discharged from the Army, in 1955. He was 26 years old.

What to do now? Paul thought of joining Herb Gutowsky's laboratory at the University of Illinois to work with that great man on elucidation of molecular structure using NMR, but when Dow Corning offered to buy an NMR spectrometer for his own personal use, he easily decided to return to Pittsburgh. Paul promised his superiors at Dow Corning that he could obtain useful NMR spectra from silicon, the life-blood of the company, and at that time an almost unbelievable feat. He accomplished this on a trip to Varian Instruments in Palo Alto, California, during his acceptance tests for the new instrument. Back in Pittsburgh, while pondering his ^{29}Si results, Paul realized that he could also do ^{13}C. He compared the expected spectral characteristics of ^{13}C with his ^{29}Si data, and calculated that the difficulties in detecting one nucleus would be offset by the difficulties for the other. If ^{29}Si was a big deal at the time, ^{13}C was a really big deal. NMR spectroscopy of carbon was to have applications in all of organic chemistry, biochemistry, and now, over half a century later, increasingly in medical diagnosis. The oil and food industries have been particular beneficiaries. Carbon 13 (^{13}C) spectroscopy made Paul a star on the international scientific stage well before he received his Ph.D.

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Paul went on to publish 13 research papers on the use of ^{13}C NMR to study organic molecular structures. He studied over a hundred compounds using ^{13}C, showing smooth curves as he systematically changed substituent groups on core organic molecules. One interesting project, among the many that Paul never published, was a collaborative study with Howard Sminos, director of research at DuPont. This was the first study of compounds enriched with ^{13}C, in which the spectral peaks showed which atoms came from the enriched material. It was another 20 years and the advent of superconducting magnets and Fourier transform NMR before Paul's work was repeated and continued. The spectroscopists who took up ^{13}C NMR in the 1970s looked in amazement at what Paul had been able to do with his primitive equipment in the 1950s. The data that Paul had obtained were essentially the same as those obtained later with much more powerful technologies. Paul was gratified.

Still in his twenties and thirties, Paul continued a high level of productivity. He was teasing out molecular structure using NMR techniques, and developing new techniques for further teasing. He focused—although no one but himself has ever called Paul's broad interests "focus"—on at least three things at once: heteronuclear NMR, especially ^{13}C NMR; the theory of chemical shift; and experimental observation of chemical shift anisotropy, particularly in solids. A study that greatly satisfied Paul was determination of the sign of CH and HH coupling constants. In the early days of NMR in chemistry, spectroscopists did not know the signs of the coupling constants, and it was a big issue. "These went from being unknown to wrong," Paul said, as a result of a widely believed calculation by the respected theorist Martin Karplus. With Bob Kurland, Paul did definitive experiments showing that, in fact, the signs were not what everyone believed.[5] This, together with studies of the HH coupling constants by Cynthia Juan (later Jameson),[6] then a graduate student in Herb Gutowski's laboratory, was the ultimate solution to this longstanding problem in spectral analysis.

Paul did the first study of a single crystal, wolfinite.[7] The lead study was the closest that Paul ever came to being a physicist. He followed this with a study of single crystals of trichloroacetic acid.[8] Solid-state techniques had not yet been born, but in the early 1960s Paul was ingeniously testing theories of electronic structures in solid objects. As befits the father of heteronuclear NMR, in addition to his work on ^{29}Si and ^{13}C, Paul showed the feasibility of NMR studies of ^{119}Sn and ^{27}Al, as well as working on ^{59}Co and ^{207}PB. All of these works by Lauterbur were exciting advances, and the NMR community took notice. Paul was sought after as a speaker at conferences and various departments were interested in recruiting him. Paul became a member during the late 1950s of the subcommittee on

NMR for the American Society for Testing and Materials. He was later made chair. The task of the committee was to find standards for presentation of NMR data in order to avoid in the future the confusions that were already taking hold, because different laboratories were presenting their data in different ways.

