John C.H. Spence

1946 - 2021

Biography

John C.H. Spence passed away on June 28, 2021 – a great loss for his family and many friends across the globe, as well as the scientific communities that he so brilliantly inspired. He was the Regent's Professor and Richard Snell Professor of Physics at Arizona State University, and the director of science for the NSF BioXFEL Science and Technology Center at Lawrence Berkeley National Lab. He made many innovative and highly original contributions to physics, materials science, and biology. He was also an outstanding teacher, and highly accomplished in a wide range of extra-curricular activities.

Spence had dual U.S. and Australian citizenship. He was born in Canberra, tragically lost his father (who was a fighter pilot) when only 4, and was raised, together with his sister Penelope, by their strong and loving mother, Vernon. In 1973 he married Susan Somerville, a University Lecturer in Child Psychology, and they had son Andrew, who is now an Associate Professor of Bioimaging at Temple University in Philadelphia. John and Susan divorced in 1998, and in 2001 he married Margaret Stanzler, a journalist and novelist.

He was inspired by EM work at CSIRO (when John Cowley was there) while working on his 1973 PhD on EELS, under Alan Spargo at the University of Melbourne, and even more so during his post-doc years in Peter Hirsch's group at Oxford. In 1976 he was recruited by John Cowley for ASU, where he worked for 45 years, collaborating with John Cowley, Sumio Iijima, Ondrej Krivanek, David Smith and many others, and established a strong research group of his own.

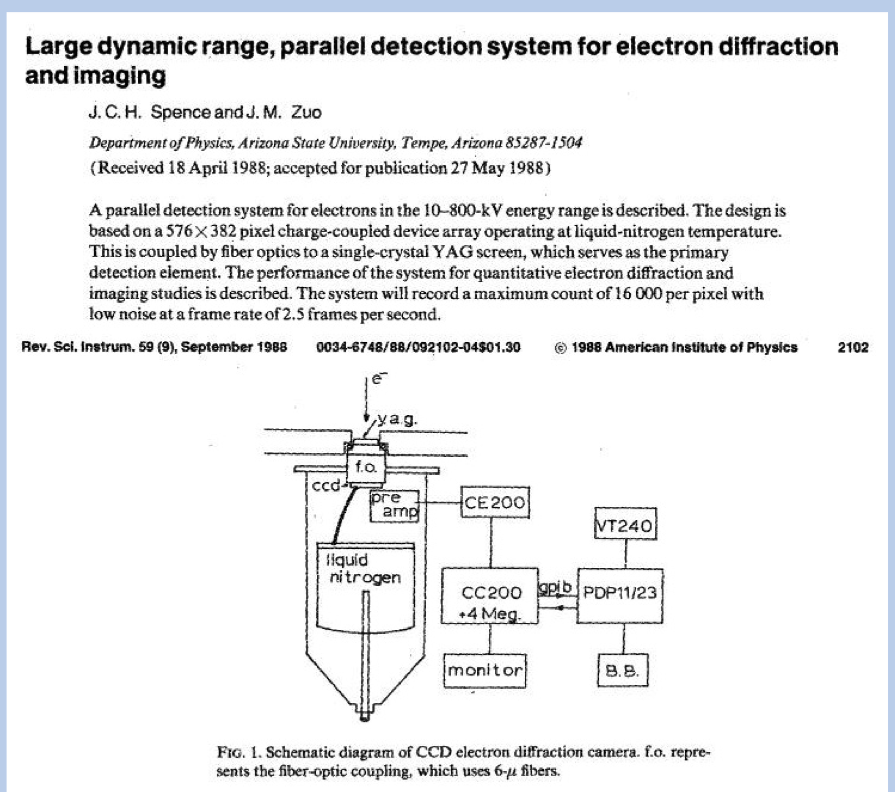
Spence was deeply interested in developing new instrumentation, for example by placing a scanning tunneling microscope in the sample holder of a transmission electron microscope, and his early work included developing sensitive cameras for TEM (Fig 3), some of which led to commercial cameras by Gatan. After working on the development of ALCHEMI (Fig. 4) and cathodoluminescence, he worked to produce the first clear picture of a chemical bond (Fig.5). He also became an expert on coherent diffractive imaging (Figs 6 and 7).

Spence never slowed down, and among the many activities in his final years, he wrote two general books (Fig. 10). He is survived by his wife Margaret, his sister Penelope, his son Andrew and Andrew's wife Rebecka, and grandchildren Maya and Lou.

Figure 1. As a classical and folk/rock musician, Spence often performed on guitar with the group *Moon Dogs* or on guitar or flute with the bassa nova group *Who Knew* along with other physicists and with the accomplished vocalist and keyboardist (and physicist) Nadia Zatsepin. The BioXFEL trio often performed at scientific conferences. Pictured is The BioXFEL Trio, with scientific collaborator Uwe Weierstall, playing *Sentimentale* by Claude Bolling at Caesar's Palace, Las Vegas, part of the BioXFEL 4th Annual International Conference, January 10 2017.

