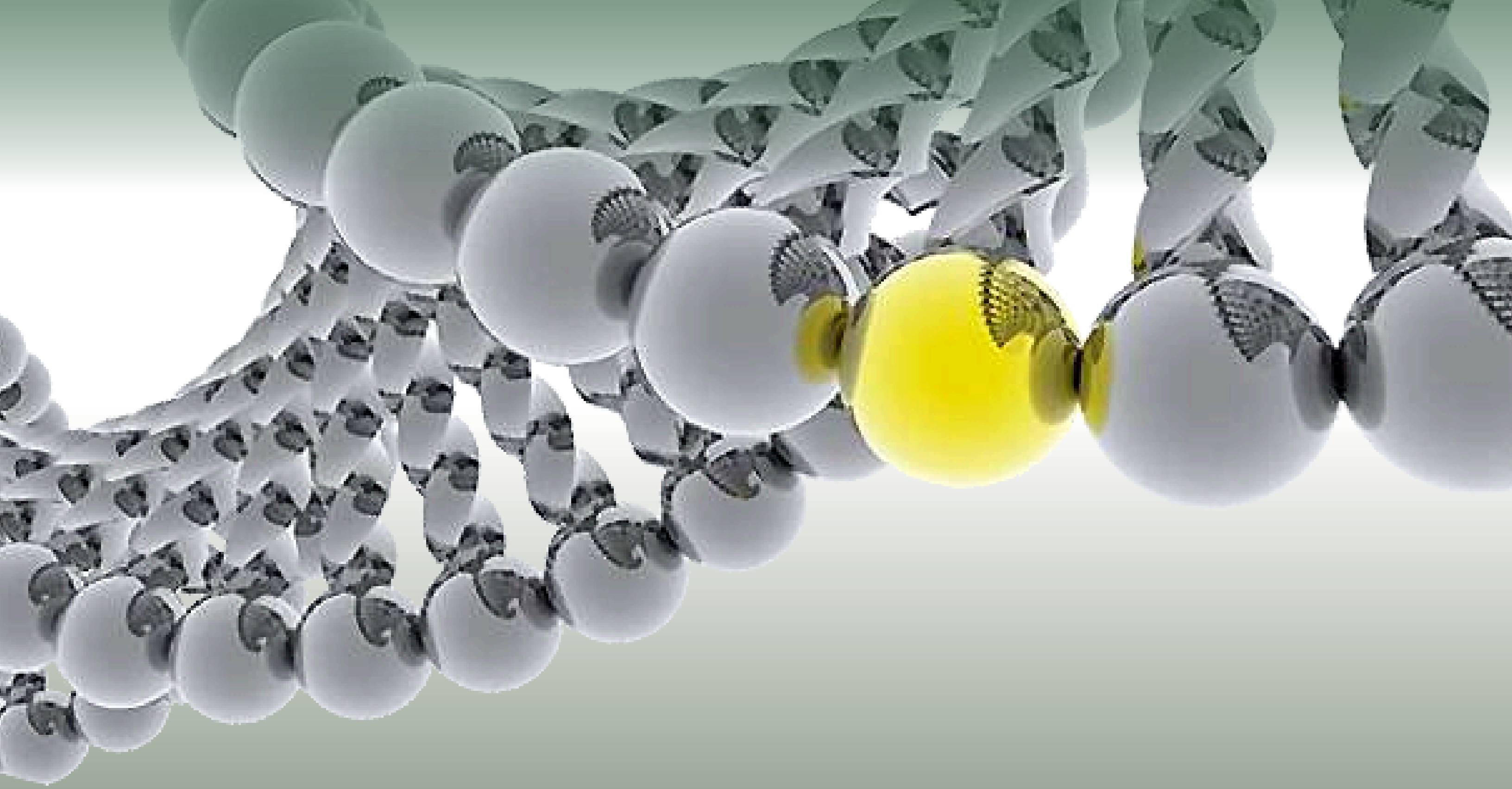
Vol. 11, Issue 1, January-April 2022

Print - ISSN : 2319-118X
Online - ISSN : 2319-1198



LS-An International Journal of LIFE Sciences

IndianJournals.com
A product of Diva Enterprises Pvt. Ltd.

Editor-in-Chief : Prof. Ashwani Kumar

Print ISSN: 2319-118X
Online ISSN: 2319-1198

LS – An International Journal of Life Sciences

Vol. 11, Issue 1, January-April 2022

Contents

LS - An International Journal of Life Sciences
DOI: 10.5958/2319-1198.2022.00001.X

IN MEMORIAM

Paul C. Lauterbur (1929–2007): Discoverer of MRI, Father of ^{13}C NMR and 2003 Nobel Laureate

M. Elise Lauterbur[1] and Govindjee Govindjee[2]***

[1]Department of Ecology and Evolutionary Biology, University of Arizona, Tucson, AZ 85721, USA
[2]Center of Biophysics and Quantitative Biology, Department of Biochemistry and Department of Plant Biology, University of Illinois at Urbana-Champaign, Urbana, IL 61801, USA
(*Corresponding author) email id: *gov@illinois.edu, **lauterbur@gmail.com

Received: 16-01-2022; Accepted: 05-04-2022

Paul's influence is felt around the world every day, every time an MRI saves the life of a daughter or a son, a mother or a father.

—Richard Herman, Chancellor, University of Illinois at Urbana-Champaign (2005–2009)

ABSTRACT

Do whatever really excites you in your life, and do it as best you can, and if you have enough luck, it will work out. — Paul Lauterbur

We provide here a brief personal tribute to Paul C. Lauterbur (6 May 1929 to 27 March 2007), who was the father of Carbon-13 Nuclear Magnetic Resonance (^{13}C NMR) and inventor of Magnetic Resonance Imaging (MRI). He was awarded the 2003 Nobel Prize in Physiology and Medicine with Peter Mansfield 'for their discoveries concerning magnetic resonance imaging'. He was engaging and personable, held himself to the utmost integrity, and believed in pressing doggedly one's ideas to the end. This tribute gives a glimpse of his life, his research and the person he was. Included are wonderful reminiscences by Chien Ho, Joseph Frank, Vikas Gulani, Daniel Lauterbur, M. Elise Lauterbur, Zhi-Pei Liang, Debora McCall and Bharati Pamidighantam.

Keywords: Magnetic resonance imaging, ^{13}C NMR, Nuclear magnetic resonance, Joan Dawson, Stony Brook University, University of Illinois at Urbana-Champaign

INTRODUCTION

Millions of people around the world have had their lives changed by Paul C. Lauterbur's work, and many of them feel a connection to him after they or a loved one has received a Magnetic Resonance Imaging (MRI, or as Paul called it, 'zeugmatography'). MRI allows non-invasive imaging of soft tissues, nerves and physiological processes and is widely used for medical diagnoses around the world. Figure 1 shows a photograph of Paul Lauterbur receiving the 2003 Nobel Prize in Physiology or Medicine from King Carl XVI Gustaf of Sweden for his invention of MRI, and Figure 2 shows Paul with the 'historical' magnet, called 'Big Red', now housed in a museum at the University of Illinois at Urbana-Champaign (UIUC).

We note that the scope of Paul's impact extends past MRI, which he called a '30-year detour'. His first major

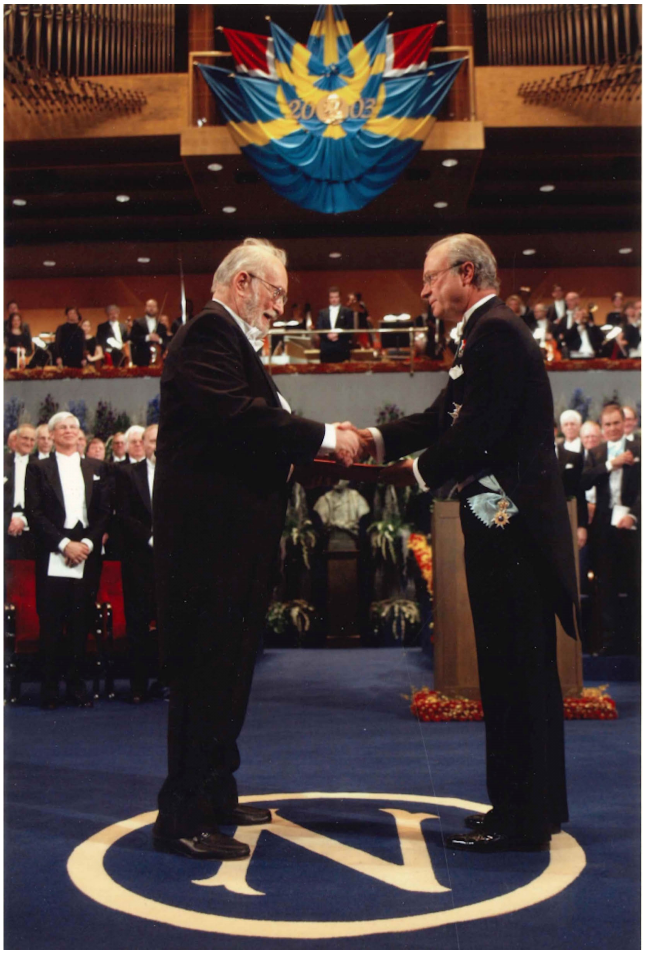


Figure 1: Presentation of the Nobel Prize in Physiology or Medicine to Paul Lauterbur (**left**) by King Carl XVI Gustaf of Sweden, 10 December 2003, Stockholm, Sweden.
Source: Official Nobel Photography

scientific breakthrough was the development of Carbon-13 Nuclear Magnetic Resonance (^{13}C NMR), which had previously been thought impractical and having few applications because of the scarcity of carbon-13 in the environment. In fact, ^{13}C NMR is necessary for characterising the structure of organic compounds and thus has applications in medicine, drug development and testing, and a great deal of research in organic chemistry and biochemistry. Towards the end of his life, Paul had turned his thoughts back to carbon and developed an experimentally testable hypothesis of the chemical origins of life.