While Paul's career as a basic scientist was blazing ahead, he was becoming frustrated with the limits put on his research by his work in industrial chemistry. No doubt his superiors were asking how his work was going to make them money. A dispute arose. Paul received an invitation from the distinguished Rex Richards to speak at a Faraday Society meeting in England. Graduate students are not ordinarily speakers at the Faraday Society meetings, and to Paul the honor was exceedingly exciting. The company said no, and in a war of wills insisted that if he took vacation time and paid his own way it would be an act of insubordination. It was time for Lauterbur to get his Ph.D., which he did in 1962, and leave Dow Corning. He had already sat as outside examiner for a Princeton Ph.D. thesis and had verbal job offers from universities that assumed he had this formal qualification.

Biological Aapplications

Paul settled on a position at the new State University of New York at Stony Brook (SUNY, now Stony Brook University) in 1963. Francis Bonner, founding head of chemistry at Stony Brook, was after simply the best young chemists available rather than following the more usual practice of trying to fill a particular niche within the study of chemistry. His philosophy produced an outstanding Chemistry Department within just a few years. Bonner recruited Paul at the level of associate professor, and Paul was given automatic tenure soon after, without ever having a postdoctoral appointment. At Stony Brook, Paul took part in the efforts to build a brand-new campus on what had recently been farming fields and to participate in building the new Chemistry Department. These early battles are now the stuff of legend.[9] Paul began his scientific work at Stony Brook doing things related to, but more complex, than those he had done at the Mellon Institute. Along with other efforts he carried out studies of unusual inorganic complexes, and described a unique approach to dynamic nuclear measurements.

A new area began to interest Paul. Since the late 1950s, serious proton NMR spectroscopy of proteins was carried out, but because of the low spectral dispersal of protons, information was difficult to obtain. Paul began a series of applications of ^{13}C NMR spectroscopy to peptides and proteins. With ^{13}C the problem is not one of dispersion, but of signal resolution, and Paul was exceptionally good at pulling NMR signals out of

the baseline noise. The computer revolution was just beginning, and Paul realized that computer-aided signal processing would add muscle to their analyses. Jerry Ackerman, then an undergraduate student, generated ^{13}C spectra of lysozyme. Using outdated equipment, Ackerman made hypothetical spectra, assuming different line widths and coupling constants for the constituent peptide signals, at different field strengths. The calculations were carried out for field strengths up to 7 tesla, a ridiculously high number at that time. The simulations aided interpretation of the experimental lysozyme spectra. During a sabbatical year in the laboratory of John Baldeschwieler at Stanford, Paul synthesized ^{13}C-labeled lysozyme, and obtained the first ^{13}C spectrum of a protein crystal. He also did preliminary biological studies using ^{3}H, well before others accomplished it. All of this work was elegant and useful, but Paul was looking for another big breakthrough equivalent to ^{13}C NMR.

Magnetic Resonance Imaging

While still at the Mellon Institute, Paul had become involved with a small company, NMR Specialties, that made spin decouplers before expanding to other products. With good funding for a startup company and a good board NMR Specialties appeared originally to be making a go of it, but by May 1971 it was clear that the company was bankrupt. Paul agreed to take over the position of chair, president, and chief executive officer (for a summer in which he had no university salary). He hadn't a clue about what he was getting into. Paul did his best to figure out what had gone on and to help steer the company to a soft landing. He said, "It was like trying to fly an airplane whose engines had stalled, a wing had come off and the fuselage was cracking up." It was for this that Paul was present on September 2, 1971, when Leon Saryan of Don Hollis's laboratory was attempting to confirm findings of Raymond Damadian concerning altered NMR relaxation times in cancer. These studies appeared promising, but Paul