Figure 2. He built and owned sailboats, and he also sailed a 120-foot schooner, the *Zodiac* (pictured). He was a vintage car enthusiast, for example, the 1923 Rolls he restored in Australia (pictured), and a 1970 Jaguar E-type in the US. He received his private pilot's license in 2009; he preferred to fly a Schwiezer 1-26 sailplane (pictured).

Scientific Contributions



Large dynamic range, parallel detection system for electron diffraction and imaging

J. C. H. Spence and J. M. Zuo

Department of Physics, Arizona State University, Tempe, Arizona 85287-1504

(Received 18 April 1988; accepted for publication 27 May 1988)

A parallel detection system for electrons in the 10–800-kV energy range is described. The design is based on a 576×382 pixel charge-coupled device array operating at liquid-nitrogen temperature. This is coupled by fiber optics to a single-crystal YAG screen, which serves as the primary detection element. The performance of the system for quantitative electron diffraction and imaging studies is described. The system will record a maximum count of 16 000 per pixel with low noise at a frame rate of 2.5 frames per second.

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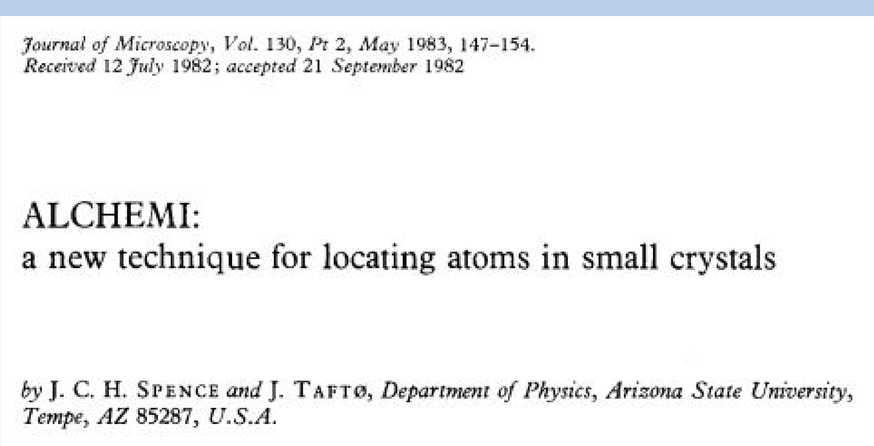
FIG. 1. Schematic diagram of CCD electron diffraction camera. f.o. represents the fiber-optic coupling, which uses 6-μ fibers.

Figure 3. One of his early contributions at ASU were the first CCD camera systems designed specifically for TEM.