It was the work on NMR in photosynthetic systems, in collaboration with Herbert S. Gutowsky (1919–2000; see Wydrzynski *et al.*, 1976; Baianu *et al.*, 1984; for Gutowsky, see Jonas and Slichter, 2006) that led one of us (Govindjee) to the feeling of connection with Paul Lauterbur. That connection grew when Paul moved to the University of Illinois at Urbana-Champaign (UIUC) in 1985, where Govindjee had already been working for 25 years; there, Paul's wife, Joan Dawson (1944–2017; see a website cited at 'In Memoriam') joined the Department of Physiology and Biophysics. At that time, Paul was the director of the Biomedical Magnetic Resonance Laboratory (BMRL) at UIUC. Paul's MRI images of fruits, vegetables and other plants (see, e.g. Borisjuk *et al.*, 2012; Van As and van Duynhoven, 2013) then and later intrigued Govindjee, and he was thrilled to attend the 2003 party at UIUC celebrating the award of the Nobel Prize and is pleased to share two of those photos here (Figures 3 and 4). More recently, Govindjee has had several MRIs and has become one of the many people connected to Paul through MRI's impact on his own health.

Figure 2: Paul Lauterbur and his first magnet at UIUC, 'Big Red'. **Top left and right**: Paul demonstrating the use of magnet in his MRI instrument. **Bottom**: Unboxed 'Big Red' in the new museum at the Beckman Institute, University of Illinois at Urbana-Champaign. <https://beckman.illinois.edu/visit/explore-beckman/illinois-mri-exhibit>

M Elise Lauterbur (co-author of this article) is Paul's younger daughter with his wife Joan Dawson. She was born shortly before Paul moved to UIUC and is currently an evolutionary biologist at the University of Arizona. Growing up, she spent a great deal of her time at the

Figure 3: A photograph taken at the celebration to honour Paul Lauterbur, 6 October 2003, at the Levis Faculty Center, University of Illinois at Urbana-Champaign (UIUC). Left to right: Yi-Gui Gao (of X-ray Spectroscopy Lab, Chemistry, UIUC; d. 2018); Amir Mirarefi (then from the lab of Charles (Chip) Zukoski, Chem. & Biochem. Eng.; now in R&D, Chicago); Paul Lauterbur (with glass in hand, celebrating his award; d. 2007); G. Govindjee (emeritus, Biochemistry, Biophysics and Plant Biology, UIUC); Nancy Cantor (then chancellor, UIUC; currently chancellor of Rutgers University–Newark); and Subramaniam Ramakrishnan (then from the lab of Chip Zukoski; now on the faculty at Florida State University). Information on this photo was provided by several colleagues at UIUC (see Acknowledgments). This photo was taken for UPI by Mark Cowan (who, unfortunately, died in 2014).
Source: Archives of the Govindjee family

Figure 4: Top: Paul Lauterbur (centre) celebrating with Chancellor Nancy Cantor (right) and Professor Gregory Girolami (left), then head of Chemistry at UIUC. **Bottom left**: In celebration with Antony (Tony) Crofts (Biophysics and Biochemistry, UIUC). **Bottom right**: Paul listening to Yi-Gui Gao (who died in 2018); behind Paul is Joan Dawson, and Gregory Girolami.
Source: Archives of the Govindjee family

BMRL, often doing homework in the conference room and drawing on the projector transparencies. Paul and Joan's students, postdocs and employees became her extended family. She is pleased to share this memorial in the hope that more people can get to know Paul and be inspired by his intellectual curiosity, perseverance, and kindness (also see below for her Reminiscence). Figure 5 shows a group photograph of the family gathered at the Nobel celebration.

Figure 5: Family get together at the 2003 Nobel celebration in Stockholm, Sweden. **Sitting**: Paul Lauterbur and wife, Joan Dawson; **standing, left to right**: Paul's older daughter, Sharyn Lauterbur-DiGeronimo; son Daniel (Dan) Lauterbur; Dan's former wife, Joanne Lauterbur; and Paul and Joan's daughter, Elise Lauterbur.
Source: Collection of Elise Lauterbur

Some of what follows are drawn from Joan Dawson's 2013 biography, *Paul Lauterbur and the Invention of MRI* (also see Dawson, 2012). In this memorial, we present a brief description of Paul's early life and education as well as a bit on his research and its significance, and share some photographs. We also include reminiscences from his family and former students and colleagues, and three appendices: Appendix 1, a list of some of the awards Paul received before the Nobel Prize; Appendix 2, a list of selected papers from his hundreds of publications; and Appendix 3, a list of selected URLs of articles published on Paul.

EARLY LIFE

The highest duty that ever comes to man is not to do a deed of prowess or win a material victory but to endure, suffer and die for truth and country.

—Edward J. Lauterbur, father of Paul C. Lauterbur

Paul C. Lauterbur was born on 6 May 1929, in Sidney, Ohio, to Edward Joseph Lauterbur and Gertrude Lauterbur, née Wagner. Edward Lauterbur was an engineer with a strong sense of duty and integrity, and he expected the same of his children. Gertrude was a homemaker who encouraged curiosity and compassion. Paul was the first of three children, with a younger brother Joe and a younger sister Margaret. Paul was a quiet, thoughtful and curious child; Joe, athletic and outgoing; and Margaret, gentle and caring. Tragically, Joe died at 16 years old. Paul and Margaret would remain close their entire lives.

Paul's lifelong goal was to understand how the world around him worked in varied and fascinating ways. Among his many explorations, including reading any book he could find, taxidermy and nursing injured snakes, he created a basement scientific laboratory during middle school. It was complete with volatile chemicals that would never be allowed in a children's science kit today. At that point, he knew just enough about chemistry to get himself into trouble. In an attempt to make model rocket fuel, he mixed red phosphorus and potassium chlorate, the former being combustible and the latter a strong oxidising agent. He knew that together these would be volatile because they were the main components of strike-anywhere match heads. What the 10- or 12-year-old Paul forgot to include in his equation was the friction of stirring these chemicals together. The friction ignited the phosphorus, and the resulting explosion landed him in the hospital for 2 weeks, permanently damaging his eyesight and leaving him with shards of the glass beaker in his hands that his young daughter Elise would ask about 50 years later!

At Sidney High School, Paul's chemistry teacher, Mr Harold McDermott, excused Paul and his two best friends from their regular chemistry class since they had already taught themselves all of the material. Instead, Mr McDermott gave them the run of the school's laboratory and later said of Paul that 'he would have spent all the time there if I let him'. This resulted in another experiment with phosphorus: he and his friends decided it would be great fun to make paper airplanes and dip the noses in white phosphorus and water, then throw them out the laboratory's second-story window. The water evaporated, the phosphorus ignited and flaming paper airplanes went spiralling to the ground outside. When Paul told this story, he would add the detail that Mr McDermott and a school administrator were walking outside at the time, and, unbeknownst to the boys, witnessed their small flock of flaming airplanes. Paul was always grateful to Mr McDermott for 'bending over backwards' to defend him and prevent expulsion. For his part, after he learned the news of Paul's Nobel Prize, Mr McDermott said 'I always knew he would do something like that'.

EDUCATION AND PRE-ACADEMIC CAREER

Lauterbur was a bright Case undergrad who refused to let his coursework get in the way of his education.

—Dr Irvin Krieger, Professor of Chemistry, Case Institute of Technology/Case Western Reserve University

Having been awarded the Case Institute of Technology's Prize Scholarship with the highest score (despite oversleeping and missing the first section of the exam), Paul took his father's advice and entered Case Institute as an engineering student. In his sophomore year, he tested out of the university's organic chemistry course and began taking graduate-level courses in chemistry. Over his father's protests, who saw no career potential for a pure chemist, he switched his major from engineering to chemistry. His junior- and senior-year projects became the sparks for the rest of his career. As a junior he devised experiments using Quinke's method to determine magnetic susceptibility in paramagnetic substances. His senior thesis, an attempt to synthesise a never-before-created carbon-silicon compound, triphenylmethyl–triphenylsilane, failed. Despite the project's failure, it was ambitious and well thought out enough to earn him his BS in chemistry in 1951 and attract the interest of the Dow Corning Corporation.

In 1951, the Dow Corning Corporation hired him to work as a researcher at the Mellon Institute in Pittsburgh, Pennsylvania. It was there that he published his first paper on silicone rubber with his mentor Earl Warrick (Warrick and Lauterbur 1955). This paper is a thorough analysis of the effects of different fillers and their properties on the stability of silicone rubber and presents filler phenomena in silicone rubber as of both technological and academic importance. Paul's first intellectual contact with Herbert (Herb) Gutowsky, mentioned above, who is called 'the father of NMR', was in 1952, during Gutowsky's lecture on NMR at the Mellon Institute. It was then that Paul thought that 'NMR is the way to find out how molecules are put together'. Paul asked Gutowsky many questions and even proposed collaborative experiments, but this possibility was interrupted by the Korean War.

Paul was drafted in 1953 into the US Army. He was initially posted to a tank battalion at Fort Knox, Kentucky, but his eyesight (poor in part because of the injuries from his childhood rocket fuel experiment) and his education made him a poor fit. He was transferred to the Army Chemical Center in Edgewood, Maryland, where he and his colleagues were assigned to develop chemical nerve agents, this time a poor fit for his moral sensibilities. At some point, he learned from another soldier that a different laboratory was using unspent budget money to purchase an NMR spectrometer, though no one there knew how to use it or what to do with it. On the strength of his junior-year project on magnetism at Case, his interaction with Herb Gutowsky, and some urgent reading of all of the available NMR literature, he managed a transfer. His NMR research during this time resulted in four papers about NMR spectra of various compounds: ^{19}F, ^{31}P and an NMR study of deuterium exchange between diborane and pentaborane (Muller *et al.,* 1956, 1957a, 1957b; Koski *et al.,* 1957).

