Springer Handbook of Microscopy

Hawkes
Spence
Editors

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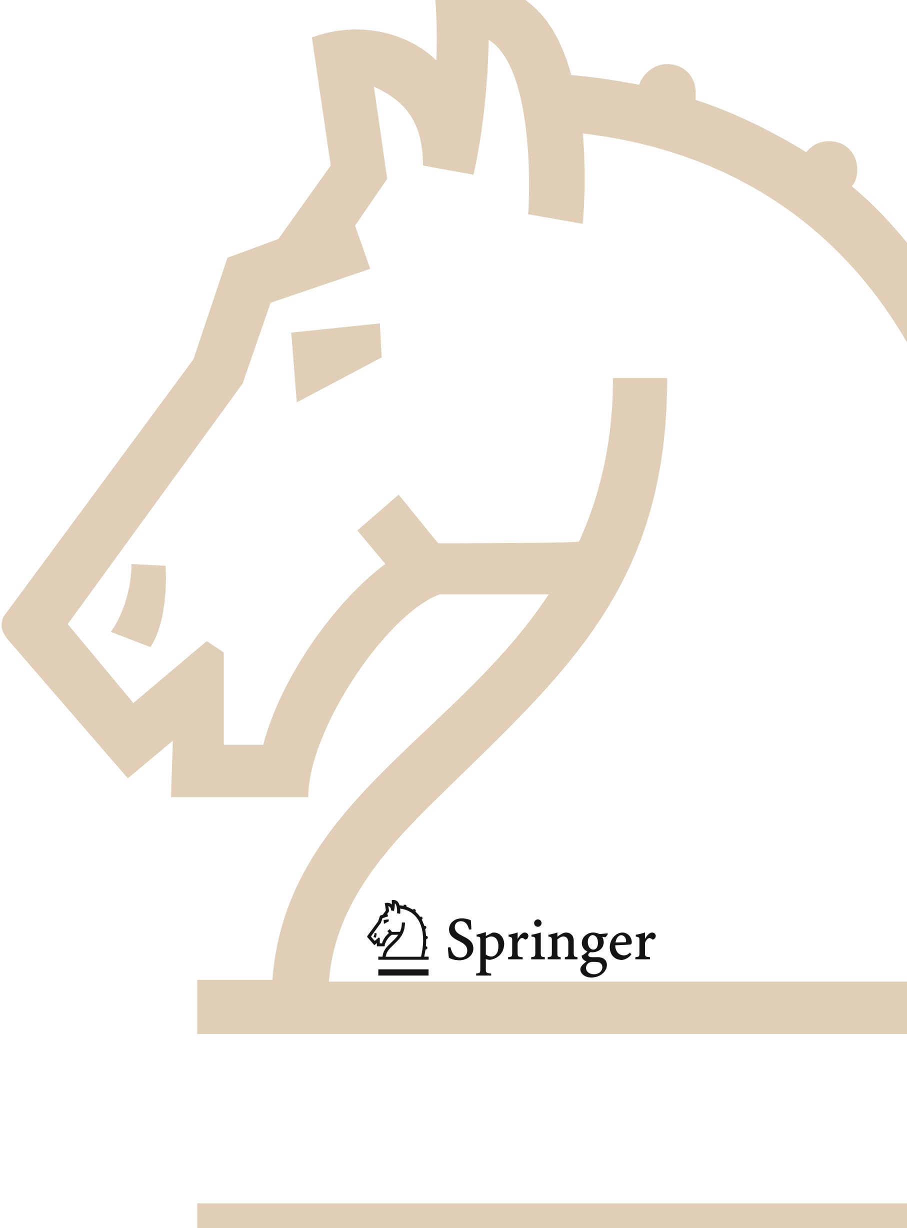
Peter W. Hawkes, John C. H. Spence (Eds.)

With 1140 Figures and 37 Tables



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Preface

Since *Science of Microscopy*, the predecessor of this book, appeared in 2007, three Nobel prizes of direct relevance to the field have been awarded. The first of these was the award to Boyle and Smith in 2009 for the invention of the charge-coupled device, which was primarily responsible for making digital imaging possible. The second was the award to Betzig, Hell, and Moerner in 2014 for the development of superresolution fluorescence microscopy, and the third to Dubochet, Frank, and Henderson in 2017 was given for their work in developing the cryo-electron microscopy technique for biology. The fact that radiation damage effects may be *out-run* by using sufficiently brief femtosecond x-ray pulses from a hard x-ray laser was also demonstrated in this period. At the same time, there has been a great surge in the application of many tomographic imaging methods in medicine (such as the microCT method covered in this book); indeed, an imaging revolution is underway in that area. In many hospitals, some form of 3-D imaging is now the first diagnostic method applied to incoming trauma victims.

For this new edition, now published as the *Springer Handbook of Microscopy*, we have again asked many of the leaders in the field of modern microscopy to summarize the latest approaches to the imaging of atoms or molecular structures, and, more especially, the way in which this aids our understanding of atomic processes and interactions in the organic and inorganic worlds.

Man's curiosity and the desire to examine the nanoworld goes back at least as far as Ancient Greece. Aristophanes, in a fourth-century BC play, refers to a burning glass; the Roman rhetorician Seneca describes hollow spheres of glass filled with water being used as magnifiers, while Marco Polo in the thirteenth century remarks on the Chinese habit of wearing spectacles. Throughout this time it would have been common knowledge that a drop of water over a particle on glass will provide a magnified image, while a droplet within a small hole does even better as a biconvex lens. By the sixteenth century, magnifying glasses were common in Europe. Kepler appears to have been the first to draw the correct ray-diagram for image formation, with rays leaving an object point over a wide angular range and gathered to a focus by a lens. His book *Paralipomena* on optics, printed in 1604, shows the correct ray diagram for a spherical glass lens, while his *Dioptrice* (1611) gives an explanation of the functioning of the lenses in Galileo's telescope. Although Kepler did not derive the *lens laws* taught to undergraduate science students today, he does reveal an understanding of the formation of virtual images, which arise with mirrors. These books contain the earliest correct ray diagrams from which the whole subject of geometric optics was later developed.