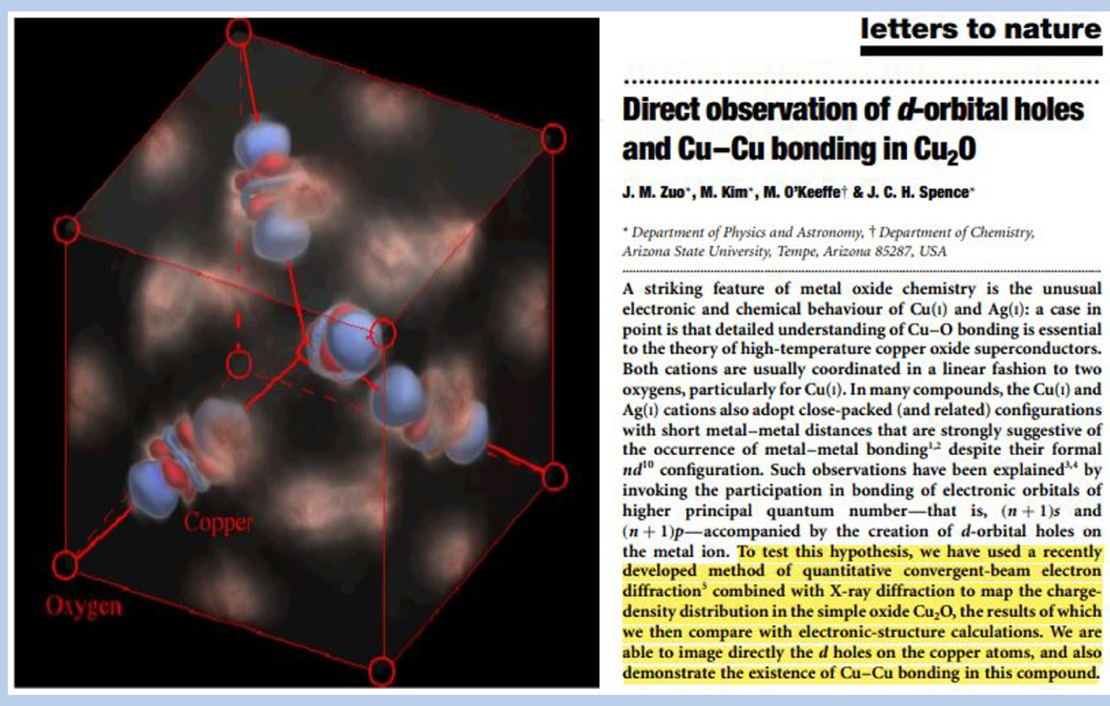


Journal of Microscopy, Vol. 130, Pt 2, May 1983, 147–154.
Received 12 *July* 1982; *accepted* 21 *September* 1982

ALCHEMI:
a new technique for locating atoms in small crystals

by J. C. H. SPENCE *and* J. TAFTØ, *Department of Physics, Arizona State University, Tempe, AZ 85287, U.S.A.*

Figure 4. together with J. Taftø, he invented ALCHEMI (Atom Location by Channeling Enhanced Microanalysis), which uses the electron wavefield propagating through a crystal as lens and locates dopant atoms by measuring X-ray fluorescence as a function of the phase of a standing wave.



letters to nature

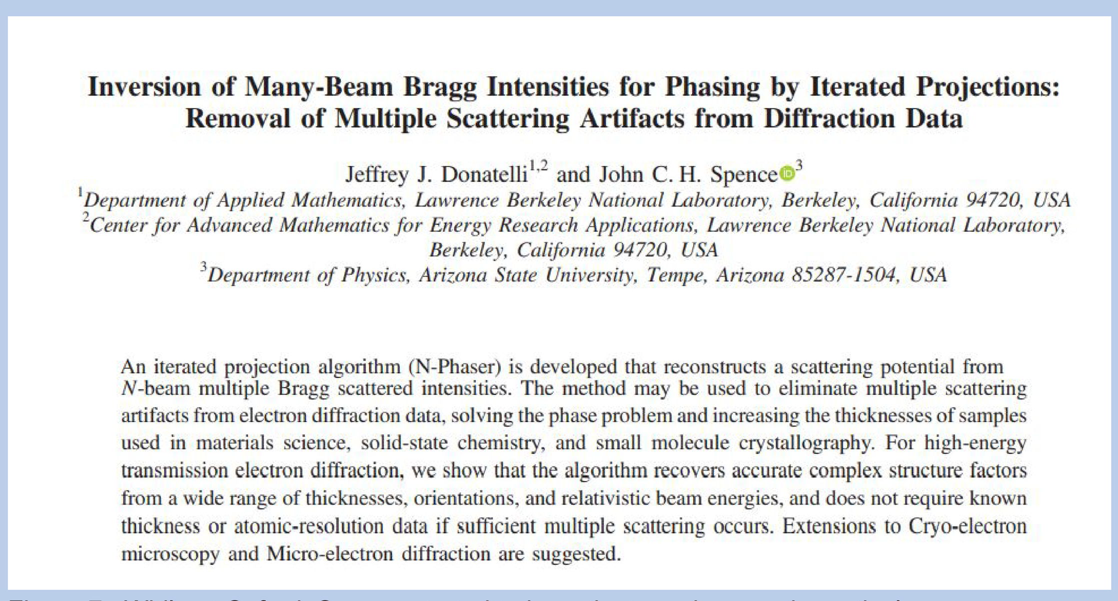
Direct observation of *d*-orbital holes and Cu–Cu bonding in Cu_2O

J. M. Zuo*, M. Kim*, M. O'Keeffe† & J. C. H. Spence*

* *Department of Physics and Astronomy,* † *Department of Chemistry, Arizona State University, Tempe, Arizona 85287, USA*

A striking feature of metal oxide chemistry is the unusual electronic and chemical behaviour of Cu(I) and Ag(I): a case in point is that detailed understanding of Cu–O bonding is essential to the theory of high-temperature copper oxide superconductors. Both cations are usually coordinated in a linear fashion to two oxygens, particularly for Cu(I). In many compounds, the Cu(I) and Ag(I) cations also adopt close-packed (and related) configurations with short metal–metal distances that are strongly suggestive of the occurrence of metal–metal bonding[1,2] despite their formal nd^{10} configuration. Such observations have been explained[3,4] by invoking the participation in bonding of electronic orbitals of higher principal quantum number—that is, $(n+1)s$ and $(n+1)p$—accompanied by the creation of *d*-orbital holes on the metal ion. To test this hypothesis, we have used a recently developed method of quantitative convergent-beam electron diffraction[5] combined with X-ray diffraction to map the charge-density distribution in the simple oxide Cu_2O, the results of which we then compare with electronic-structure calculations. We are able to image directly the *d* holes on the copper atoms, and also demonstrate the existence of Cu–Cu bonding in this compound.