After his discharge from the Army, Paul returned to the Mellon Institute for a fellowship that allowed him also to take classes towards his graduate degree in chemistry at the University of Pittsburgh. There, he innovated in the field of NMR research, publishing the first ^{13}Carbon NMR spectra in 1957 (Lauterbur, 1957) and following between 1958 and 1963 with an additional nine papers describing C^{13} spectra of various compounds (Lauterbur, 1958a, 1958b, 1961a, 1961b, 1963a, 1963b, 1963c, 1963d; Ettinger *et al.*, 1960; Tiers and Lauterbur ,1962), as well as elaborating on its potential uses in organic chemistry. These papers gained him the reputation as 'the father of ^{13}C NMR' before he earned his PhD. During this time, he also published further research on NMR of silicon and other compounds.

Carbon-12, the isotope of carbon that makes up 99% of carbon atoms in organic molecules, is 'invisible' to NMR because it does not have nuclear spin and therefore has no magnetic moment to be detected. The carbon-13 isotope, however, does have spin and magnetic moment, but these are much weaker than in a proton. As a result of its low abundance and weak magnetic moment, it is challenging to obtain signal from ^{13}C, and for this reason it was thought to be of little practical use for many years after the invention of NMR. Paul, however, was an organic chemist at heart, and saw its potential and spent many hours in the laboratory overcoming these challenges.

He published the first ^{13}C NMR spectra in an understated 1.5-page paper in which he reported the chemical shifts and spin–spin couplings of over 100 organic compounds (Lauterbur, 1957). In his subsequent series of papers, he showed that it is possible, despite additional complexities, to infer the structure of organic molecules using their NMR spectra. This set off a flurry of studies resulting in improvements of experimental methods and NMR instruments that would finally show the full importance of Paul's revolutionary ^{13}C work. ^{13}C NMR is now a fundamental part of research in complex biological systems, including molecular structure in both liquid and solid states, molecular interactions in complex biological systems, metabolism and clinical studies.

MRI AT STONY BROOK UNIVERSITY

Paul Lauterbur's work is perhaps the most significant medical diagnostic discovery of the 20th century. Every patient who undergoes a noninvasive medical imaging procedure should thank Paul. His work has led to revolutionary insights into the functions of the brain and the workings of the human body.

—Nancy Cantor, Chancellor, University of Illinois at Urbana-Champaign (2001–2004)

I wanted to be free to try any silly thing I wanted to do.

—Paul Lauterbur

Paul completed his PhD in 1962, but by that time he had already served as an outside reader on other PhD committees and received at least one faculty job offer from a department that did not realise he had not yet completed his thesis. His thesis was a detailed and thorough survey of the NMR of many key important carbon compounds (Lauterbur, 1963a, 1963b, 1963c, 1963d); it was submitted formally under Henry Frank, but interestingly, Paul was given little supervision and was really his own PhD adviser. He would later say that he finally submitted his thesis only because he needed a PhD to accept one of these job offers.

The job offer he accepted was that of associate (not assistant) professor of Chemistry and Radiology at the State University of New York (SUNY) at Stony Brook, now known as Stony Brook University (SBU). He started work in 1963, was shortly promoted to full professor, and worked there until 1985. There, he continued his work with ^{13}C NMR, studying its application to peptides and proteins, and pioneering computer-aided signal processing. In 1970, he published the first ^{13}C spectra of a protein, egg white lysozyme (Lauterbur, 1970).

During this time, Paul developed an interest in exploring NMR signal from complex objects, building on previous work by a number of labs attempting to distinguish and diagnose cancerous tumours. But, 'as a naive chemist, I couldn't imagine cutting people up to see if they were sick or not'. He thought he could use NMR to find a better way, if only it was possible to localise NMR signals. This is the most famous story of the invention of MRI, and a favourite of his to tell: it was 1971, and he was having dinner at a Big Boy restaurant with friend and colleague, Don Vickers, after observing an experiment attempting to replicate a finding of NMR signals from tumours. While explaining to Don why imaging by NMR wouldn't work, and between bites of his hamburger, he 'realized that inhomogeneous magnetic fields labeled signals according to their spatial coordinates and made a leap of faith to the conclusion that the information could be recovered in the form of images' (See Dawson, 2013). These ideas are described in detail in the notebook he bought that night, now held at the Museum of the Science History Institute (formerly of the Chemical Heritage Foundation) in Philadelphia, Pennsylvania. The notebook can be seen in digital form at https://digital.sciencehistory.org/works/0c483j46q. In this single notebook, Paul detailed the groundwork for the next 30 years of MRI research, including 3D imaging, spectroscopic imaging and isotope exchange imaging. Many subsequent developments in MRI by future researchers were in fact first suggested in his notebook.

A thirty-year detour

—Paul Lauterbur

The first paper describing the principles of MRI was published in the journal *Nature* shortly thereafter (Lauterbur, 1973), and it has been considered one of the 21 most influential papers published in that journal (Garwin and Lincoln, 2003). Like Paul's first ^{13}C paper, this article was the result of foresight and a lot of hard work. Because his technique involved the mistuning (from the perspective of an NMR researcher) of the gradient controls on the Chemistry Department's NMR machine, he went in late after other researchers had gone home, adjusted the controls as necessary, and then returned everything to the original settings before other researchers returned to work the next day. The paper was rejected at first, in part because the images showing distinct differences between capillary tubes filled with H_2O and the surrounding D_2O, now iconic, were deemed 'too blurry'. Paul would later say that 'you could write the entire history of science in the last 50 years in terms of papers rejected by *Science* or *Nature*'. Perhaps he felt the same about patents: SBU declined to submit a patent application for MRI, citing an 'inability to identify a potential market of sufficient size'. Paul then decided that sharing his research was more important than applying and waiting for the patent decision and went on to present his work at conferences. He called his method 'zeugmatography', referencing the joining ('zeugma', from Greek) of a magnetic field and spatially defined field gradients. (For zeugmatography, see Lauterbur, 1974, 1979.)

The above-mentioned 1973 paper is really a proof of concept. It showed that NMR signal from protons could be localised by combining the standard uniform magnetic field used in NMR with an orthogonal magnetic field gradient. Standard NMR applies a uniformly oscillating magnetic field, with oscillations at a frequency dependent on the strength of the uniform field and the nuclei being observed. Imaging requires that the wavelength (oscillation frequency, in this case) used to create the image be smaller than the object to be imaged. This naturally precludes the use of NMR, with typical wavelengths in the range of 20+ MHz. Paul showed that by using orthogonal field gradients to restrict the interaction of the uniform field to a particular location, the imaging resolution is no longer dependent on wavelength, but simply a function of the field gradient. In this seminal MRI paper, he used a 60 MHz magnetic field to generate a simple, two-dimensional image of afore-described capillary tubes filled with D_2O (heavy water, with deuterium replacing the usual ^1H) suspended in H_2O (ordinary water). Despite the original two-dimensional nature of the images, Paul thought from the beginning that three-dimensional imaging should be the goal. In addition, the paper anticipated a wide variety of potential applications that are now in use, including soft tissue imaging, chemical composition, and solid-state imaging. After all, Paul 'had confidence that whatever physics allowed, engineers could achieve'.

THE CUTTING EDGE AT THE UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

The most gratifying experiences emotionally were those when a stranger would volunteer 'you saved my daughter's life'.

—Paul Lauterbur

In 1985, Paul joined the University of Illinois at Urbana-Champaign (UIUC) as a professor serving on the faculties of the Departments of Chemistry and Bioengineering and the Center of Biophysics and Quantitative Biology. It was during 1985–1999 that Govindjee knew Paul and his wife, Joan Dawson. In addition, Paul also held an appointment as a professor in the College of Medicine at the University of Illinois at Chicago. His major duty at UIUC was as the director of the Biomedical Magnetic Resonance Laboratory (BMRL).

During this time, he continued to publish on many aspects at the forefront of MRI research and mentored many students and postdocs. He and Joan built a 'BMRL family', who celebrated together and supported each other. Despite his myriad responsibilities, Paul always gave full attention to any student or postdoc who walked through his office door. As Joan writes in her biography of Paul (Dawson, 2013), 'Doug Morris [one of Paul's postdocs] said that when you appeared in his office he would throw his pen down, throw up his hands, and inquire "Whatyagot?"'

The day he won the Nobel Prize, Paul told Gregory Girolami (then head of Chemistry at UIUC), who lived three houses away and had walked over to Paul and Joan's home at 7:00 in the morning: 'I have a scheduled meeting with my students at 4 o'clock today and, no matter what happens, I want to keep that appointment'. Dr Girolami had taken charge of working with UIUC's public relations staff to arrange Paul's schedule for that day. All was done as Paul wanted.

Paul published over 100 papers during this time, always on the cutting edge. He was working to expand the scope and power of MRI in all its aspects, so it is impossible to describe their full impact even in aggregate in this tribute.

Among this work is the foundation of modern high-resolution, real-time dynamic imaging: Signal Localisation by Imaging (SLIM) (Hu *et al.,* 1988; Liang and Lauterbur, 1991) and its follow-on methods, including Reduced-Encoding MR Imaging with Generalised-series Reconstruction (RIGR) (Webb *et al.,* 1993) and Dynamic Imaging by Model Estimation (DIME) (Liang *et al.,* 1997). Conceived originally with Joan for the goal of high-resolution metabolic imaging, SLIM uses a priori information (conventional MRI or other images) to constrain the calculations to localise signals from metabolites. Much of this work was completed with Zhi-Pei Liang, a postdoc and then professor of Electronic and Computational Engineering at UIUC (see Liang's Reminiscence). RIGR advanced dynamic imaging uses an innovative method: calculating the change in shape of the target organ (a beating heart, for example) from an original, static image. This method allowed dynamic imaging to be conducted far faster and with less data than was previously possible. DIME built on that by using model estimation to overcome the speed and data limitation challenges of dynamic imaging. If you have ever seen an MRI of a beating heart, it is this research of Paul Lauterbur that ultimately made that possible!

