Appendix 6 Historical Background

The precise origins and originators of the light microscope are disputed and lost in history; simple glass lenses and water-filled globes have been used to assist the examination of small objects for more than two millennia, and images seen in natural water drops can hardly have escaped notice before then. Later in the Middle Ages, the Arabic scholar and polymath Alhazen described the use of magnifying lenses (besides much else) in his *Kitab al-Manazir* or *Book of Optics*, around 1000 AD.

The microscope and the telescope are related optically, yet until people experimented with combinations of different lenses, no great effort would have been given to systematically exploring the unknown and hidden world beyond the limits of the eye. Hartley (1993) postulates that simple magnifying glasses were known since time immemorial and had no need of description, whereas maritime and military necessity drove forward the invention of the telescope in the 16th century. The telescope was *invented*; the microscope only *discovered* later. There was clearly profit to be made in telescope production, yet no immediate benefit (aside of natural curiosity) from developing the microscope.

The origin of the telescope is unclear, but it is certain that it pre-dates the microscope. In 1608 a patent dispute between the opticians Johannes Lippershey, Jacob Metius and Zacharias Janssen of Middleburg (in modern-day Holland) is recorded. This telescope patent was denied because other spectacle-makers had made similar claims; the design was considered too simple to keep secret, and the authorities in Holland recognised the military advantages of the telescope. Galileo Galilei, working at the University of Padua, heard of the 'Dutch spyglass' and constructed his own telescope of nine times magnification about the second half of 1609. In Venice he had access to exceptionally pure and clear Murano glass, which could be ground into high quality lenses.

There are two designs of refracting telescope, the first being the Dutch or Galilean model, which uses a convex objective lens and concave eyepiece lens. This telescope produces an upright image, but suffers from a small field of view, a relatively low magnification (maximum of about 30 times) and generally poor image quality. For this reason it is sometimes referred to as the terrestial telescope. The second design is the astronomical Keplerian refracting telescope with a convex eyepiece. This produces an inverted image (which does not matter in astronomy) but could be made of greater overall magnification with a wider field of view and brighter image. At some point the microscope was discovered when somebody looked through the 'wrong' end of the Keplerian telescope, for the one is merely an inversion of the other. Until the separate coining of the terms 'telescope' and 'microscope' by the end of the first quarter of the 17th century, the words *perspicillum*, *tubus opticus* and *occhiale* were interchangeable neologisms. Since both instruments produced their image by dioptric magnification through refractive enlargement of the visual angle this can only have added to the confusion about the exact date of their orgin.

The first popular and comprehensive book on microscopes and what they could reveal was Robert Hooke's *Micrographia* (literally: *Small Drawings*), dated 1665 and released in October 1664. Hooke was not sufficiently confident to use the word 'microscope' coined forty years earlier, referring instead to 'magnifying glasses' in the subtitle of his book. Significantly, Hooke called the compartments *cells* that he could see in a thin slice of cork. In *Observ. XVIII* [No. 18] *'Of the Schematisme or Texture of Cork, and of the Cells and Pores of some other such frothy Bodies'*, he likened them to the orderly arrangements of small rooms inhabited by hermit monks within a religious community. It is a good analogy: individual cells are the basic functional unit of life within the entire organism.

It seems that Antoni van Leeuwenhoek, a draper living in Holland (Bracegirdle, 1986) and contemporary of Hooke's, inspired by reading *Micrographia*, was not deterred by the 'troublesome' difficulties using high

power single magnifying glasses '*offensive to my eye because of their smallness, and the nearness of the Object*' as encountered by Hooke. Leeuwenhoek would have been familiar with using a magnifying glass for inspecting cloth. He studied objects that had never before been seen, including bacteria, protozoa and human sperm, even the explosion of gunpowder under the microscope – nearly blinding himself in the process! Leeuwenhoek's microscope consisted of little more than a simple metal frame to hold the lens and the specimen. This demonstrates convincingly that the only truly essential part of a microscope is that first tiny lens just after the specimen; all of the other parts simply add to the convenience of use. It is this objective lens which is all-important in collecting information about the object, and any information that does not enter the objective lens will not be seen. Those of Leeuwenhoek's microscopes which survive have been intensively investigated, and shown to have magnifications up to several hundred times, able to resolve between 1 and 2 micrometres.