Figure 5. Together with M. O'Keefe and J.M. Zuo, Spence continued developing convergent-beam electron diffraction in the STEM to quantitatively and accurately map charge density distributions. Combining CBED and ALCEMI, he produced the first images mapping the charge density of non-ionic bonds in Cu2O.



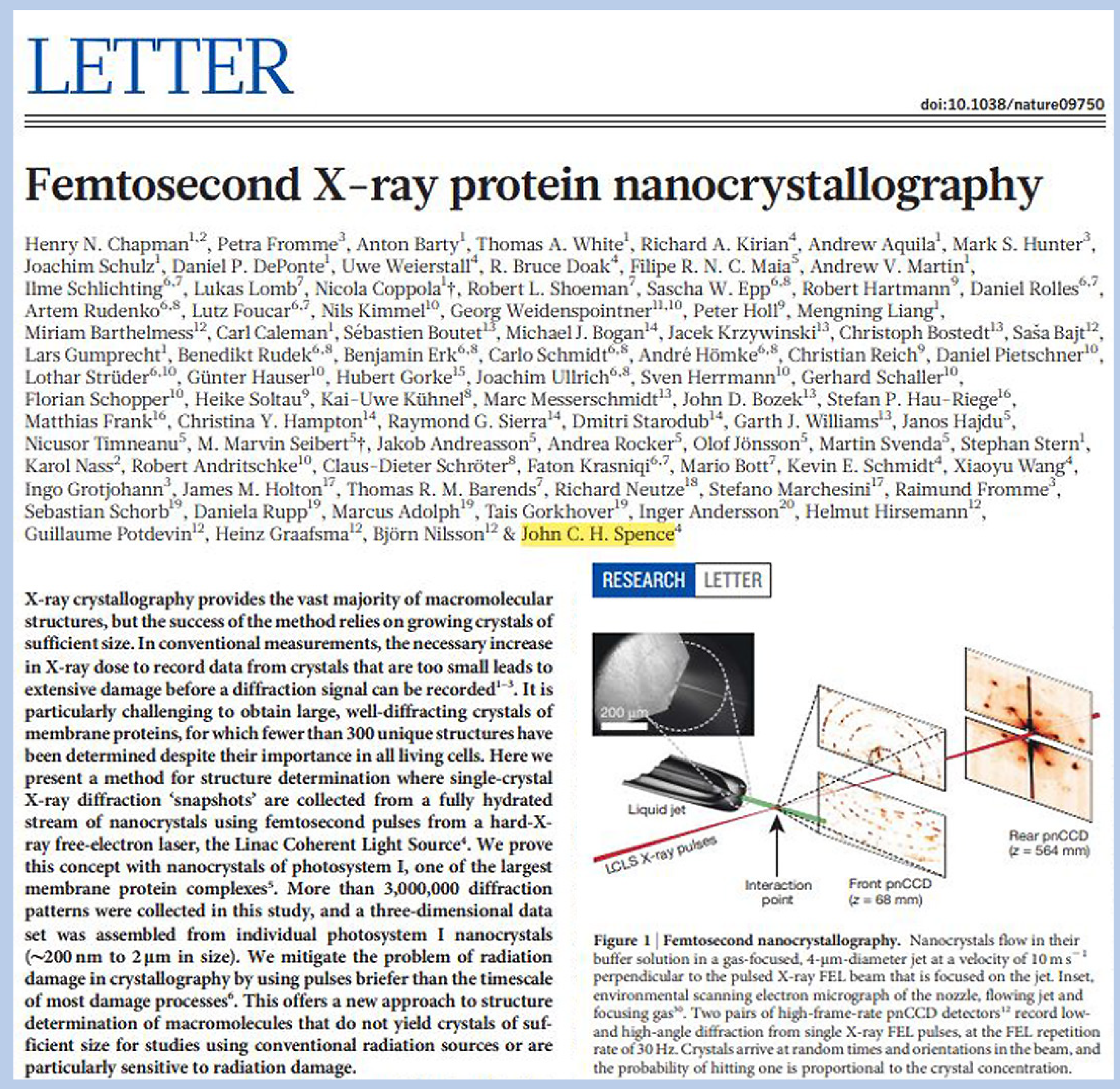
Inversion of Many-Beam Bragg Intensities for Phasing by Iterated Projections: Removal of Multiple Scattering Artifacts from Diffraction Data

Jeffrey J. Donatelli[1,2] and John C. H. Spence[3]