Elise Lauterbur has fond memories of one project that was a little bit off the beaten path for Paul: *Chick* Scope, an educational project that allowed students to generate MR images of developing chicken embryos (Bruce *et al.,* 1997). In collaboration with education researchers and Joan's science outreach programme, Project SEARCH, *Chick*Scope was implemented in kindergarten through high school classrooms, including Elise's fifth-grade class. This project had two goals: first, to understand how Internet-based educational opportunities could affect teaching and learning, and second, to develop and test methods of controlling MRI systems remotely, at a time (~1996) when the Internet was only beginning to be widely used. Like most of Paul's work, *Chick*Scope was at the forefront of its field. We agree with Bruce *et al.* (1997): 'Although *Chick*Scope represents an unusual approach today, current trends suggest that Web use and remote instrumentation are technologies that will become increasingly common in schools and workplaces of the near future. The particular instruments and scientific domains may change, but the basic organization of collaborative, technology-supported science investigations should be generalizable'.

It was during his tenure at UIUC that Paul had what he called his 'best idea since imaging'; he called it Diffusional Enhancement of Signal Intensity and Resolution (DESIRE). Here, he theorised a method to generate MR images at a resolution finer than allowed by light microscopy level, even to individual molecules. Resolution at this level is limited because the signal diffuses far enough over its short lifetime that localisation to an individual molecule is impossible. Rather than directly imaging the target molecules (cell membranes, for example), Paul thought to localise the signal indirectly, by using the patterns of diffusion through interstitial space. This method would increase resolution by two to three orders of magnitude. Unfortunately, DESIRE microscopy was not published except in abstracts in conference proceedings; other laboratories had experimented with it, and with similar methods, but, like many of Paul's ideas, the technology had yet to catch up to his insights!

After being awarded the Nobel Prize in Physiology or Medicine in 2003, Paul returned to a childhood interest, the nature of carbon, silicon and the origins of life (see Lauterbur, 2005, 2008). In the first of two papers on this subject, Paul proposed that the spontaneous formation of molecular imprints could have provided binding and catalytic sites allowing 'transformations that may have preceded, and provided a spontaneous path to, contemporary biological organization'. These 'guided' reactions would have been replicable, with the potential to grow in scale and complexity, providing a foundation for the development of self-organising life. Paul expanded on these ideas in a manuscript published posthumously in 2008, with a call for experimental testing of his hypothesis that these processes could have resulted in 'proto-cells, with proto-enzymes and proto-ribosomes' that could further evolve by natural selection. It was this work that occupied him until his death in 2007, including during his last days. Additional notes, grant proposals and ideas for experiments are available in the archive of his work held at the Science History Institute, Philadelphia, Pennsylvania.

PERSONAL LIFE

Physically, Paul was a big, burly man, and a jovial one, but these attributes contrasted markedly with the humility with which he regarded his achievements.

—Ian Young, 'Father of Clinical MRI'

Paul met his first wife, Rose Mary Caputo, through mutual friends while he was at the Mellon Institute in Pittsburgh. Rose Mary was a creative person, a writer for a local television station, and devoted to her community theatre. After a romantic courtship, they married in 1959 and shortly had two children: a son, Daniel, in 1961, and a daughter, Sharyn, in 1963. Much like Paul's own upbringing, his children were encouraged and expected to go out and explore the world. When Paul decided it was time to use MRI to image a living organism, he chose a clam. They were small, common on the beach near Stony Brook, and more importantly, would lie still during the scan. Paul asked both children to go to the beach to find clams for the experiment. Dan brought back the biggest he could find, and Sharyn, the smallest and cutest. One of Sharyn's clams was the perfect size and became the first living organism to be imaged. The image was published along with those of a pine branch, a pecan nut and a live mouse (Lauterbur, 1974). Rose Mary and Paul separated in the early 1980s.

Paul met the woman who would become his second wife, Dr Joan Dawson, at a conference in Oxford in 1977. Joan was a muscle physiologist, biophysicist and fellow NMR researcher at University College London. They began a conference-hopping courtship after his divorce, and 2 years later Paul asked Joan to marry him in a letter written while he was travelling by train from one conference to another in continental Europe. They married in 1984, and their daughter Elise was born the next year. Both Paul and Joan accepted faculty positions at the University of Illinois at Urbana-Champaign in 1985 and developed the BMRL and an extended lab family together. While their introduction in 1977 was their first meeting as scientists, they may have first met some 20 years earlier. Joan had grown up in Midland, Michigan, the headquarters of Dow Corning. Her friend Nancy Warrick was the daughter of Paul's mentor Earl Warrick. At one dinner at the Warrick household, Nancy's father, Earl, had a guest from Pittsburgh visiting, a clever young man wearing thick glasses. The 12-year-old Joan thought this visitor was impossibly smart and sophisticated. Paul remembered visiting the Warrick household in Midland many times in those days, though he did not particularly remember a shy 12-year-old friend of Nancy's named Joan. It was only after many years of marriage that Paul and Joan realised this early connection.

REMINISCENCES

Chien Ho (Alumni Professor; Department of Biological Sciences, Carnegie Mellon University, Pittsburgh, Pennsylvania, USA; chienho@andrew.cmu.edu)

I have known Paul since the 1960s. I joined the faculty of the Department of Biophysics at the University of Pittsburgh in 1965, shortly after Paul left for Stony Brook. Because of our mutual interests in science, in particular NMR, and because of our connections with Pittsburgh, we became good friends. We had many contacts and scientific discussions over the course of 50 years. I always enjoyed my scientific discussions with Paul. He had a sharp mind and always came up with novel ideas, so I learned a great deal from him through our conversations. I served on the advisory committee of Paul's NIH-supported Biomedical Research Resource Center at the University of Illinois at Urbana-Champaign for several years. Paul also served on the advisory committee of my NIH-supported Biomedical Research Resource Center at Carnegie Mellon University from 1997 to 2001.

Paul's interests in magnetic resonance started when he took his first job after he graduated from Case Institute of Technology in 1951 to work as a staff member in the research and development group sponsored by Dow Corning Corporation working on synthesising and testing organosilicon compounds and polymers, like silicon rubber, at the Mellon Institute. He became interested in NMR and relaxation phenomenon and in applying these new techniques to polymers in the early 1950s. During the Korean War in the early 1950s, he was drafted into the U.S. Army and was sent to the Army Chemical Center's Medical Laboratories to install a Varian NMR spectrometer (operating at 40 MHz for ^{1}H and ^{19}F, and at 17 MHz for ^{31}P) to support chemical warfare research. After his Army service, he returned to the Mellon Institute and persuaded the Dow Corning Group to purchase a new NMR spectrometer to be used to investigate silicone compounds; this instrument gave Paul the opportunity to begin a most productive and innovative research on NMR as well as his path to MRI. Paul's early work earned him a reputation as the father of heteronuclear NMR or father of ^{13}C NMR well before his MRI work.

In the 1970s through the 1990s, we often got together when we attended the Annual meetings of the International Society for Magnetic Resonance in Medicine (ISMRM). After Elise was born, Joan and Paul usually took her with them when they attended meetings in the United States and abroad. Elise could be the most travelled person in her age group! My wife, Nancy, and I were happy to see them at the ISMRM Meeting in Sydney in 1998.

In looking at Paul's scientific contributions, I would like to share with you two experiences that I had with his innovations. First, during the mid-1970s, I was a member of the Biophysics and Biophysical Chemistry B Study Section (BBCS) of NIH. The BBCS was assigned to review Paul's first NIH grant application for his MRI research. It was obvious that the members of BBCS did not have expertise in this new technology. The executive secretary of BBCS sent Paul's proposal to several leading NMR experts for their comments. They all claimed that they had no expertise to review or comment on this grant application. After extensive discussion in the BBCS, it was recommended that based on Paul's past expertise in NMR, he should be given a chance to carry out his innovative research project. He got his first MRI grant from the NIH, and that facilitated his subsequent development of the MRI technology.

My second experience was being assigned as a member of the site visit team to review Paul's grant application to build an MRI facility at Stony Brook University. His designed MRI instrument is now being displayed in the Beckman Institute. I remember that Joe Frank was with Paul during the site visit. Again, his expertise in NMR and his innovation for MRI convinced the site visit team that his grant application should be funded!

Paul was truly a great innovator of the 20th century. His development of MRI has provided a non-invasive tool for diagnosing diseases and for monitoring therapeutic treatments of patients. MRI instruments are now available in major hospital centres all over the world, thus, saving thousands of lives daily. Paul's impact on science, technology and medicine is truly immeasurable!

I end my Tribute to Paul with a 2004 photograph of two of us at his home in Champaign-Urbana, Illinois (Figure 6).

Joseph (Joe) Frank (Senior Investigator and Chief, Laboratory of Diagnostic Radiology Research Co-Director, Center for Infectious Disease Imaging—National Institutes of Health; jfrank@mail.nih.gov)

I am Joe Frank, a physician-scientist, senior investigator and lab chief at the National Institutes of Health Clinical Center in the Radiology Department and the National Institutes of Biomedical Imaging and Bioengineering. I worked in Paul Lauterbur's lab from 1973 to 1977, where

Figure 6: A photograph of Paul Lauterbur with Chien Ho, taken at a celebration for the 2003 Nobel Prize to Paul, taken at his home on 20 February 2004.
Source: Zhi-Pei Liang

I received a BS and an MS in chemistry. I started out in his lab in 1973 as a photographer needing to modify the original NMR zeugmatograms from Paul's papers to Gaussian blurred images.