It was Anthony van Leeuwenhoek (1632–1723) who first succeeded in grinding lenses accurately enough to produce a better image with his single-lens instrument than that produced with the primitive compound microscopes that were available then. His 112 papers, published in *Philosophical Transactions of the Royal Society*, brought the microworld to the general scientific community for the first time, covering everything from sperm to the internal structure of the flea. Robert Hooke (1635–1703) developed the compound microscope, publishing his results in careful drawings of what he saw in his *Micrographia* (1665). The copy of this book in the University of Bristol library shows remarkable sketches of faceted crystallites, below which he had drawn piles of cannon balls, whose faces make corresponding angles. This strongly suggests that Hooke believed that matter consists of the small spheres (atoms) which could produce these facet angles, and had made this discovery long before its official rediscovery by the first modern chemists, notably Dalton in 1803. Greeks such as Leucippus (450 BC) had long before convinced themselves that a stone, cut repeatedly, would eventually lead to *a smallest fragment* or fundamental particle; Democritus once said that "nothing exists except atoms and empty space. All else is opinion."

This atomic hypothesis has a fascinating history, and is intimately connected with the history of microscopy. It was Brown's observation in 1827 of the motion of pollen in water by optical microscopy that laid the basis for the modern theory of matter based on atoms. As late as 1900 many chemists and physicists did not believe in atoms, despite the many independent estimates that could be made of their size. Avogadro's idea, around 1811 that equal volumes of gas contained the same number of molecules (regardless of their size) had a powerful influence. This number was first estimated by Johann Loschmidt in 1865. Faraday's experiments on electrolysis related mass to an electron current and the charge it carried. The electron and its charge-to-mass ratio were discovered by

J.J. Thomson in 1897. The evidence for the existence of atoms was summarized by Kelvin and Tait in an appendix to their *Treatise on Natural Philosophy*, together with an erroneous and rather superficial estimate of the young age of the Earth, to be used against Darwin. This text was the standard English-language physics text of the late nineteenth century, despite its failure to cover much of Maxwell's work. Einstein's 1905 theory of Brownian motion, and Perrin's (1909) more accurate repetition of Brown's experiment, using microscope observations to estimate Avogadro's number, finally settled the matter regarding the existence of atoms. Einstein does not reference Brown's paper but indicates that he had been told about it. As Professor Archie Howie from Cambridge, UK, commented, it is interesting to speculate how different the history of science would be if Maxwell had read Brown's paper and applied his early statistical mechanics to it. By the time of Perrin's paper, Bohr, Thomson, Rutherford, and others were firmly committed to atomic and even subatomic physics.

In biology, the optical microscope remained an indispensable tool from van Leeuwenhoek's time with many incremental improvements. It was able to identify bacteria and their role in disease, but not viruses, which were too small. These were first seen with the transmission electron microscope (TEM) in 1938 by Ernst Ruska's brother Helmut. With Zernike's phase contrast theory in the 1930s, a major step forward was taken, but the really dramatic and spectacular modern advances had to await the widespread use of the modern TEM with new sample preparation methods and the development of the cryo-EM method. The invention of the laser and superresolution optical modes, the charge-coupled device (CCD) and more recent direct-electron detectors, the introduction of scanning modes and probes, computer control, and data acquisition, powerful new algorithms for data analysis and the production of fluorescent proteins led to further major advances.

The importance of this early history should not be underestimated – in the words of Richard P. Feynman

> If in some cataclysm, all scientific knowledge were to be destroyed and only one sentence passed on to the next generation of creatures, what statement would contain the most information in the fewest words? I believe it is the atomic hypothesis – that all things are made of atoms.

Images of individual atoms were first provided by Erwin Müller's field-ion microscope in the early 1950s, soon to be followed by Albert Crewe's scanning transmission electron microscope (STEM) images of heavy atoms on thin-film surfaces in 1970. With its sub-ångström resolution, the modern transmission electron microscopes can now routinely image atomic columns in thin crystals in projection, individual atoms in 2-D materials, and even foreign atoms within a thin crystal using beam-electrons that have excited inner-shell atomic processes. For favorable surface structures, the scanning tunneling microscope has provided us with images of individual surface atoms since its invention in 1982 and resulted in a rich spin-off of related techniques, such as the scanning tunneling spectroscopy method, the near-field probes, and the atomic force microscope.

The particles used to probe condensed and biological matter must possess a long lifetime if they are to be used as free-particle beams. For the most part, this has limited investigators to the use of light, x-rays, neutrons, and electrons. The major techniques can then be classified as imaging, diffraction, and spectroscopy. These may be used in both the transmission and reflection geometries, giving bulk and surface information, respectively. Under these general headings, in Chap. 9 we review both the low-energy electron microscope (LEEM) and spin-polarized LEEM methods which, using reflected electrons, have revolutionized surface science and thin-film magnetism. Here, the high cross-section allows movies to made of surface processes at submicrometer resolution, while Auger electron spectroscopy is conveniently incorporated. Chapter 11 describes the spectacular progress that has been made with spectroscopic LEEM since the previous edition of this book. Here, the electron prism in the instrument provides dispersion for spectroscopy of the electrons reflected from a clean surface. A remarkable resolution of 1.5 nm has now been obtained by such a LEEM at 3.5 eV, and an energy resolution of about 100 meV, both being invaluable for studies aimed at imaging crystal growth, the study of catalysis, and work-function imaging. Chapter 10 deals with the closely related photoelectron microscopy, where a LEEM instrument is used to image the photoelectrons excited by a synchrotron beam. Here, the superb energy selectivity of optical excitation can be used to great advantage. With the importance of 2-D materials, including graphene and all its descendants that are now recognized, PEEM studies of the growth of new 2-D materials have taken on a new lease of life. In angle-resolved mode, maps of Fermi surfaces can now be made routinely at synchrotrons, as described also in Chap. 11. Chapter 5, based on the earlier chapter by the late Rudi Reichelt, describes advances in scanning electron microscope (SEM) research, where the lower-energy secondary electrons provide images with a large depth of focus in the most versatile of all electron-optical instruments. Chapter 6 reviews the functioning of this instrument at higher pressures than in the conventional SEM and its use for environmental electron microscopy. The numerous modes of operation include x-ray analysis, cathodoluminescence, low-voltage modes for insulators, and the controlled-atmosphere environmental SEM (ESEM). A similar instrument can be devised using a gas field-ion source instead of an electron source. This scanning ion microscope uses the methods of field-ion microscopy to obtain an atomically sharp source of ions (such as 30 kV helium ions), which are focused and scanned across the sample. Chapter 14 gives us a full account of this exciting new microscopy, which has emerged since the first edition. It includes a full account of ion–sample interactions, the resulting signals that can be detected, contrast mechanisms for transmitted and reflected modes, the analytical capabilities of the instrument, and its applications. The atom probe itself is described in Chap. 15, including a full history of the field-ion microscope, the methods of the analytical atom probe (which identifies the atoms in the image) including laser pulsing of the tip, and the use of a smaller counter electrode at lower voltage placed close to the needle-shaped sample, and giving a higher electric field and better mass resolution. As the summary of applications shows, the resulting instruments have also emerged as a successful new form of microscopy since the first edition of this book.