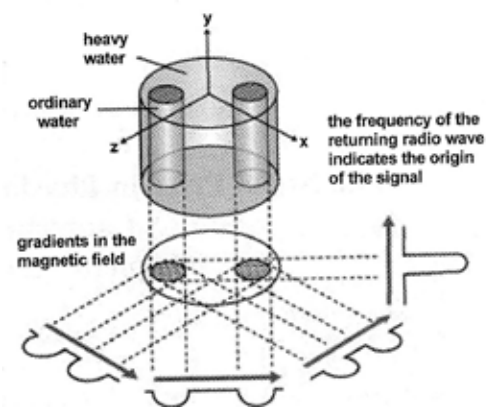

Diagram for the setup of Paul's first magnetic resonance image. (Courtesy Joan Dawson)

believed that they could not be of much use in medical diagnosis because they were done on excised tissue specimens; he did not believe that NMR relaxation measurements were likely to contribute much to the rich variety of information available from optical microscopy. What was needed was a way to locate spatially the NMR signal from within a complex object. It is now the stuff of legend that while at a Big Boy hamburger place that evening, Paul realized that deliberately imposed magnetic field gradients would make possible magnetic resonance imaging.

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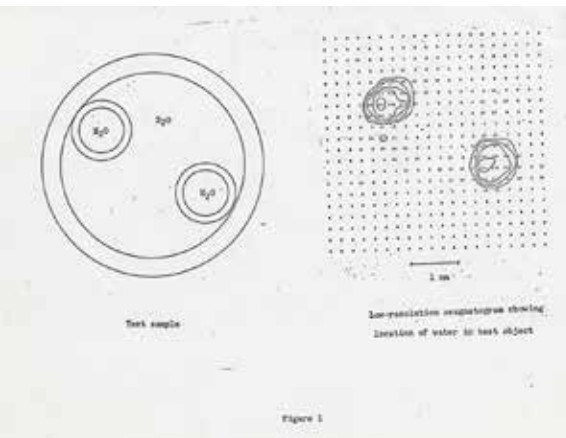
Paul's discovery of MRI is well known; he called it "zeugmatography" (Greek for "I excite") to emphasize that its physical foundation was unlike that of other imaging techniques. (It is the coupling of the static and variable magnetic fields that makes microscopy with energy of radio wavelength possible). Not so well known is the completeness of his vision at the time. When Paul received the Nobel Prize in 2003 for his invention of magnetic resonance imaging, the citation referred to his conception of two-dimensional images; in fact Paul's original notebook refers to imaging in three dimensions. He always thought that two-dimensional imaging was a stopgap until true three-dimensional imaging became practical. On that September night Paul envisioned contrast by density, relaxation times, and diffusion. He suggested spectroscopic imaging and isotope exchange imaging.

Lauterbur's first imaging paper,[10] published in *Nature* in 1973, is a proof of concept showing a two-dimensional image of two microtubes of H_2O in a background of D_2O. The paper was at first rejected, and when the editors did accept it, they deleted all mention of macroscopic (medical) studies by zeugmatography from the concluding sentence. In May 1973 Paul gave an astonishing talk at Argonne National Laboratory.[11] There he introduced zeugmatography and demonstrated that it could produce three-dimensional images and that isotopic exchange could be imaged zeugmatographically and that water diffusion could be imaged and measured. The physical example he used was the two-capillary setup shown in the *Nature* paper. The biological example was a parsley stem.

As exciting as all of this is in retrospect, the early years of zeugmatography were not easy; Paul's proofs of concept did not bring forth visions of modern MRI. There were objections that the physics could not be right ("It violates the Heisenberg uncertainty

principle!") and that there could never be significant applications because NMR signals are too small. Magnets could never be built large enough for human applications. Mathematical disentangling of signals from different regions was, at the least, a formidable problem. Some even confused the common practice of spinning a sample to even out inhomogeneity with a basic requirement of NMR ("But how do you spin the patient?") Even Paul's closest friends tended to think of zeugmatography as an interesting little niche that would have no important applications.