In early 1974, I started my research career in Paul's lab and quickly became enthralled with NMR zeugmatographic imaging by performing some of the early in vivo experiments in mice. I was hooked! This was the most innovative time of my young scientific career, performing experiments that had never been done before and tackling hurdles to get instruments working and get results. Paul taught me about dedication to science investigation and to think outside the box. Late at night on Christmas Eve in 1974, I had the IBM 1800 (an early Data Acquisition and Control System) in the Chemistry Department all to myself, so I decided to punch cards of raw CW spectra NMR data and process them into zeugmatographs. The Stony Brook campus police arrived to ask what I was doing. After several tense minutes, I was able to get them to phone the Lauterbur home and Paul vouched for me, saying 'what else should he be doing!' We were able to review the imaging results of tumours growing in a mouse the following week during the winter break. The years that I was mentored by Paul changed the trajectory of my medical scientific career, and I am extremely grateful to have had the opportunity to work with him. I credit that time in Paul's lab as the basis for my scientific career in MRI and the way to mentor many of my students, postdocs and fellows in my lab. Figure 7 shows a 2005 group photograph of Paul with some of us when he visited NIH after winning his Nobel Prize.

Figure 7: Visit to the NIH and reunion with former lab members, 20 May 2005. **Sitting**: Paul Lauterbur and wife, Joan Dawson. **Standing, left to right**: Doug Morris (former postdoc at UIUC), Chuck Dulcey (former student at Stony Brook), Kyle Hedges (former student at Stony Brook), Joseph (Joe) Frank (former student at Stony Brook), Marcelino Bernardo (currently Associate Director of Imaging Physics at The Frederick National Laboratory for Cancer Research), Yihong Yang (former student at UIUC) and Su Xu (former student at UIUC).
Source: Joseph Frank

Vikas Gulani (Fred Jenner Hodges Professor and Chair of Radiology at the University of Michigan; vikasgulani@med.umich.edu)

Dr Paul Lauterbur was a generational scientist, one who invented the field of MRI and before that had been a pioneering NMR scientist, consistently preferring to explore big ideas over safe ones and unafraid of the failures that inevitably accompany doing difficult science. To get there, he worked harder every day than most students and postdocs half his age or younger. On most Saturdays and Sundays, I knew he was 'in the house' with his silver car parked outside in the first parking space, indicating he had beat us all there, opera wafting out of his office. The door was always open physically and symbolically. Intimidated by all that he had accomplished, I preferred early on to set meetings rather than use the open-door policy, though towards the end I started to simply walk in.

In personal meetings, if I did not prepare by properly reading up on the subject, having some real data, and anticipating difficult scientific questions, I knew the discussion could go off into wildly interesting but confusing discussions in which I could get lost. This was not because Paul was in any way unfair or wanting to challenge a student, but because his curiosity would inevitably bring up tangents we needed to explore. I learned from those discussions that all these tangents need to be considered to fully understand a subject, and some of these are where the optimal scientific path actually lies. Paul encouraged me to be fully transparent, to 'publish your numbers' so that others can see them in black and white and prove you wrong if you are wrong, so that science can move forward. He also taught me to be precise with my terminology. When I described an old imaging probe as 'not very good', he curtly told me, 'the word "good" has no scientific meaning; tell me what characteristics of the probe are non-ideal and why, with numbers'. Abstracts and papers came back with red edits on the margins, tightening my language and asking difficult questions. There is no doubt that spending time as a graduate and medical student and then postdoc with Paul taught me how to think as a scientist, and I am grateful for the mentorship.

And this last word 'mentor' brings me to the person that Paul was. When I was in the last year of residency/fellowship, perhaps a year prior to his passing, I drove to Urbana, Illinois, from Ann Arbor, Michigan, to ask him for a letter of recommendation for a faculty job. I had not seen him for a few years, and I wanted to find out in person whether my asking was proper or whether I should defer to other people's letters. He was curious as ever, now exploring biochemical origins of life as the scientific question that he said MRI had diverted him from exploring. I asked him to just use an old letter, if he was willing. He not only complied but said he would of course write a proper letter for the job, saying 'mentorship is forever'. I more fully appreciated later in life just how kind an adviser he had been, as the full depth of some of the gestures was not apparent to me at a younger age. Our meetings inevitably began with 'How are you and how is your family?' and he spent the first 10–30 minutes genuinely wanting to know the answer. How much of a busy person's time they are willing to share in this manner says a lot about them. When I had a baby and went to him at some point to discuss science, he advised 'Don't forget to say *goochy goochy goo* once in a while, or it will pass you by'. He had personal, catered dinners and parties for me when I got married and had a child, again underscoring a care for me and for my family. The entire lab was always invited to his and Dr Joan Dawson's house for Thanksgiving and Boxing Day, because there were international students among us who may have nowhere to go. Now with my own lab and family, I can understand what a major human gesture this yearly invitation was.

These are but a few examples; many others abound. While I enjoyed my time with him when I was in the lab, my appreciation and respect for Paul the scientist and person have grown even more in the years since his passing.

Daniel (Dan) Lauterbur (Retired, former Archaeologist for the State of Michigan; dan.lauterbur@gmail.com)

Anyone who knew my dad knew that he was thoroughly dedicated to his work. During my childhood in the 1960s and 1970s, most of my memories of time shared with Dad involve sitting with him in the evenings in his study as he read and listened to music, getting help with homework, and having bits of conversation as the opportunity arose. While I'd occasionally get him to toss a baseball with me, or go fishing, he was an academic father—those typical 'American dad' acts of bonding with his children weren't really his forte.

The one consistent and sweet interaction we had was bedtime stories, in particular tales of the adventures, and misfortunes, of a certain worm named Oscar. Dad would spin these creative stories frequently, and they were always enthralling and entertaining to my young mind—though I believe that was when I first learned how to react with an eye roll to some of his imagined scenarios. For me, these bedtime tales were called 'Short Oscar stories', not for the length of the telling, but for what would ultimately befall poor Oscar. I am guessing that also applied to the stories my younger sister, Sharyn, heard.

In a typical Short Oscar story, Oscar would be out on a lovely wet rainy day, exploring the world around him. He would meet all sorts of fascinating individuals and discover amazing new locations to explore. Eventually, he'd wriggle down a perfect little hole for a worm such as he, and go down, down, and even further down into this incredible subterranean world. He would then hear a strange sound, a buzzing, vibrating sound, and get fearful and quickly wiggle up towards the surface, towards the light, surrounded by this shaking noise! He got to where he was able to see the sunlight and the green of the grass surrounding the outlet of the hole! Oscar was so excited to pop back out into the world again, to get away from this strange noise and continue his adventures! He poked his head out and saw the blue sky and the sun overhead! And just at that point a lawnmower, making a loud, shaky sound, passed over the hole. Uh oh! Short Oscar!

My much younger sister, Elise, however, being extremely sensitive to animals in peril, received only happy Oscar stories. But it's interesting that these stories are a thread of connection we share, that Dad maintained for decades. They were essentially shaggy dog stories—I think he made most of them up extemporaneously. His life was dedicated to great and good scientific pursuits, but we children got a most unique little piece of a different side of our father, and I'll always be grateful.

M. Elise Lauterbur (NSF Postdoctoral Fellow in Biology in the Department of Ecology and Evolutionary Biology at the University of Arizona; lauterbur@gmail.com)

There is too much to say about my dad in one short message. I hope this article has accurately conveyed who he was as a researcher and person, but despite science being his calling and lifelong love, there was so much more to his personality. So here are a few small thoughts from me, as his daughter.

He and his stories were the focus of any gathering. I remember many dinners, for one occasion or another, where he held the table rapt or had everyone laughing uproariously. He was funny, clever and told terrible puns. This last I have proudly inherited from him. He also loved classical music and was partial to bombastic opera and big symphonies. He would often conduct along to the radio while he was driving. One year he had earrings made for my mom out of the copper shielding from a failed magnet, a romantic but bittersweet gift. He gave her roses on the third of every month, the same day as their wedding anniversary. Sometimes he brought me a single rose as well.

He and my mom built their labs into a true family and raised me as they were raised—to be independent of thought and action, to ask questions about the world around me, and to find my own ways to answer them. I have a distinct memory from one dinner at home when I was around 7 or 8 years old. I had asked a question about something, expecting a short lecture on the subject from my mom, or a longer one from my dad. Instead, I was told to 'go look it up in the encyclopaedia' and directed to the *Encyclopedia Britannica*, 1985 edition, which they had purchased at great expense the year I was born for just this purpose.

All my life I have been asked, 'What is it like to have a famous scientist for a father?' As a child the answer was easy—he's just my dad. He reads the Sunday comics in the newspaper with me, he comes to my music recitals, he taught me to ride a bike and tie my shoes. As an adult and a scientist myself, it is more complicated. One of my strongest regrets is that I did not take more time to talk about science with him. Despite him being 'just Dad' for so long, by the time I could understand the significance of his scientific contributions, I could also understand the degree of his intelligence enough to be a little intimidated. I thought he wouldn't be interested in listening to my naive ideas as I studied to become a biologist. I was wrong, of course. One of his many virtues was welcoming and supporting the ideas and conversation of budding scientists. There are many days during my own research when I wish I could get his thoughts on some idea I am working through. I know that he would have looked at the problem upside down in a way no one else had thought to, and provided insight that no one else could.

I keep a reprint of his second to last article, about the origins of life in chemistry, as a reminder that creativity and pursuing one's passions lead to the best work (Figure 8).