Turning now to the transmission geometry, we review the latest work in atomic-resolution transmission electron microscopy (TEM) in Chap. 1, the technique that has transformed our understanding of defect processes in crystalline solids and nanostructures. In that connection, Chap. 12 provides a review of the role of modeling in TEM to obtain higher resolution and decide among the alternative likely structures seen in the images. Chapter 26 describes the extension of the high-resolution TEM approach to 3-D image reconstruction, using multiple projections. Given the need to obtain many different projections all at atomic resolution without significant radiation damage, this has proven to be an enormously difficult problem, for which there has been dramatic progress since the previous edition. Chapter 29 reviews the application of this high-resolution TEM approach, combined with other diffraction methods, to the important class of mesoporous materials (zeolites and the newly discovered class of metal-organic framework structures). These highly radiation-sensitive materials are finding many new applications for gas storage and petrochemical catalysis and provide one of the most challenging samples for TEM work. Spectacular results have been obtained (resulting in high honors for the scientists), and there appears to be no other way to determine the structure of this critical new class of nanostructured material. The scanning transmission mode is treated in Chap. 2. The scanning transmission electron microscope (STEM) provides additional powerful analytical capability, which, like STM, can provide spectroscopy with atomic-scale spatial resolution and many other signals, such as cathodoluminescence, energy-loss spectroscopy and characteristic inner-shell x-ray detection. Recently, atomic-resolution images have been produced using this x-ray fluorescence signal. The closely-related electron microdiffraction method, which uses the subnanometer probe of the STEM in the transmission geometry, is described in Chap. 18. The analysis of the resulting nanodiffraction patterns has proven particularly powerful for the study of the nanoparticles used in catalysis and their associated strain fields. An entire chapter (Chap. 7) is then devoted to analytical TEM (AEM), with a detailed analysis of the physics and performance of its two main detectors, for characteristic x-ray emission and energy-loss spectroscopy. The remarkable recent achievements of in-situ TEM are surveyed in Chap. 3, including transmission imaging of liquid cell electrolysis, observations of the earliest stages of crystal and nanotube growth, phase transitions and catalysts, superconductors, magnetic and ferroelectric domains and plastic deformation in thin films, all at nanometer resolution or better. Again, the large scattering cross-section of electron probes provides plenty of signal even from individual atoms, so that movies can be made. Chapter 8 summarizes the dramatic recent revival of time-resolved electron microscope imaging, which uses laser-pulses to excite processes in a sample prior to imaging them. The excited state may be imaged by passing the delayed optical pulse to the photocathode of the TEM in the *pump-probe* mode. Single-shot transmission electron diffraction patterns have now been obtained using electron pulses as short as a picosecond.

Most of these techniques are undergoing a quiet revolution as aberration corrector devices are being fitted to electron microscopes. The dramatic revelation that, after 60 years of effort, aberration correction is now a reality, was made about 20 years ago, and we review the relevant electron-optical theoretical background in Chap. 13. The same chapter includes an account of monochromators, which help to combat the effects of chromatic aberration, and energy analyzers. Also in the transmission geometry, there have been rapid advances in high-energy pulsed electron diffraction, with pulses as brief as 10 fs at MeV energies having been generated recently. Pump-probe methods can now be used by this technique to detect time-resolved diffuse scattering between Bragg reflections from phonons in a thin crystal. This field is reviewed in Chap. 19. Finally, in biology, perhaps the largest scientific payoff of all has occurred in the field of cryo-electron microscopy, which now seriously challenges all protein crystallography performed at synchrotrons. This is largely the result of the recent *resolution revolution* fueled by the development of new TEM detectors, which can record the arrival of every beam electron under the low-dose conditions used. There are three kinds of cryo-electron microscopy—single-particles, tomography, and 2-D crystals. Images of many projections of similar particles are merged in the single particle mode, whereas many projections of the same particle are merged in tomography. The increased radiation damage in the tomography mode leads to lower resolution. The grand challenge of locating every protein and molecular machine in a single cell remains outstanding, but many molecular mechanisms and drug binding processes have now been elucidated at a resolution of a few ångströms. We summarize this exciting field in Chap. 4.