[1] *Department of Applied Mathematics, Lawrence Berkeley National Laboratory, Berkeley, California 94720, USA*
[2] *Center for Advanced Mathematics for Energy Research Applications, Lawrence Berkeley National Laboratory, Berkeley, California 94720, USA*
[3] *Department of Physics, Arizona State University, Tempe, Arizona 85287-1504, USA*

An iterated projection algorithm (N-Phaser) is developed that reconstructs a scattering potential from *N*-beam multiple Bragg scattered intensities. The method may be used to eliminate multiple scattering artifacts from electron diffraction data, solving the phase problem and increasing the thicknesses of samples used in materials science, solid-state chemistry, and small molecule crystallography. For high-energy transmission electron diffraction, we show that the algorithm recovers accurate complex structure factors from a wide range of thicknesses, orientations, and relativistic beam energies, and does not require known thickness or atomic-resolution data if sufficient multiple scattering occurs. Extensions to Cryo-electron microscopy and Micro-electron diffraction are suggested.

Figure 7. While at Oxford, Spence started to investigate various mathematical approaches to directly solve the many-beam dynamical diffraction inversion problem for determining unknown crystal structures. He kept returning to this quest for the rest of his life and was finally able to publish an elegant and complete solution based upon an iterative method: Donatelli, J. J. & Spence, J. C. (2020) Inversion of many-beam Bragg intensities for phasing by iterated projections: removal of multiple scattering artifacts from diffraction data. Phys. Rev. Lett. 125: 065502.



LETTER

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Femtosecond X-ray protein nanocrystallography

Henry N. Chapman[1,2], Petra Fromme[3], Anton Barty[1], Thomas A. White[1], Richard A. Kirian[4], Andrew Aquila[1], Mark S. Hunter[3], Joachim Schulz[1], Daniel P. DePonte[1], Uwe Weierstall[4], R. Bruce Doak[4], Filipe R. N. C. Maia[5], Andrew V. Martin[1], Ilme Schlichting[6,7], Lukas Lomb[7], Nicola Coppola[1]†, Robert L. Shoeman[7], Sascha W. Epp[6,8], Robert Hartmann[9], Daniel Rolles[6,7], Artem Rudenko[6,8], Lutz Foucar[6,7], Nils Kimmel[10], Georg Weidenspointner[11,10], Peter Holl[9], Mengning Liang[1], Miriam Barthelmess[12], Carl Caleman[1], Sébastien Boutet[13], Michael J. Bogan[14], Jacek Krzywinski[13], Christoph Bostedt[13], Saša Bajt[12], Lars Gumprecht[1], Benedikt Rudek[6,8], Benjamin Erk[6,8], Carlo Schmidt[6,8], André Hömke[6,8], Christian Reich[9], Daniel Pietschner[10], Lothar Strüder[6,10], Günter Hauser[10], Hubert Gorke[15], Joachim Ullrich[6,8], Sven Herrmann[10], Gerhard Schaller[10], Florian Schopper[10], Heike Soltau[9], Kai-Uwe Kühnel[8], Marc Messerschmidt[13], John D. Bozek[13], Stefan P. Hau-Riege[16], Matthias Frank[16], Christina Y. Hampton[14], Raymond G. Sierra[14], Dmitri Starodub[14], Garth J. Williams[13], Janos Hajdu[5], Nicusor Timneanu[5], M. Marvin Seibert[5]†, Jakob Andreasson[5], Andrea Rocker[5], Olof Jönsson[5], Martin Svenda[5], Stephan Stern[1], Karol Nass[2], Robert Andritschke[10], Claus-Dieter Schröter[8], Faton Krasniqi[6,7], Mario Bott[7], Kevin E. Schmidt[4], Xiaoyu Wang[4], Ingo Grotjohann[3], James M. Holton[17], Thomas R. M. Barends[7], Richard Neutze[18], Stefano Marchesini[17], Raimund Fromme[3], Sebastian Schorb[19], Daniela Rupp[19], Marcus Adolph[19], Tais Gorkhover[19], Inger Andersson[20], Helmut Hirsemann[12], Guillaume Potdevin[12], Heinz Graafsma[12], Björn Nilsson[12] & John C. H. Spence[4]

X-ray crystallography provides the vast majority of macromolecular structures, but the success of the method relies on growing crystals of sufficient size. In conventional measurements, the necessary increase in X-ray dose to record data from crystals that are too small leads to extensive damage before a diffraction signal can be recorded[1–3]. It is particularly challenging to obtain large, well-diffracting crystals of membrane proteins, for which fewer than 300 unique structures have been determined despite their importance in all living cells. Here we present a method for structure determination where single-crystal X-ray diffraction 'snapshots' are collected from a fully hydrated stream of nanocrystals using femtosecond pulses from a hard-X-ray free-electron laser, the Linac Coherent Light Source[4]. We prove this concept with nanocrystals of photosystem I, one of the largest membrane protein complexes[5]. More than 3,000,000 diffraction patterns were collected in this study, and a three-dimensional data set was assembled from individual photosystem I nanocrystals (~200 nm to 2 μm in size). We mitigate the problem of radiation damage in crystallography by using pulses briefer than the timescale of most damage processes[6]. This offers a new approach to structure determination of macromolecules that do not yield crystals of sufficient size for studies using conventional radiation sources or are particularly sensitive to radiation damage.