Zhi-Pei Liang (Franklin W. Woeltge Professor in the Electrical and Computer Engineering Department at UIUC, Urbana, Illinois; z-liang@illinois.edu)

This is a special year that marks the 50th anniversary of Paul's invention of zeugmatography, now known as MRI. On 2 September 1971, Paul wrote down in his notebook the ingenious idea for image formation using magnetic resonance. He wrote: 'The distribution of magnetic nuclei … may be obtained by imposing magnetic field gradients … on a sample, such as an organism or a manufactured object, and measuring the intensities and relaxation behavior of the resonances as functions of the gradient magnetic field'. These fantastic ideas have not only led to the development of a new scientific field, which is still expanding after 50 years, but also revolutionised biology and medicine, saving many lives daily worldwide.

Figure 8: Signed copy of Paul Lauterbur's last article, 'Demystifying Biology: Did Life Begin as a Complex System?' Inscription reads 'Elise—Do it all and enjoy it all. Paul Lauterbur (Dad)'.
Source: Collection of Elise Lauterbur

I am blessed to have the distinct honour and privilege to be Paul's postdoc, colleague and close friend for 17 years before he passed away in 2007. Many people knew Paul and I were special friends; I admired and loved Paul not just because he was a brilliant researcher, but also because he was a wonderful human being, a caring mentor, a sincere colleague and friend, and a humble and gracious person. Figure 9 shows photographs of Paul taken at UIUC right after the announcement of his Nobel Prize.

No doubt, Paul was the most creative scientist I have ever met. Today's recent breakthrough in ultrafast MR spectroscopic imaging (MRSI) is based on Paul's vision and ideas. How much I wish I could say to him directly: Paul, your ideas on MRSI work, and work beautifully! I miss Paul, miss him greatly.

Debora McCall (Executive Assistant Dean for Administration, University of Illinois at College of Medicine at Urbana- Champaign; demccall@illinois.edu)

I was Paul's administrative assistant from 1986 to 2001. Paul started his lab at the University of Illinois with two graduate students, both bright MD/PhD students in the College of Medicine's Medical Scholars Program. We were housed in a two-story building named the Biomedical Magnetic Resonance Laboratory. There was no imager to use for research in those days, but Paul was determined to find a way to build a research laboratory at the University of Illinois. It was around 1989 that he received an NIH Shared Instrumentation Grant, which financially helped obtain the SISCO 4.7T system that got the research under way. With the system up and running, the number of people working in the laboratory began to grow, and research results were achieved.

Along with research results came deadlines—specifically, grant deadlines. I recall working many long nights and weekends putting together grant proposals. Paul would write, I would type, Paul would edit, I would type the revisions. There was no electronic grant submission then.

Figure 9: Top left and right: photographs of Zhi-Pei Liang with Paul Lauterbur. **Bottom left:** Paul celebrating with Joan Dawson (on his left) and Liang on his right. **Bottom right**: Paul in a group at a special symposium at UIUC celebrating his Nobel Prize.
Source: Archives of Zhi-Pie Liang

My co-worker and I also spent many late nights and weekends copying proposals and preparing for site visits. Our work and diligence paid off, as the NIH Research Resource and the NSF Science and Technology grants were both funded in the early 1990s, and the laboratory grew and flourished. At one point, there were a total of 50 graduate students, approximately 100 undergraduate students, and half a dozen postdocs conducting research in Paul's laboratory! We became our own scientific community, and as a result, we were cheerleaders for each other's successes at work and in life.

Paul and Joan treated everyone in the lab as family. They made certain that everyone in the lab had somewhere to spend holidays. Because there were a number of foreign students working in the laboratory who didn't leave campus for the holidays, Paul and Joan opened their home for the Thanksgiving holiday and Boxing Day each year. This feeling of family is what made it such a joy to come to work every day and to contribute in my small way to the mentoring of the many young, eager minds that were learning, growing, and developing under Paul and Joan's tutorship. Paul (along with Joan) mentored numerous students, staff, faculty and colleagues during his prestigious career. I have been one of the most fortunate of those mentees. Paul challenged me to work beyond what I believed I was capable of, and for that I am the one that benefited. I consider it an honour and a privilege to have worked with him.

Paul Lauterbur, the man, can be described as true greatness, yet he was humble and approachable. No matter how busy he was, Paul always made the time to talk to his students. He thrived on the stimulation of trying to solve an intriguing research problem, he was committed to helping his students determine what had gone wrong with a failed experiment, and he enjoyed the casual conversation with a student, staff member, or colleague who just stopped by to say hello. The *Champaign-Urbana News Gazette* ran an editorial on 2 April 2007, which accurately describes Paul's greatness. In my opinion, the media finally got it right. Editorial writer Jim Dey wrote the following: 'University faculties across the country are home to a great many brilliant minds, but very few giants. The University of Illinois … has lost a giant…. We shall not see his like again soon. The UI and the world are poorer because Professor Lauterbur's work has ended. But what a life he lived. What a legacy he left'.

Bharathi Pamidighantam (Department of Histotechnology, Indiana University Health, Bloomington Hospital, Bloomington, Indiana; b.pamidighantam@comcast.net)

I was associated with Professor Paul Lauterbur for 2 years. In my view, he was a very noble person, kind, easy to approach, who always encouraged me and other undergraduate students in the lab. I enjoyed very much our research meetings and our in-depth discussions on many topics, including, of course, MRI. I am delighted to share with others my appreciation of Professor Lauterbur's mentorship.

CONCLUDING REMARKS

For Paul's own words about his scientific journey, we recommend his Nobel Prize lecture. There the reader will also get to experience a little of Paul's own charm and humour. https://www.nobelprize.org/prizes/medicine/2003/lauterbur/biographical/. His wife, Dr M. Joan Dawson, published his biography in 2013, *Paul Lauterbur and the Invention of MRI*, MIT Press. Joan Dawson passed away in 2017, and Paul's first wife, Rose Mary, passed away in 2020. Paul is survived by his son, Daniel Lauterbur, and daughters Sharyn Lauterbur DiGeronimo and M. Elise Lauterbur.

ACKNOWLEDGMENTS

Elise Lauterbur thanks Roger Ledgister for extensive editing and support. Govindjee thanks the following of UIUC for information and support during the preparation of this tribute: Gregory S. Girolami (Faculty, Chemistry); Danielle L. Gray (X-Ray Lab, Chemistry); Catherine Jones Murphy (Faculty, Chemistry); and Mary C. Schlembach (Library). Both the authors are grateful to Nancy Winchester for the final editing of this article and to Gregory Girolami for checking the text before its submission for publication.

REFERENCES

Baianu IC, Critchley C, Govindjee [G], Gutowsky HS (1984) NMR study of chloride-ion interactions with thylakoid membranes. *Proceedings of the National Academy of Sciences USA* 81:3713–3717.

Borisjuk L, Rolletschek H, Neuberger T (2012) Surveying the plant's world by magnetic resonance imaging. *The Plant Journal* 70:129–146.

Bruce BC, Carragher BO, Damon BM, Dawson MJ, Eurell JA, Gregor CD, Thakkar U (1997) Chickscope: an interactive MRI classroom curriculum innovation for K-12. *Computers and Education* 29(2–3):73–87.

Dawson MJ (2012) Paul Lauterbur 1929—2007. Biographical Memoirs of the National Academy of Sciences USA.

Dawson MJ (2013) Paul Lauterbur and the invention of MRI. Cambridge, MA: MIT Press. ISBN 9780262019217. <http://cognet.mit.edu/book/paul-lauterbur-and-invention-of-mri>

Ettinger R, Blume P, Patterson A Jr, Lauterbur PC (1960) C13 chemical shifts in CO and CO_2. *The Journal of Chemical Physics* 33(5):1597–1598.

Garwin L, Lincoln T, eds. (2003) A century of nature: twenty-one discoveries that changed science and the world. Chicago, IL: University of Chicago Press.

Hu X, Levin DN, Lauterbur PC, Spraggins T (1988) SLIM: spectral localization by imaging. *Magnetic Resonance in Medicine* 8(3):314–322.

In Memoriam: M. Joan Dawson, Ph.D. 09 February 1944—27 July 2017 <https://www.ismrm.org/members-only/in-memoriam/m-joan-dawson-ph-d-1944-2017/>

Jonas J, Slichter C (2006) Herbert Sander Gutowsky—November 8, 1919-January 13, 2000. *Biographical Memoirs of the National Academy of Sciences USA* 88:1–17.

Koski WS, Kaufman JJ, Lauterbur PC (1957) Nuclear magnetic resonance study of the B2D6-B5H9 exchange reaction. *Journal of the American Chemical Society* 79(10):2382–2385.

Lauterbur PC (1957) C13 nuclear magnetic resonance spectra. *The Journal of Chemical Physics* 26(1):217–218.

Lauterbur PC (1958a) Some applications of C13 nuclear magnetic resonance spectra to organic chemistry. *Annals of the New York Academy of Sciences* 70(4):841–857.

Lauterbur PC (1958b) Anisotropy of the C13 chemical shift in calcite. *Physical Review Letters* 1(9):343.

Lauterbur PC (1961a) C13 nuclear magnetic resonance spectroscopy. I. Aromatic hydrocarbons. Journal *of the American Chemical Society* 83(8):1838–1846.

Lauterbur PC (1961b) C13 nuclear magnetic resonance spectroscopy. II. Phenols, anisole and dimethoxybenzenes. *Journal of the American Chemical Society* 83(8):1846–1852.

Lauterbur PC (1963a) Steric effects on C13 nuclear magnetic resonance spectra of substituted benzenes (Doctoral thesis). University of Pittsburgh.

Lauterbur PC (1963b) C13 nuclear magnetic resonance spectroscopy. III. Iodobenzene and methyliodobenzenes. *The Journal of Chemical Physics* 38(6):1406–1414.

Lauterbur PC (1963c) C13 nuclear magnetic resonance spectroscopy. IV. Aniline, N, N dimethylaniline, and their methyl derivatives: steric inhibition of conjugation. *The Journal of Chemical Physics* 38(6):1415–1431.