Electrons, with the largest cross-section, a coherent source brighter than current generation synchrotrons, and now single-electron detectors, provide the strongest signal and, hence, the best resolution. They do this in a manner that can conveniently be combined with spectroscopy, and we now have aberration corrected lenses for them. However, multiple scattering and inelastic background scattering often complicate interpretation. Electrons in a beam continue on to the detector after losing energy while traversing a sample, making an unwanted background, unlike x-rays, which are annihilated after creating a photoelectron, which is not usually detected. X-ray imaging of nanostructures, even at synchrotrons, involves much longer data acquisition times, but the absence of background and multiple scattering effects greatly improves quantification of data, and thicker samples can be examined. It can be shown that the small magnitude of the fine-structure constant will almost certainly never permit imaging of individual atoms using x-rays, unless data from identical particles is merged. We should recall that in protein crystallography, about 98% of the x-ray beam hits the beam-stop after traversing the sample and does not interact with the sample at all. Of the remaining 2%, 84% is annihilated in production of photoelectrons, and 8% in Compton scattering, while only the remainder produces Bragg diffraction. By comparison, electron scattering depends sensitively on sample thickness, and the direct beam is rapidly both diffracted and inelastically scattered away by multiple scattering to negligible intensity with increasing thickness. This thickness sensitivity means that, apart from work on monolayers, electron diffraction intensities are far less reproducible than x-ray scattered intensities, making quantification more difficult. Generally speaking, it is not difficult to record the same Bragg intensity ratios from two crystals of the same structure but different size, using x-ray diffraction; this is impossible using electron diffraction, unless they both have dimensions of tens of nanometers or less. For light elements the inelastic cross-section for kilovolt electrons is about three times that of the elastic cross-section, unlike hard x-rays, where the photoelectric effect is far stronger than elastic scattering. Success with x-rays has come mainly through the use of crystallographic redundancy to reduce radiation damage in protein crystallography. Nevertheless, soft x-ray imaging using zone-plate lenses now provides about 20 nm resolution in the *water window*, with the advantages of thicker samples and imaging in an aqueous environment. Applications of *full-field* zone-plate microscopy have also been found in environmental science, materials science, and magnetic materials. In addition, the equivalent of the STEM has been developed for soft x-rays: the scanning transmission x-ray microscope (STXM), which uses a zone-plate to focus x-rays onto a sample that can be raster scanned by piezo-electric motors. This arrangement can then provide spatially-resolved x-ray absorption spectroscopy. That work is reviewed in Chap. 23. Chapter 24 reviews the highly successful microcomputed tomography method, in which the absorption of an x-ray beam passing through a sample is recorded from many different directions, allowing a 3-D image to be reconstructed.

Both x-ray and electron-beam imaging methods are limited in biology by the radiation damage they create, unlike microscopy with visible light, which also allows observations in the natural state. Optical microscopy has now undergone a revolution, with the development of superresolution, two-photon, fluorescent labeling, and scanning confocal methods. These methods are reviewed in Chaps. 21 and 22. Chapter 21 is divided into two parts, one closely based on *Science of Microscopy*, the other chronicling later developments. The authors discuss two-photon confocal microscopy, in which the spot-scanning mode is adopted, and a symmetrical lens beyond the sample collects light predominantly from the excitation region, thereby eliminating most of the *out-of-focus* background produced in the normal full-field *optical sectioning* mode. 3-D image reconstruction is then possible. Two-photon microscopy combines this with a fluorescence process in which two low-energy incident photons are required to excite a detectable photon emitted at the sum of their energies. This has several advantages, by reducing radiation damage and background, and allowing observation of thicker samples. The method can also be used to initiate photochemical reactions for study. Chapter 22 describes the latest superresolution schemes for optical microscopy, which have now brought the lateral resolution down to almost the nanometer size of a molecule. The many methods are known by acronyms such as STED, RESOLFT, PALM, STORM, and PAINT. By the symmetrical lens arrangement, they have increased resolution measured along the optic axis by a large factor. The lateral resolution can be improved by modulating the illumination field or by using the stimulated emission depletion microscopy mode (STED), in which saturated excitation of a fluorophore produces nonlinear effects allowing the diffraction barrier to resolution to be broken.

For the scanning near-field probes new possibilities arise. Although restricted to the surface (the site of most chemical activity) and, in some cases, requiring complex image interpretation, damage is reduced, while the sub-ångström resolution normal to the surface is unparalleled. The method is also conveniently combined with spectroscopy. Early work was challenged by problems of reproducibility and tip artifacts, but several chapters in this book show the truly remarkable recent progress in surface science, materials science, and biology. Chapter 25 describes the various modes of atomic force microscopy which can be used to extract atomic-scale information from the surfaces of modern materials, including oxides and semiconductors. Work functions can be mapped out (by means of a Kelvin probe with good spatial resolution) and a variety of useful signals obtained by modulation spectroscopy methods. This way maps of magnetic force, local dopant density, resistivity, contact potential and topography may be obtained. Chapter 27 (unchanged from *Science of Microscopy*) describes applications of the scanning tunneling microscope (STM) in materials science, including inelastic tunneling, surface structure analysis in surface science, the information on electronic structure which may be extracted, atomic manipulation, quantum size and subsurface effects, and high temperature imaging. Chapter 28 provides a review of low-temperature STM methods applied to quantum materials and superconductors, allowing impurity atoms to be imaged, energy gaps to be mapped out, and new phases to be identified. Finally, Chap. 31 reviews the special problems that arise when the atomic force microscope (AFM) is applied to the imaging of biomolecules; much practical information on instrumentation and sample preparation is provided, and many striking examples of cell and macromolecule images are shown.

We include three chapters on unconventional *lensless* imaging methods. Chapter 16 deals with electron holography and Chap. 20 with diffractive imaging. Gabor's original 1948 proposal for holography was intended to improve the resolution of electron microscopes. Only recently have his plans been realized, though it has proved easier to use an aberration-corrected microscope than to employ his two-stage procedure. Meanwhile, electron holography using Möllenstedt's biprism and the Lorentz mode has proved an extremely powerful method of imaging the magnetic and electrostatic fields within matter. Dramatic examples have included TEM movies of superconducting vortices as temperature and applied fields are varied, and ferroelectric and magnetic domain images, all within thin self-supporting films. Chapter 20 describes the recent development of new iterative solutions to the noncrystallographic phase problem, which now allows diffraction-limited images to be reconstructed from the far-field scattered intensity distribution. This has produced lensless atomic-resolution images of carbon nanotubes (reconstructed from electron microdiffraction patterns) and phase contrast images from both neutron and soft x-ray Fraunhofer diffraction patterns of isolated, nonperiodic objects. In this work, lenses are replaced by computers, so that images may now be formed with any radiation for which no lens exists, free of aberrations. As discussed, these methods have been extensively applied to the data collected at x-ray lasers, using femtosecond x-ray pulses in the *diffract-and-destroy* mode. Here, the elastic scattering is collected (and the incident pulse terminates) before the onset of the photoelectron cascade starts to create radiation damage and, subsequently, destroys the sample. The companion Chap. 17 reviews another lensless imaging method, ptychography, and its many applications. This method, which is now rapidly gaining in popularity since the development of ptychography algorithms for nonperiodic samples, does not require a rough estimate of the boundary of an isolated sample, unlike most diffractive imaging methods. Chapter 30 describes recent advances in phase-contrast lensless x-ray imaging, where the use of x-ray phase shifts rather than absorption effects provides images of tissue rather than bone. A pure phase shift, without absorption, would deposit no damaging energy into a patient, while providing potentially high interferometric contrast. Propagation (*defocus*), Talbot (*self-imaging*) grating methods, and split-beam interferometers are all described for this growing field. Chapter 32 on the uses of microscopy in forensic sciences concludes the book.