RESEARCH LETTER

Figure 1 | Femtosecond nanocrystallography. Nanocrystals flow in their buffer solution in a gas-focused, 4-μm-diameter jet at a velocity of $10\ m\ s^{-1}$ perpendicular to the pulsed X-ray FEL beam that is focused on the jet. Inset, environmental scanning electron micrograph of the nozzle, flowing jet and focusing gas[30]. Two pairs of high-frame-rate pnCCD detectors[12] record low- and high-angle diffraction from single X-ray FEL pulses, at the FEL repetition rate of 30 Hz. Crystals arrive at random times and orientations in the beam, and the probability of hitting one is proportional to the crystal concentration.

Figure 6. Spence initiated a series of international workshops on coherence and phase retrieval, bringing together CBED, electron holography and ptychography, as well as X-ray diffractive imaging communities. This led to work on time-resolved x-ray imaging with free-electron lasers of streams of individual, hydrated nanocrystals, thus avoiding the need for the larger crystal formation needed for X-ray crystallograpgy. Orientation with a laser required liquid microjets for delivery, which was perfected with Bruce Doak, Dan Deponte and Uwe Weierstall. Consequently, from the 1990s, he established the new field of serial femtosecond crystallography, using X-ray free-electron lasers the Linac Coherent Light Source at LBNL, the first X-ray free-electron laser. Imaging with femtosecond coherent x-rays enabled one to do ("diffraction before destruction"), outrunning the radiation damage that is typically a problem in biological EM. Photons scattered from the same molecule accumulate, but not those from different molecules. The X-ray laser structural biology work was ranked among the top 10 scientific breakthroughs of 2012 by *Science* magazine. Together with Janos Hajdu and Henry Chapman, Spence was awarded the 2021 Gregori Aminoff Prize of the Royal Swedish Academy of Sciences for their contributions to FEL-based structural biology.