Lauterbur PC (1963d) C13 nuclear magnetic resonance spectroscopy. V. Nitrobenzene and methylnitrobenzenes: steric inhibition of conjugation. *The Journal of Chemical Physics* 38(6):1432–1443.

Lauterbur PC (1970) ^{13}C nuclear magnetic resonance spectra of proteins. *Applied Spectroscopy* 24(4):450–452.

Lauterbur PC (1973) Image formation by induced local interactions: examples employing nuclear magnetic resonance. *Nature* 242(5394):190–191.

Lauterbur PC (1974) Magnetic resonance zeugmatography. *Pure and Applied Chemistry* 40(1–2):149–157.

Lauterbur PC (1979) Feasibility of NMR zeugmatographic imaging of the heart and lungs. In Medical imaging techniques. Boston, MA: Springer, pp. 209–218.

Lauterbur PC (2005) Demystifying biology: did life begin as a complex system? *Complexity* 11:30–35.

Lauterbur PC (2008) The spontaneous development of biology from chemistry. *Astrobiology* 8:3–8.

Liang ZP, Jiang H, Hess CP, Lauterbur PC (1997) Dynamic imaging by model estimation. *International Journal of Imaging Systems and Technology* 8(6):551–557.

Liang ZP, Lauterbur PC (1991) A generalized series approach to MR spectroscopic imaging. *IEEE Transactions on Medical Imaging* 10(2):132–137.

Muller N, Lauterbur PC, Goldenson J (1956) Nuclear magnetic resonance spectra of phosphorus compounds. *Journal of the American Chemical Society* 78(15):3557–3561.

Muller N, Lauterbur PC, Svatos GF (1957a) Nuclear magnetic resonance spectra of some fluorocarbon derivatives. *Journal of the American Chemical Society* 79(8):1807–1810.

Muller N, Lauterbur PC, Svatos GF (1957b) Nuclear magnetic resonance spectra of some perfluoroalkyl derivatives of sulfur hexafluoride. *Journal of the American Chemical Society* 79(5):1043–1045.

Tiers GV, Lauterbur PC (1962) Fluorine NMR spectroscopy. X. Analysis of carbon 13 satellites in the spectra of cis and trans CFCl= CFCl. Assignment of coupling constants for fluorinated olefins. *The Journal of Chemical Physics* 36(4):1110–1112.

Van As H, van Duynhoven J (2013) MRI of plants and foods. *Journal of Magnetic Resonance* 229:25–34.

Warrick EL, Lauterbur PC (1955) Filler phenomena in silicone rubber. *Industrial & Engineering Chemistry* 47(3):486–491.

Webb AG, Liang ZP, Magin RL, Lauterbur PC (1993) Applications of reduced encoding MR imaging with generalized series reconstruction (RIGR). *Journal of Magnetic Resonance Imaging* 3(6):925–928.

Wydrzynski T, Zumbulyadis N, Schmidt PG, Gutowsky HS, Govindjee [G] (1976) Proton relaxation and charge accumulation during oxygen evolution in photosynthesis. *Proceedings of the National Academy of Sciences USA*, 73:1196–1198.

Appendix 1: Selected Pre-nobel Awards to Paul Lauterbur*

1982: Gold Medal, Society of Magnetic Resonance in Medicine (first recepient, https://www.ismrm.org/about/society-award-winners/gold-medal/)

1983: Howard N. Potts Medal (now the Benjamin Franklin Medal; https://www.fi.edu/laureates/paul-c-lauterbur; https://en.wikipedia.org/wiki/Howard_N._Potts_Medal)

1984: Albert Lasker Clinical Research Award (https://laskerfoundation.org/winners/magnetic-resonance-imaging-mri)

1985: Member, U.S. National Academy of Sciences (http://www.nasonline.org/member-directory/deceased-members/45770.html); Kettering Prize, General Motors Cancer Research Foundation (https://www.nytimes.com/1985/06/12/us/3-cancer-researchers-win-130000-awards.html); Gairdner Foundation International Award (https://gairdner.org/winners/index-of-winners/#Paul_C._Lauterbur)

1986: European Magnetic Resonance Award (first recipient, http://www.trtf.eu/awards.html); Harvey Prize in Science and Technology (Technion, Israel; https://harveypz.net.technion.ac.il/harvey-prize-laureates/)

1987: Fiuggi International Prize; President's National Medal of Science (USA; https://www.nsf.gov/od/nms/recip_details.jsp?recip_id=207); Gold Medal of the Radiological Society of North America https://www.rsna.org/about/distinguishedaward-recipients/gold-medalists; and the Roentgen Medal https://roentgenmuseum.de/en/theroentgenmedal/traeger-1980-1989

1988: National Medal of Technology and Innovation (https://en.wikipedia.org/wiki/National_Medal_of_Technology_and_Innovation ; given jointly to Paul Lauterbur and Raymond Damadian), given by U.S. President Ronald Reagan (also see: https://www.rfsuny.org/rf-news/suny-invention-of-mri/suny-invention-of-mri.html; Gold Medal, Society of Magnetic Resonance Imaging (https://www.ismrm.org/about/society-award-winners/gold-medal/)

1989: Dr. A.H. Heineken Prize for the discovery of MRI <https://www.heinekenprizes.org/portfolio-items/paul-c-lauterbur/>

1990: Henry Bower Award, Franklin Institute of Philadelphia (first recipient; https://www.fi.edu/laureates/paul-c-lauterbur-0)

1992: International Society of Magnetic Resonance in Medicine Award listed at: https://ethw.org/Paul_C._Lauterbur

1993: Carnegie Mellon Dickson Prize in Science (https://www.cmu.edu/dickson-prize/past-winners/index.html)

1994: Kyoto Prize for Advanced Technology (Japan) (https://www.kyotoprize.org/en/laureates/paul_christian_lauterbur/).

1999: Gold Medal, European Congress of Radiology (https://www.myesr.org/taxonomy/term/33)

2001: U.S. National Academy of Sciences Award for Chemistry in Service to Society (http://www.nasonline.org/programs/awards/chemistry-in-service-to-society.html)

2003: Nobel Prize in Physiology or Medicine (jointly with Peter Mansfield, UK) 'for their discoveries concerning magnetic resonance imaging' (https://www.nobelprize.org/prizes/medicine/2003/summary/)

2007: National Inventors Hall of Fame, class of 2007 (posthumous; https://www.invent.org/inductees/paul-christian-lauterbur)

2017: Enshrinee in the Engineering and Science Hall of Fame (posthumous; https://eshalloffame.org/index.php/enshrinees/21-paul-c-lauterbur)

***In addition to the above, Paul Lauterbur received honorary doctorate degrees from the University of Liege, Belgium, in 1984, from Carnegie Mellon University in Pittsburgh in 1987, and from Nicolaus Copernicus University Medical School in Kraków, Poland, in 1988.**

And last but not least, an asteroid discovered in 2006 by an Italian amateur astronomer, Silvano Casulli, has been named in Paul's honor: ***Asteroid 255598 Paul Lauterbur*** (see the Minor Planet Center, published 12 January 2017, M.P.C. 103028).

Appendix 2: Fifty Selected Papers, Listed Alphabetically Over the Decades, Which Show Paul Lauterbur's Breadth of Research in Chemistry, Physiology, and Medicine

Note: Papers referenced in the main text are in the **References** section and are not duplicated here

1950s

Holzman GR, Lauterbur PC, Anderson JH, Koth W (1956) Nuclear magnetic resonance field shifts of Si29 in various materials. *The Journal of Chemical Physics* 25(1):172–173.

(Please see **References** for the majority from this decade)

1960s

Burke JJ, Lauterbur PC (1961) Sn1 nuclear magnetic resonance spectral. *Journal of the American Chemical Society* 83(2):326–331.

Burke JJ, Lauterbur PC (1964) C^{13} and H^1 nuclear magnetic resonance spectra of cycloalkanes. *Journal of the American Chemical Society* 86:1870–1871.

Lauterbur PC (1961) Magnetic shieldings and the electronic structures of aromatic molecules. *Tetrahedron Letters* 2:274–279.

Lauterbur PC (1965) Isotope effects on ^{59}Co magnetic shielding in $K_3Co(CN)_6$. *The Journal of Chemical Physics* 42(2):799–800.

Lauterbur PC, Burke JJ (1965) Anisotropic ^{207}Pb magnetic shielding in a single crystal of wulfenite, $PbMoO_4$. *The Journal of Chemical Physics* 42(1):439–440.

Lauterbur PC, Hopkins RC, King RW, Ziebarth OV, Heitsch CW (1968) The nuclear magnetic resonance spectra of aluminum borohydride-trimethylamine. *Inorganic Chemistry* 7:1025–1027.

Lauterbur PC, Kurland RJ (1962) On the signs of CH and HH coupling constants. *Journal of the American Chemical Society* 84:3405–3406.

Lauterbur PC, Pritchard JG, Vollmer RL (1963) The isomeric pentane-2,4-diol cyclic sulphites. Journal of the Chemical Society (of Bangalore), article # 1012l; pp. 5307–5310; ISSN: 0253-4134 / 0973-7103; DOI:10.1039/JR9630005307

Lauterbur PC, Ramirez F (1968) Pseudorotation in trigonal-bipyramidal molecules. *Journal of the American Chemical Society* 90:6722–6726.

1970s

Hoult DI, Lauterbur PC (1979) The sensitivity of the zeugmatographic experiment involving human samples. *Journal of Magnetic Resonance* 34:425–433.

Lauterbur PC (1974) Magnetic resonance zeugmatography. *Pure and Applied Chemistry* 40:149–157.

Lauterbur PC (1979) Medical imaging by nuclear magnetic resonance zeugmatography. *IEEE Transactions on Nuclear Science* 26:2807–2811.