Coverage has been limited to high-resolution methods, with the result that some important microscopies have been omitted (such as magnetic resonance imaging (MRI) and acoustic imaging).

The ingenuity and creativity of the microscopy community as recorded in these pages are remarkable, as is the spectacular nature of the images presented. Neither shows any signs of abating. As in the past, we fully expect major advances in science to continue to result from breakthroughs in the development of new microscopies.

Peter W. Hawkes
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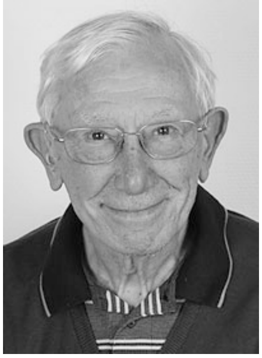

Peter Hawkes looks back at a long career in microscopy. After graduation in 1959, Peter Hawkes joined Ellis Cosslett's Electron Microscopy Section in the Cavendish Laboratory, Cambridge and completed his PhD on electron lens aberrations in 1963. Two books on quadrupole optics resulted from this as well as an introductory text on *Electron Optics and Electron Microscopy*. He remained in Cosslett's group, publishing extensively on electron lens properties and later on digital processing of electron microscope images. He was a Research Fellow of Peterhouse and Churchill College. In 1975, he moved to the CNRS Laboratory of Electron Optics in Toulouse, of which he later became the Director. In 1980, he joined Hermann Wollnik (University of Gießen) and Karl Brown (SLAC) in organising the first of the series of conferences on Charged-Particle Optics; this was an instant success and the series continues today. He is author with Erwin Kasper of a three-volume treatise on the Principles of Electron Optics.

Peter was the Founder-President of the European Microscopy Society and is an Honorary Member of the French Microscopy Society, of which he had been President. He was elected Fellow of the Optical and Microscopy Societies of America and was awarded the CNRS Silver Medal. He has been an active member of the editorial boards of *Ultramicroscopy* and the *Journal of Microscopy* and editor-in-chief of the long-running *Advances in Imaging and Electron Physics*. In recent years, he has had more time to spend on a very different interest, the artists and craftsmen of the nineteenth century, with the result that the *William Morris Society Newsletter* and the *Journal of Pre-Raphaelite Studies* now appear in his list of publications.

Since 2013, **John Spence** FRS has been the Director of Science of *BioXFEL*, a seven-campus consortium in the USA devoted to the application of the recently invented free-electron X-ray laser to the study of structure and dynamics in biology.

John completed his PhD in Physics at Melbourne University in Australia, followed by postdoctoral research at the Materials Department in Oxford, UK. He then moved to the Physics Department at Arizona State University in 1976, joining John Cowley's rapidly growing center for electron microscopy. John's laboratory has since focused on the development of new forms of atomic-resolution microscopy, from time-of-flight analysis in scanning tunneling microscopy to the direct imaging of moving dislocation kinks, new electron microscope detectors, and lensless imaging, to name only a few. He has authored or coauthored over 500 papers and holds several patents and is the author of the leading text (4th edition) on atomic-resolution electron microscopy, and a new text with J.M. Zuo on Advanced Transmission Electron Microscopy. He is also the author of "Lightspeed", a history of measurements of the speed of light and the search for an absolute frame of reference in the universe, which led to Einstein's relativity.

John held a joint appointment with Lawrence Berkeley Laboratory and has spent sabbaticals in Cambridge, UK, the Max Planck Institute at Stuttgart, Oxford, UK, and Trondheim, Norway. He is an overseas Fellow of Churchill College Cambridge, a foreign member of the Royal Society and the Australian Academy of Science, and recipient of several professional society awards. He enjoys flying large gliders among the strong thermals over the Arizona desert mountains and sailing. He is a keen musician devoted to classical piano music, also playing flute and guitar with his jazz quartet *Who Knew*.

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List of Abbreviations

1-D	one-dimensional
2-D	two-dimensional
2PE	two-photon excitation
3-D	three-dimensional
3-D-EBSD	three-dimensional electron backscattered diffraction
3-D-XRDM	three-dimensional x-ray diffraction microscopy
3-DAP	three-dimensional atom probe
3M	multimessenger microscopy
4-D	four-dimensional
5-D	five-dimensional
6-D	six-dimensional

A

ABF	annular bright-field
ACF	absorption correction factor
ADC	analog-to-digital-converter
ADF	annular dark-field
ADT	automated diffraction tomography
AE	Auger electron
AEEM	Auger electron emission microscopy
AEES	Auger electron emission spectroscopy
AEM	analytical electron microscopy
AET	analytical electron tomography
AFAM	atomic force acoustic microscopy
AFM	atomic force microscopy
AIR	algebraic iterative reconstruction
ALS	Advanced Light Source
AM	amplitude modulation
APFIM	atom-probe field ion microscope
APT	atom probe tomography
ARPES	angle-resolved photoemission spectroscopy
ARRES	angle-resolved reflected-electron spectroscopy
ART	algebraic reconstruction technique
ARXPS	angle-resolved x-ray photoemission spectroscopy
ASEM	atmospheric scanning electron microscope
ASR	averaged successive reflection
AU	Airy unit
AWG	arbitrary waveform generation

B

BART	binary algebraic reconstruction technique
bcc	body-centered cubic
BCS	Bardeen–Coopper–Schrieffer
BEEM	ballistic electron emission microscopy
BF	bright-field
BIV	best imaging voltage
BQPI	Bogoliubov quasiparticle interference
BS	backscatter spectrometry
BSE	backscattered electron