Books

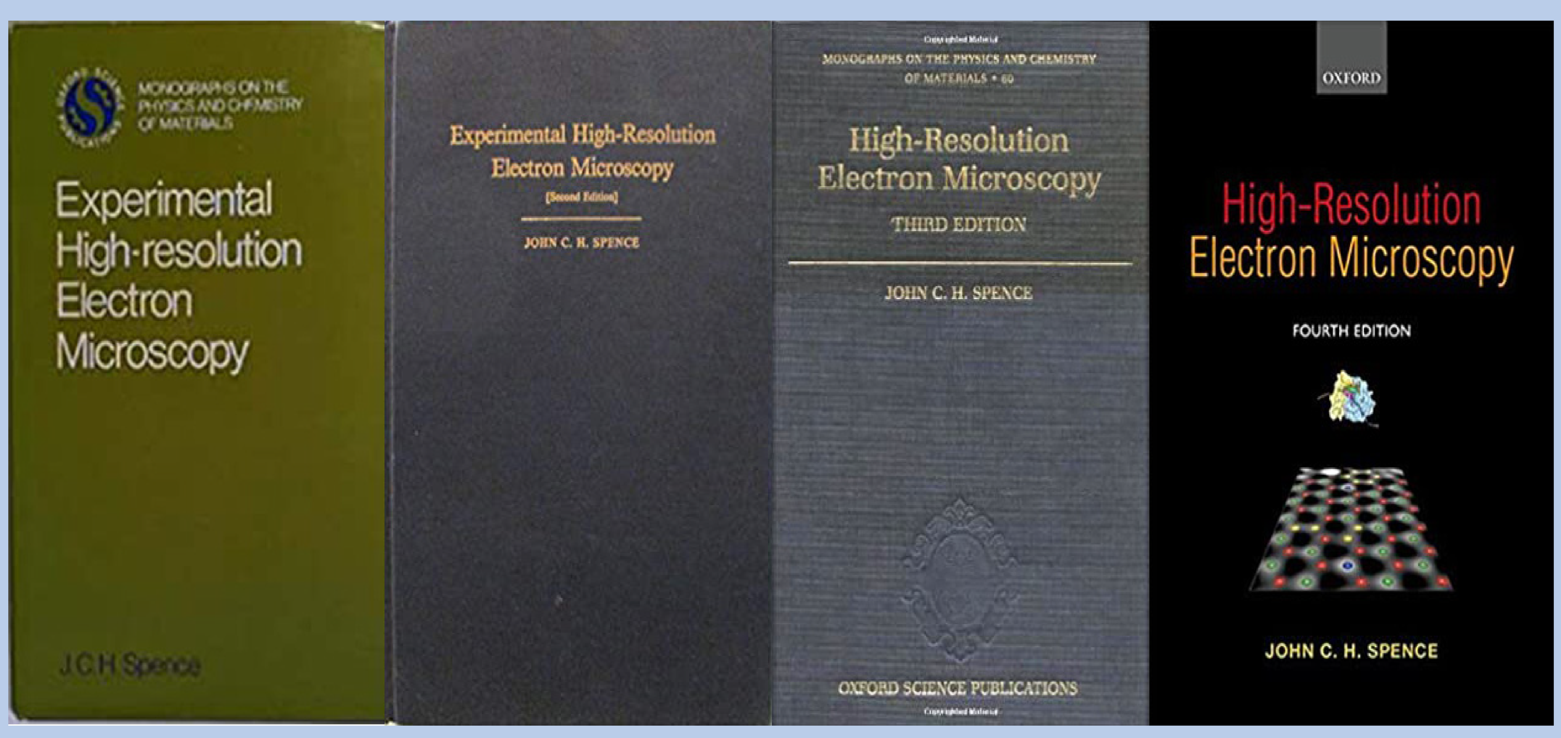

Figure 8. Author of four editions of books on HREM: *Experimental High-Resolution Electron Microscopy* (1980, 1988); *High-Resolution Electron Microscopy* (2003, 2013).

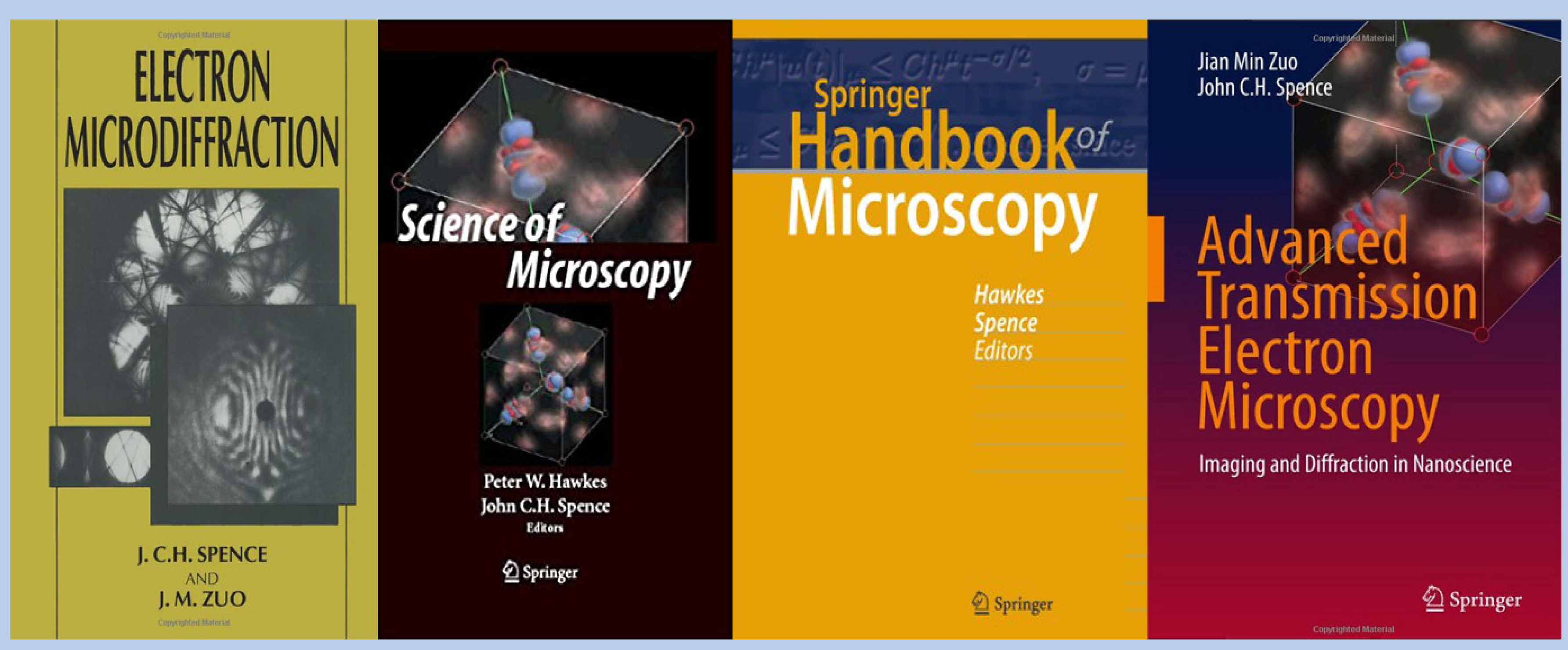

Figure 9. Co-author of other Science books: *Electron Microdiffraction* (1992), *Science of Microscopy* (2006), *Advanced TEM* (2017), *Handbook of Microscopy* (2019).