Lee N, Inouye M, Lauterbur PC (1979) ^{19}F- and ^{13}C-NMR studies of a specifically labelled lipoprotein in the *Escherichia coli* membrane. *Biochemical and Biophysical Research Communications* 78:1211–1218.

(See the section on **References** for the majority of papers from this decade)

1980s

Bendel P, Lai CM, Lauterbur PC (1980) ^{31}P spectroscopic zeugmatography of phosphorus metabolites. *Journal of Magnetic Resonance* 38:343–356.

Bernardo ML, Lauterbur PC (1983) Rapid medium-resolution 3-D NMR zeugmatographic imaging of the head. *European Journal of Radiology* 3:257–263.

Brownell GL, Budinger TF, Lauterbur PC, McGeer PL (1982) Positron tomography and nuclear magnetic resonance imaging. *Science* 215:619–626.

Budinger TF, Lauterbur PC (1984) Nuclear magnetic resonance technology for medical studies. *Science* 226:288–298.

Heidelberger E, Petersen SB, Lauterbur PC (1983) Aspects of cardiac diagnosis using synchronized NMR imaging. *European Journal of Radiology* 3:281–285.

Heneghan MA, Biancaniello TM, Heidelberger E, Peterson SB, Marsh MJ, Lauterbur PC (1982) Nuclear magnetic resonance zeugmatographic imaging of the heart: application to the study of ventricular septal defect. *Radiology* 143:183–186.

Herman GT, Udupa JK, Kramer DM, Lauterbur PC, Rudin AM, Schneider JS (1981) Three-dimensional display of nuclear magnetic resonance images. *Proceedings of SPIE—The International Society for Optical Engineering* 273:35–40.

Klimek R, Lauterbur PC, Mann WJ, Mendoca-Dias MH, Kaplan C (1982a) Nuclear magnetic resonance technique in human surgery. Case report. *Przeglad lekarski* 39:335–357.

Kramer DM, Schneider JS, Rudin AM, Lauterbur PC (1981) True three-dimensional nuclear magnetic resonance zeugmatographic images of a human brain. *Neuroradiology* 21:239–244.

Lai CM, Lauterbur PC (1981a) True three-dimensional image reconstruction by nuclear magnetic resonance zeugmatography. *Physics in Medicine and Biology* 26:851–856.

Lauterbur PC (1980) Progress in NMR zeugmatography imaging. Philosophical Transactions of the Royal Society of London. *Series B, Biological Sciences* 289:483–487.

Lauterbur PC (1982) NMR zeugmatographic imaging in medicine. *Journal of Medical Systems* 6:591–597.

Lauterbur PC (1986a) Cancer detection by nuclear magnetic resonance zeugmatographic imaging. *Cancer* 57:1899–1904.

Lauterbur PC (1986b) NMR imaging in biomedicine. *Cell Biophysics* 9:211–214.

Lauterbur PC (1988) NMR images of microscopic flow. *Nature* 336:310. DOI: 10.1038/336310A0.

Lauterbur PC, Lai CM (1980) Zeugmatography by reconstruction from projections. *IEEE Transactions on Nuclear Science* 27:1227–1231.

Lauterbur PC, Levin DN, Marr RB (1984) Theory and simulation of NMR spectroscopic imaging and field plotting by projection reconstruction involving an intrinsic frequency dimension. *Journal of Magnetic Resonance* 59:536–541.

Mendonca-Dias MH, Mann WJ, Chumas J, Bernardo ML, Lauterbur PC (1982) Three-dimensional nuclear-magnetic-resonance zeugmatographic imaging of surgical specimens. *Bioscience Reports* 2:713–717.

Muller RN, Marsh MJ, Bernardo ML, Lauterbur PC (1983) True 3-D imaging of limbs by NMR zeugmatography with off-resonance irradiation. *European Journal of Radiology* 3:286–290.

1990s

Chandra S, Liang ZP, Webb A, Lee H, Morris HD, Lauterbur PC (1996) Application of reduced-encoding imaging with generalized-series reconstruction (RIGR) in dynamic MR imaging. *Journal of Magnetic Resonance Imaging* 6:783–797.

Frank S, Lauterbur PC (1993) Voltage-sensitive magnetic gels as magnetic resonance monitoring agents. *Nature* 363:334–336.

Gulani V, Iwamoto GA, Lauterbur PC (1999) Apparent water diffusion measurements in electrically stimulated neural tissue. *Magnetic Resonance in Medicine* 41:241–246.

Hawrylak N, Ghosh P, Broadus J, Schlueter C, Greenough WT, Lauterbur PC (1993) Nuclear magnetic resonance (NMR) imaging of iron oxide-labeled neural transplants. *Experimental Neurology* 121:181–192.

Hyslop WB, Woods RK, Lauterbur PC (1995) Four-dimensional spectral-spatial imaging using projection reconstruction. *IEEE Transactions on Medical Imaging* 14:374–383.

Kmiecik JA, Gregory CD, Liang ZP, Lauterbur PC, Dawson MJ (1999) Lactate quantitation in a gerbil brain stroke model by

GSLIM of multiple-quantum-filtered signals. Generalized spectral localization by imaging. *Journal of Magnetic Resonance Imaging* 9:539–543.

Liang ZP, Lauterbur PC (1993) A theoretical analysis of the SLIM technique. *Journal of Magnetic Resonance, Series B* 102:54–60.

Liang ZP, Lauterbur PC (1994) An efficient method for dynamic magnetic resonance imaging. *IEEE Transactions on Medical Imaging* 13:677–686.

Webb AG, Liang ZP, Magin RL, Lauterbur PC (1993) Applications of reduced-encoding MR imaging with generalized-series reconstruction (RIGR). *Journal of Magnetic Resonance Imaging* 3:925–928.

Yang Y, Xu S, Dawson MJ, Lauterbur PC (1997) Diffusion measurement in phantoms and tissues using SLIM localization. *Journal of Magnetic Resonance* 129:161–164.

Zhou X, Magin RL, Alameda JC, Reynolds HA, Lauterbur PC (1993) Three-dimensional NMR microscopy of rat spleen and liver. *Magnetic Resonance in Medicine* 30:92–97.

2000s

Feng L, Pamidighantam B, Lauterbur PC (2010) Microwave-assisted sol-gel synthesis for molecular imprinting. *Analytical and Bioanalytical Chemistry* 396:1607–1612.

Gulani V, Webb AG, Duncan ID, Lauterbur PC (2001) Apparent diffusion tensor measurements in myelin-deficient rat spinal cords. *Magnetic Resonance in Medicine* 45:191–195.

Lauterbur PC (2004) Nobel Lecture. All science is interdisciplinary—From magnetic moments to molecules to men. *Bioscience Reports* 24:165–178.

Lauterbur PC (2005a) All science is interdisciplinary—from magnetic moments to molecules to men (Nobel lecture). Angewandte Chemie (International Ed. in English), 44:1004–1011.

Lauterbur PC (2005b) Reflections on MRI. *IEEE Signal Processing Magazine* 22:12–13.

Swain RA, Harris AB, Wiener EC, Dutka MV, Morris HD, Theien BE, Konda S, Engberg K, Lauterbur PC, Greenough W (2003) Prolonged exercise induces angiogenesis and increases cerebral blood volume in primary motor cortex of the rat. *Neuroscience* 117:1037–1046.

Appendix 3: Selected Articles About Paul Lauterbur, Arranged Chronologically

255598 Paullauterbur (2006 PE1). Minor Planet Center. Retrieved 3 September 2019. <https://www.minorplanetcenter.net/db_search/show_object?object_id=255598>

Becker ED (July 2007) Obituary: Paul Christian Lauterbur. *Physics Today* 60(7):77–78. Bibcode:2007PhT....60g..77B. DOI: 10.1063/1.2761815.

Chang K (March 28, 2007) Paul Lauterbur, MRI pioneer and Nobel Laureate, dies. International Herald Tribune (now *New York Times* International Edition). Retrieved 4 May 2018.

Dawson MJ (2012) Biographical memoir. U.S. National Academy of Sciences. http://www.nasonline.org/publications/biographical-memoirs/memoir-pdfs/lauterbur-paul.pdf

Dawson MJ (2013) Paul Lauterbur and the invention of MRI. Boston, MA: MIT Press, ISBN 9780262019217. https://www.journals.uchicago.edu/doi/abs/10.1086/688329>

Gill C (2004) Magnetic personality. http://www.umc.pitt.edu/pittmag/fall2004/feature1.html

Lauterbur PC (2003) Autobiography. Nobel Prize official website. Paul C. Lauterbur—Biographical. Nobelprize.org. Nobel Media AB. https://www.nobelprize.org/nobel_prizes/medicine/laureates/2003/lauterbur-bio.html

Lauterbur PC (2003) On Nobelprize.org including the Nobel Lecture All Science Is Interdisciplinary — From Magnetic Moments to Molecules to Men.

Lauterbur PC (September 1971) Genesis of the MRI (Magnetic Resonance Imaging) notebook (all pages freely available for download in a variety of formats from Science History Institute Digital Collections at digital.sciencehistory.org).

Physics History Network (2007) Paul C. Lauterbur. American Institute of Physics <https://history.aip.org/phn/11805001.html>; <https://www.journals.uchicago.edu/doi/abs/10.1086/688329>

Prasad A (March 14, 2014) Imperial technoscience: transnational histories of MRI in the United States, Britain, and India. Boston, MA: MIT Press, p. 17. ISBN 9780262026956. <https://mitpress.mit.edu/books/imperial-technoscience>

How to cite this article: Lauterbur ME, Govindjee [G] (2022) Paul C. Lauterbur (1929–2007): Discoverer of MRI, Father of ^{13}C NMR and 2003 Nobel Laureate. *LS - An International Journal of Life Sciences* 11(1):8-27.