C

CAD	computer aided design
CAST	Centre for Applied Science and Technology
CBED	convergent-beam electron diffraction
CC	charge collection
CCD	charge-coupled device
cCDI	conventional coherent diffractive imaging
ccp	cubic close-packed
CDI	coherent diffractive imaging
CDW	charge density wave
CE	collection efficiency
CEC	constant energy contours
CF	charge-flipping
CFEG	cold field emission gun
CFM	chemical force microscopy
CFT	forward cylindrical FT
CITS	current imaging tunneling spectroscopy
CL	cathodoluminescence
CLEM	correlative light and electron microscopy
CLS	confocal laser scanning
CMC	constant mean curvature
CMOS	complementary metal–oxide semiconductor
CNT	carbon nanotube
COF	covalent organic framework
CPD	critical point drying
CPO	charged particle optics
CRB	Cramér–Rao bound
CRLB	Cramér–Rao lower bound
cryo-EM	cryo-electron microscopy
cryo-ET	cryo-electron tomography
cryo-FIB	cryo-focused ion beam milling
cryo-FLM	correlative fluorescence microscopy
CS	compressed sensing
CSEM	conventional high-vacuum scanning electron microscopy
CSF	crystal structure factor
CT	computed tomography
CTAFM	computed tomography AFM
CTEM	conventional transmission electron microscope
CTF	coherent transfer function
CVD	chemical vapor deposition
CW	continuous wave

CW-STED	continuous wave-stimulated emission depletion
CXDI	coherent x-ray diffractive imaging

D

DAC	digital to analog conversion
DAM	drive amplitude modulation
DART	discrete algebraic reconstruction technique
DAXM	differential-aperture x-ray microscopy
DCT	diffraction contrast tomography
DDC	direct detection camera
DDEC	direct-detection electron-counting
DF	dark-field
DFT	density functional theory
DIC	differential interference contrast
DIRECTT	direct iterative reconstruction of computed tomography trajectories
DLA	delay-line anode
DLS	distance least-squares
DLVO	Derjaguin, Landau, Verwey, Overbeek
DMI	Dzyaloshinskii–Moriya interaction
DOS	density of states
DP	diffraction pattern
dpa	displacements per atom
DPC	defocusing phase contrast
DPN	dip pen nanolithography
DQE	detective quantum efficiency
DREEM	double reflection electron emission microscope
dSTORM	direct stochastic optical reconstruction microscopy
DTEM	dynamic transmission electron microscopy
DWNT	double walled nanotube
DWT	discrete wavelet transform

E

EBIC	electron beam-induced current
EBIV	electron beam-induced voltage
EBSD	electron backscatter diffraction
EC	electron crystallography
ECoPoSAP	energy-compensated position-sensitive atom probe
ECP	electron channeling pattern
ED	electron diffraction
EDS	energy-dispersive spectroscopy
EDT	electron diffraction tomography
EDX	energy-dispersive x-ray
EDXS	energy-dispersive x-ray spectroscopy
EEL	electron energy-loss
EELM	electron energy-loss microscopy
EELS	electron energy-loss spectroscopy
EF	energy filtering
EFM	electrostatic force microscopy
EFTEM	energy-filtered transmission electron microscopy
EFTEM-SI	energy-filtered TEM spectrum imaging
ELNES	energy-loss near-edge structure
EM	electron microscopy
EMC	expectation maximization and compression
EMCCD	electron multiplying charge coupled device
EMFP	elastic mean free path
EMPAD	electron microscope pixel array detector
EOM	electro-optic modulator
EOS	electro-optic sampling
ePIE	extended ptychographical iterative engine
EQM	electronic quantum matter
ESD	electron-stimulated desorption
eSE	electron-induced secondary electron
ESEM	environmental scanning electron microscope
ESI	electron spectroscopic imaging
ESM	electrochemical strain microscopy
EST	equally sloped tomography
ET	electron tomography
ETD	Everhart–Thornley detector
ETEM	environmental transmission electron microscope
EUV	extreme ultra-violet
eV-TEM	electron-volt TEM
EXAFS	extended x-ray absorption fine structure
EXELFS	extended energy-loss fine structure
ExM	expansion microscopy

F

FC	flux closure
FCS	fluorescence correlation spectroscopy
FD	Fourier diffractogram
FE	finite element
FEBID	focused electron-beam-induced deposition
FEG	field emission gun
FEL	free-electron laser
FEM	field electron microscopy
FESEM	field emission scanning electron microscope
FET	field-effect transistor
FFM	friction force microscopy
FFP	front-focal plane
FFT	fast Fourier transform
FIB	focused ion beam
FIM	field ion microscopy
FITC	fluoresceine isothiocyanate
FLICS	fluorescence lifetime correlation spectroscopy
FLM	fluorescence light microscopy
FM	frequency modulation
FMT	fluorescence molecular tomography

FMTI	ferromagnetic topological insulator
FOM	figures of merit
FOV	field of view
FP	Fourier ptychography
FPALM	fluorescence photoactivation localization microscopy
fps	frames per second
FRAP	fluorescence recovery after photobleaching
FRC	Fourier-ring-correlation
FRET	fluorescence resonance energy transfer
FRM	fast rotation matching
FT	Fourier transform
FTIR	Fourier transform infrared microspectroscopy
FWHM	full width at half maximum
FWTM	full width at tenth maximum

G

gCW-STED	gated continuous wave-stimulated emission depletion
GED	gas-phase electron diffraction
GENFIRE	generalized Fourier iterative reconstruction
GFIS	gas field ion source
GFP	green fluorescent protein
GIS	gas injection system
GOF	goodness of fit
GOS	generalized oscillator strength
GPILRUFT	global ptychographic iterative linear retrieval using Fourier transforms
GPT	general particle tracer
GS	Gerchberg–Saxton algorithm
GSD	ground state depletion
GSDIM	ground state depletion followed by individual molecule return
GSED	gaseous secondary electron detector

H

HAADF	high-angle annular dark-field
hcp	hexagonal close-packed
HIM	helium ion microscopy
HOLZ	high-order Laue zone
HPI	hexagonally packed intermediate
HPR	hybrid projection reflection
HREM	high-resolution electron microscopy
HRSEM	high-resolution scanning electron microscopy
HRTEM	high-resolution transmission electron microscopy
HS	Hartree–Slater
HV	high vacuum