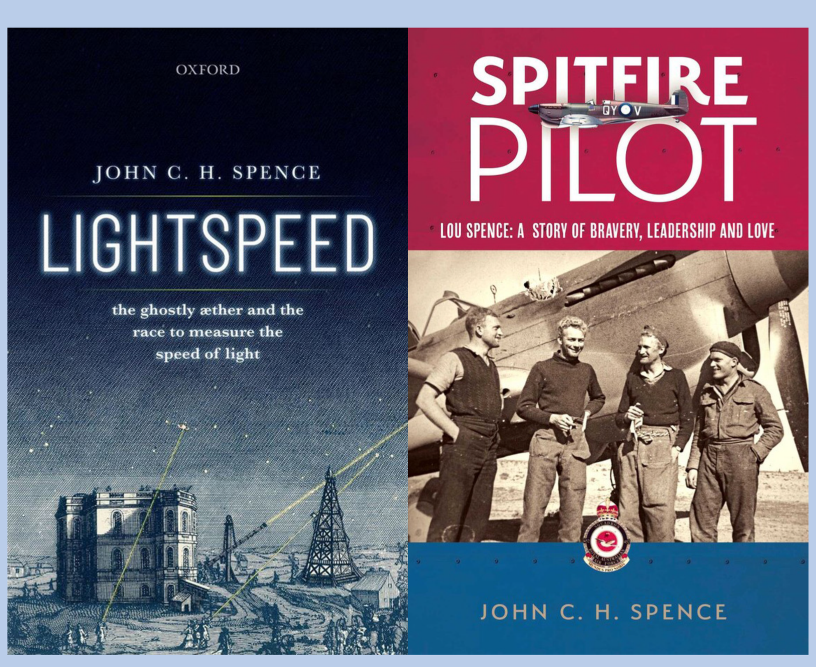

Figure 10. Author of other books: *Lightspeed* (2019), on the history of attempts to measure the speed of light, leading to Einstein's theories and *Spitfire Pilot* (2021), on his father, Wing Commander Lou Spence, a fighter pilot in World War 2 who flew in combat in the Middle East and in Spitfires against the attempted Japanese invasion of Australia. He passed away (when John was four years old) leading the Australian Airforce Mustangs of RAAF 77 Squadron in their contribution to the Korean War. His grandfather, John Swain, flew with the Royal Flying Corp at Gallipoli, and John proudly displayed a damaged propeller from his grandfather's airplane in his Arizona home.

Honors

- Fellow of the American Physical Society
- Fellow of the Institute of Physics (UK)
- Overseas fellow of Churchill College Cambridge, UK
- Burton Medal, Microscopy Society of America (1980)
- Distinguished Scientist Award and Fellow of the Microscopy Society of America (2006)
- Buerger Award of the American Crystallographic Society (2012)
- J.M. Cowley Medal of the International Federation of Societies of Microscopy (2014)
- Foreign Member of the Royal Society (ForMemRS) (2015)
- Honorary Fellow of the Royal Microscopical Society (HonFRMS) (2017)
- Gregori Aminoff Prize (2021)

A *Festschrift* volume of *Ultramicroscopy* appeared in July 2011.

Committees, Editorships

- Worked on making *IUCrJ* a natural home for FEL Science and Technology.
- At the 5 December 2012 launch of *IUCrJ*, the main editors were Baker, Catlow, Desiraju, Larsen, and Spence.
- From the start, Spence was the main editor for physics and FEL Science and Technology.
- IUCr Commission on Electron Diffraction (now Electron Crystallography) (1996–2002; Chair 2002–2005)
- IUCr Commission on Charge, Spin and Momentum Densities (now Quantum Crystallography) (1999–2008).
- Co-editor of *Acta Cryst. (A)* for North America (Diffraction Physics, 1990-2000)
- Scientific Advisory Committees at LBNL
- Member of the DOE BESAC Committee

Acknowledgements

- *Hawkes PW (2021) Ultramicroscopy 231:113323.*
- *Chapman HN, Hasnainmn SS, Weierstall U. (2021) IUCrJ 8:705–708.*
- *Memoriam, ASU News, 2021*
- *Ondrej Krivanek, personal commmunication*
- *Wikipedia*
- *Obituary, Royal Microscopy Society, 2021*
- *Obituary, Dee Funeral Home, Concord, MA, 2021*