Lauterbur's first magnetic resonance image, drawn by hand. (courtesy Joan Dawson)

Paul's vision was quite different, and he pressed doggedly onward. He devised a back projection technique for processing images, only to discover that it already existed. He was both disappointed that he was not the first and encouraged that an important problem was already overcome. He and an increasing number of students progressed in the size and complexity of their imaging, starting with a tiny clam to fruits and vegetables, including oranges and pork chops that Paul ate for lunch. He diagnosed a tumor in a green pepper. Images of heart,[12] lung,[13] and cancers[14] (all by 1976) were meant to stimulate interest in the medical community, which they did.

At first the data were recorded on an oscilloscope and the images drawn by hand. They then used a Selectric typewriter, with the blackness of different letters providing contrast. Undergraduate Joe Frank photographed these images using panty hose as a filter to blur the sharp boundaries. Undergraduate Chuck Dulsey wrote primitive data processing codes. Graduate student Regenald Dias did the first electron spin resonance (ESR) imaging in 1974. Paul and his students proved feasibility of chemical shift imaging in 1975,[15] and published the first use of magnetic contrast agents in 1978.[16] Ed Heidelberger, another undergrad, demonstrated fluorine gas images of the lungs in 1982.[17] ("Ed didn't know it couldn't be done, so he did it.") Paul's ideas tended to simmer for a decade or two before catching on. It is now generally believed, and even written into authoritative reviews, that all of these practices started much later. The atmosphere in the

laboratory was almost giddy; the students knew they were on to something important. They called themselves "zuegies" and made tee shirts sporting a big Z.

Most of the advances in MRI of the next quarter century were initiated in that laboratory. Some people complained that there was nothing new you could do in MRI because Paul was always there first. Much was never published. Paul's early work on contrast agents deserves particular note; he was lecturing on this subject in 1976, showing examples. It is not well known that Paul did the first experiments using paramagnetic contrast agents and the first experiments using paramagnetic chelates. Paul had visions of inventing a set of *in vivo* magnetic stains like those used for optical microscopy; he discussed targeting agents, a field that became prominent many years later. As with imaging itself, Paul's enthusiasm for contrast agents was not immediately accepted. "Why," people asked, "introduce an invasive contrast agent to a technique that is importantly noninvasive?" There was also, rightly, concern about toxicity. Paul proved concept using toxic agents such as manganese ("And he calls that noninvasive!") because he knew from the beginning that safe agents could be devised. In a 1978 grant application Paul outlined the direction the field would follow for the next quarter century.

Paul's student Kyle Hedges produced a microscopic image of ~ 20 ul^3, not to be surpassed for about two decades.[19] (In-plane microscopy of the next decades was on slabs hundreds of micrometers thick). In the late 1970s, although not published for some years, Paul worked with Bob Marr of Brookhaven National Laboratories on using a priori information (such as a high-resolution proton image) to improve image resolution of a lower signal dataset, such as a spectral image of metabolites. They called the project SLIM (spectral localization by imaging, later renamed signal localization by imaging).[20] They were criticized vehemently because of a general misunderstanding of the underlying mathematical assumptions. It was also said to violate the second law of thermodynamics, the "you can't get something for nothing" law.

Move to the Cornfields

In a widely publicized move Paul left Stony Brook for the University of Illinois in 1985. His reasons for leaving Stony Brook were largely the great difficulty in moving his zeugmatographic studies into their natural home of medical diagnosis. Everyone could see that Paul needed strong collaboration with physician scientists for medical applications of NMR, and there was effort to facilitate such collaboration. But it was not to be; Paul's joint appointment in the Department of Radiology was a disaster, and he began looking

over the horizon at other universities. After negotiations with several institutions, Paul settled on the University of Illinois at Urbana-Champaign. He was particularly attracted to the lively research environment, the ease of collaboration, and the strengths in sciences and computing. He also found the large Medical Scholars program at UIUC enticing. Here he found serious students willing to endure the lengthy training required to obtain a quality Ph.D. at the same time that they completed their medical training.