I

IAP	imaging atom probe
IBA	ion beam analysis
IBF	incoherent bright-field
IBSC	ion beam slope cutting
IC	intermittent contact
ICA	independent component analysis
ICL	integration classification likelihood criterion
ICP-MS	inductively coupled plasma mass spectroscopy
IDC	indirect detection camera
IETS	inelastic electron tunneling spectroscopy
IL	ionoluminescence
IMFP	inelastic mean free path
IML-SPIM	individual molecule localization selective plane illumination microscopy
IOM	inverted optical microscope
IR	infrared
IS	image scanning
iSE	ion-induced secondary electron
iSEED	ion-induced secondary electron energy distribution
iSEY	induced secondary electron yield
ITA	iterative transformation algorithms

K

KCBED	kinematic convergent beam blank disk
KE	kinetic emission
KFM	Kelvin probe force microscopy
KKA	Kramers–Kronig analysis
KRIPES	k-resolved inverse photoelectron emission spectroscopy

L

LAADF	low-angle annular dark-field
LACBED	large-angle convergent-beam electron diffraction
LARBED	large-angle rocking-beam electron diffraction
LCTEM	liquid cell transmission electron microscopy
LEAP	local-electrode atom probe
LEED	low-energy electron diffraction
LEELM	low-electron energy loss microscopy
LEEM	low-energy electron microscopy
LFL	Landau–Fermi liquid
LIQUITOPY	liquid tunable microscopy
LMAIS	liquid metal alloy ion source
LMIS	liquid metal ion source
LO	longitudinal optical
LPS	longitudinal phase space
LSC	longitudinal space charge
LSI	linear space invariant
LSM	laser scanning microscopy
LV	low vacuum
LVFESEM	low-voltage field emission scanning electron microscope
LVSEM	low-voltage scanning electron microscopy

M

MAADF	medium-angle annular dark-field
MAL	maximum likelihood
MALDI	matrix-assisted laser desorption/ionization
MAPS	monolithic active pixel sensor
MDF	minimum detectable fraction
MDFF	mixed dynamic form factor
MDN	minimum detectable number
MEM	mirror electron microscopy
MEMS	microelectromechanical system
MFM	magnetic force microscopy
MFP	mean free path
microCT	microcomputed tomography
MIEEM	metastable impact electron emission microscopy
MIL	Materials of the Institute Lavoisier
MINFLUX	nanoscopy with minimal photon fluxes
MIP	mean inner potential
MMF	minimum mass fraction
MMM-4Pi	multifocal multiphoton microscopy 4Pi
MOF	metal organic framework
MOGA	multi-objective genetic algorithm
MOS	metal oxide semiconductor
MOSFET	metal–oxide–semiconductor field-effect transistor
MOST	multiple off-state transitions
MOTIS	magneto-optical trap ion source
MPA	magnetic prism array
MPE	multiphoton excitation
MRI	magnetic resonance imaging
MRP	mass resolving power
MSA	multivariate statistical analysis
MSI	multivariate statistical methods
MTE	mean transverse energy
MTF	modulated transfer function

N

NA	numerical aperture
NAD	nonlinear anisotropic diffusion
NAED	nanoarea electron diffraction
NBD	nanobeam diffraction
NC-AFM	noncontact atomic force microscopy
NCC	normalized cross-correlation
NEMS	nanoelectromechanical system
NEXAFS	near-edge x-ray absorption fine structure
NFFT	nonequispaced fast Fourier transformation
NFMM	near-field microwave microscopy
NIM	nanoimpedance microscopy and spectroscopy
NMR	nuclear magnetic resonance
NPC	nuclear pore complex
NSOM/SNOM	near-field scanning optical microscopy
NTF	noise transfer function

O

OBD	optical beam deflection
OIM	orientation imaging microscopy
OL	objective lens
OTF	optical transfer function

P

PACBED	position averaged CBED
PAD	pixel area detector
PAINT	points accumulation for imaging in nanoscale topography
PALM	photoactivated localization microscopy
PALMIRA	PALM with independently running acquisition
PBS	polarization beam-splitter
PCA	principal component analysis
PCAFM	photoconductive AFM
PCD	projected charge density
PCF	phase-correlation function
pCF	pair correlation function
PCI	phase contrast index function
PCTF	phase contrast transfer function
PDF	probability density function
PDW	pair density wave
PE	potential emission
PED	precession electron diffraction
PEELS	parallel electron energy-loss spectrum
PEEM	photoelectron emission microscopy
PFI	polychromatic far-field interferometer
PFM	piezoelectric force microscopy
PG	point-group
PGA	phase grating approximation
PIE	ptychographical iterative engine
PINEM	photon-induced near-field electron microscopy
PL	photoluminescence
PLA	pressure-limiting aperture
PLD	pulsed laser deposition
PMQ	permanent magnet quadrupole
PMT	photomultiplier tube
POA	phase object approximation
POCS	projections onto convex set
PoSAP	position-sensitive atom probe
PPFFT	pseudopolar fast Fourier transform
PR	piezoresponse
PSD	power-spectral-density
PSE-CVD	pulsed-spray evaporation chemical vapor deposition
PSF	point spread function
PSM	presharpened microtip
PSRT	progressive stochastic reconstruction technique
PVD	physical vapor deposition
PXRD	powder x-ray diffraction

Q

QD	quantum dot
QPI	quasiparticle scattering interference
QSE	quantum size effect

R

RAAR	relaxed averaged alternating reflector
RBS	Rutherford backscattering spectrometry
REAP	remote-electrode atom probe
REM	reflection electron microscopy
RESOLFT	reversible saturable optical fluorescence transition
RF	radio frequency
RI	refractive index
RICS	raster imaging correlation spectroscopy
RIM	reflection ion microscopy
RMLF	reactive multilayer foil
RMS	root mean square
ROI	region of interest
RP-CVD	reduced pressure chemical vapor deposition
RSFP	reversibly switchable fluorescent protein
RVM	ray–voxel interaction matrix

S

SA	selected area
SAED	selected area electron diffraction
SAP	scanning atom probe
SAP	selected area ptychography
SART	simultaneous algebraic reconstruction technique
SAT	single atom tip
SAXS	small-angle x-ray scattering
SBR	signal-to-background-ratio
SCBED	scanning convergent-beam electron diffraction
SCEM	scanning confocal electron microscopy
SCFS	single-cell force spectroscopy
SCM	scanning capacitance microscopy
SDD	silicon drift detector
SDM	spatial distribution map
SE	secondary electron
SEC	Schottky emission cathode
SECM	scanning electrochemical microscopy
SED	scanning electron diffraction
SEED	secondary electron energy distribution
SEEM	secondary electron emission microscopy
SEM	scanning electron microscopy
SEM-EDX	scanning electron microscopy with energy dispersive x-ray spectroscopy
SEND	scanning electron nanodiffraction
SFIM	scanning field ion microscopy
SFXM	scanning fluorescence x-ray microprobe
SG	space group
SGM	scanning gate microscopy
SHARP	scalable heterogeneous adaptive real-time ptychography
SI	spectrum image
SI-STM	spectroscopic imaging scanning tunneling microscopy
SIM	scanning impedance microscopy
SIMS	secondary ion mass spectroscopy
SIRT	simultaneous iterative reconstruction technique
SJTM	scanned Josephson tunneling microscopy
SLEEM	scanning low-energy electron microscopy
SMACM	single-molecule active-control microscopy
SMART	spectromicroscope for all relevant techniques
SMFS	single-molecule force spectroscopy
SMI	structure model index
SMIM	scanning microwave impedance microscopy
SNDM	scanning nonlinear dielectric microscopy
SNOM	scanning near-field optical microscope
SNR	signal-to-noise-ratio
SP	single-particle
SPA-LEED	spot-profile analysis LEED
SPAD	single photon avalanche diode
SPELEEM	spectroscopic photoemission and low-energy electron microscopy
SPEM	scanning photoemission microscope
SPIM	selective-plane-illumination microscopy
SPLEEM	spin-polarized low-energy electron microscopy
SPLIT	separation of photons by lifetime tuning
SPM	scanning probe microscopy
spt-PALM	single-particle tracking-photoactivation localization microscopy
SR-SIM	super-resolved structured illumination microscopy
SRIM	stopping and range of ions in matter
SRT	spin-reorientation transition
SSIM	saturated structured-illumination microscopy
SSPM	scanning surface potential microscopy
SSRM	scanning spreading resistance microscopy
STED	stimulated emission depletion
STEM	scanning transmission electron microscopy
STEM-SI	scanning transmission electron microscopy spectrum-imaging
stFCS	spatiotemporal fluorescence correlation spectroscopy
SThM	scanning thermal microscopy
STIM	scanning transmission ion microscopy
STM	scanning tunneling microscopy
STORM	stochastic optical reconstruction microscopy
STXM	scanning transmission x-ray microscopy

SW	single wavelength
SWM	standing wave microscope
SWNT	single-walled carbon nanotube

T

t-EBSD	transmission EBSD
TAP	tomographic atom probe
TCC	transmission cross coefficient
tcp	tetrahedrally close-packed
TDS	thermal diffuse scattering
TEEM	thermionic emission electron microscopy
TEM	transmission electron microscopy
TEY	total electron yield
TFE	thermal field emitter
TGA	thermogravimetric analysis
TI	topological insulators
TIE	transport of intensity
TIRF	total internal reflection fluorescent
TKD	transmission Kikuchi diffraction
TO	transverse optical
ToA	time-of-arrival
ToF	time-of-flight
ToF-SIMS	time of flight secondary ion mass spectrometry
TPE	two-photon excitation
TPMS	triply periodic minimal surface
TR-GED	time-resolved gas-phase electron diffraction
TR-NIM	torsional resonance nanoscale impedance microscopy
TTM	two-temperature model
TV	total variation
TXM	transmission x-ray microscope

U

UBMS	unbalanced magnetron sputtering
UED	ultrafast electron diffraction
UEM	ultrafast electron microscopy
UFM	ultrasonic force microscopy
UHV	ultrahigh vacuum
UHVTEM	ultrahigh vacuum transmission electron microscope
ULV	ultralow vibration
USAXS	ultrasmall angle x-ray scattering
UTEM	ultrafast TEM
UTW	ultrathin window
UV	ultraviolet
UVPEEM	ultraviolet photoemission electron microscopy

V

VB	valence band
VFP	visible fluorescent protein
VLSI	very-large-scale integration
VLVSEM	very low-voltage scanning electron microscopy
VOA	virtual objective aperture
VP	variable pressure
VPP	Volta phase plate
VPSE	variable pressure secondary electron
VPSEM	variable pressure scanning electron microscopy

W

WAXS	wide-angle x-ray scattering
WBP	weighted back-projection
WD	working distance
WDD	Wigner distribution deconvolution
WDS	wavelength-dispersive spectrometer
WDX	wavelength-dispersive x-ray
WKB	Wentzel–Kramers–Brillouin
WPOA	weak phase object approximation
WSIRT	weighted-SIRT
WTF	wave transfer function

X

X-PEEM	x-ray photoemission electron microscopy
X-STM	cross-sectional scanning tunneling microscopy
XAFS	x-ray absorption fine structure
XANES	x-ray absorption near-edge structure
XAS	x-ray absorption spectroscopy
XASPEEM	x-ray absorption PEEM
XCF	cross-correlation function
XEDS	x-ray energy dispersive spectroscopy
XFCT	x-ray fluorescence CT
XFEL	x-ray free-electron laser
XMCD	x-ray magnetic circular dichroism
XMCDPEEM	x-ray magnetic circular dichroism photoemission electron microscopy
XMLDPEEM	x-ray magnetic linear dichroism photoemission electron microscopy
XPEEM	x-ray-induced photoemission electron microscopy
XPS	x-ray photoelectron spectroscopy
XRD	x-ray diffraction

Y

YAG	yttrium-aluminum-garnet
YAP	yttrium-aluminum-perovskite
YSZ	yttria stabilised zirconia

Z

ZIF	zeolitic imidazolate framework
ZL	zero-loss
ZLP	zero-loss peak
ZOLZ	zero-order Laue zone
ZPP	Zernike phase plate