Paul Lauterbur (courtesy Joan Dawson)

The appointment was accepted on April Fools' Day 1985. Things began to go wrong almost immediately. Due to administrative turnover, the collaboration between UIUC and neighboring Mercy Hospital, the basis of Paul's recruitment, became instead open warfare. New equipment waited on the loading docks of suppliers while a lengthy lawsuit was settled. Promised funding did not materialize. Paul tried to run a universitywide NMR laboratory on his private grants and was criticized for his lack of success. He succeeded in obtaining a National Science Foundation Center Grant for development and application of new MRI methods. The most expensive part of this project was to build a 4 tesla MRI system. The recognized NMR companies would not touch the problem at the time, and in a dreadful story the chosen builders (experts in magnetics of all kinds) botched the job. Paul became a pariah with former colleagues and the university administration. Life was made difficult for him in both petty and meaningful ways.

On the other hand, with new collaborators and students Paul was able to run projects of a much wider variety than he did previously. Many of these became the founding efforts for exciting medical technology and research that is being carried on today. Among his pursuits were NMR studies of flow, multidimensional imaging, isotope exchange, diffusion and diffusion tensor imaging, contrast enhancement, time-resolved MRI, simulated environment display (in 1995), surface coils, microscopy and ultramicroscopy, Web-based imaging (in 1996), electron spin resonance imaging, functional magnetic

resonance imaging, spectroscopic imaging, and the use of a priori information in MRI. In most of these areas Paul and his collaborators were the first to show proof of concept, while in others he showed an early understanding of the importance of new ideas originated elsewhere. All continue to be pursued.

Two areas of great effort are particularly promising today. One is imaging constraint by a priori information. Zhi Pei Liang collaborated with Paul to generalize and improve the early SLIM technique (GSLIM) for spectroscopic imaging, and to produce constrained methods for fast dynamic imaging, RIGR (reduced-encoding imaging with generalized-series reconstruction), and DIME (dynamic imaging by motion estimation). Research using these methods and their descendents, under a host of different acronyms, is making high-resolution real-time dynamic imaging possible today. The other effort was NMR microscopy at molecular resolution, which was thought impossible due to molecular diffusion between the interrogating and receiving pulse. Paul proposed to use the barriers to water diffusion to deduce, rather than image directly, the presence of obstructing macromolecules. Paul named the project DESIRE (diffusional enhancement of signal intensity and resolution) and thought it was the best idea he had had since MRI.

How Did the Physics and Chemistry of Early Earth Give Rise to Life?

Late in life, in his early seventies, and with his usual intellectual audacity, Paul changed his research field completely. "We cannot understand Biology," he wrote, "if we do not understand how it could have begun. We cannot truly know chemistry if we cannot imagine how it could give rise to biology."[21] He returned to study of the origins of life, the subject that had intrigued him over 60 years earlier, during his middle school years. It was, in fact, a continuing interest for which he had kept up with the ideas and literature all of his adult life. Nearly 12 feet of shelf space in his personal library were devoted to it. He came across an article on the use of molecular imprints in analytical chemistry. It occurred to him that such entities could have facilitated the evolution of reproducing molecular structures and that by developing this idea he could make a contribution to the science of life's origin. His first ideas on the subject were

"We cannot understand biology if we do not understand how it could have begun. We cannot truly know chemistry if we cannot imagine how it could give rise to biology."

published in 2005.[22] His final thoughts appeared posthumously in 2008.[23] Here he laid out an hypothesis of how the physics and chemistry of early Earth could lead by known and testable mechanisms to the first forms of cellular life. He was working on this paper just days before he died on March 27, 2007.

Personal

Paul is survived by Rosemary Lauterbur, his first wife, and Joan Dawson, his widow and author of this memoir. He has three children, Daniel Lauterbur, Sharyn Lauterbur DiGeronimo, and Mary Elise Lauterbur, and a sister, Margaret McDonough of Coshocton, Ohio. We are far from alone. All of Paul's students— graduate, undergraduate, and postdoctoral—were his intellectual children, the bedrock of his life.

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