Compound microscopes, with multiple lenses, were inferior to the single lens (or simple) microscopes due to the cumulative effects of the aberrations present in each lens. The more lenses that were added to the microscope, the worse it performed because each lens successively magnified the aberration present. Thus the resolving power of the simple microscope was approximately five times better than the compound microscope. The simple microscope tended to be used for higher power studies by transmitted-light, whereas the compound microscope, close relative of the telescope, was largely used to investigate solid objects by reflected-light at relatively low magnification.

Throughout the 18th century, after the deaths of both Hooke and Leeuwenhoek, the microscope degenerated largely into a beautifully-constructed plaything, primarily for the cabinets of English gentlemen of leisure. The apotheosis of such instruments is George Adams' silver microscope made for King George III. Hence, microscopy came to be despised and distrusted by scientists of the 18th and early 19th centuries because of the erroneous interpretations that could arise all too easily from the poor and defective images. It was not until the 1820s that significant advances were made so that the compound microscope could surpass the simple microscope in convenience, versatility and performance.

Various enterprising individuals tried constructing tiny achromatic doublets for the microscope. In order to minimise spherical aberration in the objectives of compound microscopes, it was usual practice to insert a restricting aperture between the lenses. This was none too effective, but did, however, cause serious loss of both resolving power and brightness. A wine merchant named Joseph Jackson Lister (Bracegirdle, 1987) made it his hobby to study the optics of the microscope, and successfully combined two plano-convex achromatic doublets in an aplanatic arrangement to minimise spherical aberration. Lister's work (Lister, 1830) revolutionised microscope design, since progress was made not only in minimising chromatic and spherical aberrations, but also by increasing the useful aperture of the objectives. The improved microscopes allowed for advances to be made in cell biology and medicine.

It was thought that the angular aperture of an objective was important, and a situation akin to that of the 18th century arose: objectives had far too much magnifying power (empty magnification) in relation to their aperture. However, objective manufacture was entirely empirical, no-one knew the true basis of image formation, and the uncertainty threatened to put people like Carl Zeiss out of business. Zeiss turned for help to an academically-successful 26-year-old named Ernst Carl Abbe (Volkmann, 1966; Gerth & Wimmer, 2005) who started work with the firm in 1866. Abbe abandoned all preconceived ideas about objective design, and set to work to establish the entire process of design and manufacture upon a firm basis of theoretical calculations: to rationalise and standardise the process for absolute consistency. He was successful, and from the early 1870s all the lenses made in Jena were made to pre-calculated computations instead of relying (as elsewhere) solely upon the skill of individual craftsmen. Abbe elucidated the diffraction theory of image formation, and the '*Abbe sine condition*', which he published in December 1873

(Abbe, 1873). This single technical advance was to have a greater impact upon microscopy than the work of Lister 40 years previously.

From the early 1870s, Abbe devoted his energy to improving the achromatic objectives, which still exhibited residual colour fringes and some spherical aberration. This necessitated finding new types of optical glass, and Abbe learnt that high-quality fluorite could be obtained from the Oltschenalp in Switzerland. He used this because the exceptionally clear crystal from the area offerred the required dispersive properties to minimise residual errors in the objective. Again Abbe was successful, and the light microscope reached the zenith of optical developmentin 1886, which would last for the next century, with the production of highly-corrected apochromat lenses (Haselmann, 1993).

The closing years of the 19th century saw the introduction of a reliable method of adjusting the microscope to exploit the full aperture of the objective – Köhler illumination (Köhler, 1893). Improvements during the 20th century broadly centered on photographic image recording and developing contrast-enhancement methods. The development of electron microscopy in the second half of the 20th century led many to believe that the light microscope had only a limited future. However, realisation of the power of fluorescence microscopy, together with the advent of the laser, powerful computers and electronic detectors for digital imaging, has led to the renaissance of the light microscope in the late 20th century (Lippincott-Schwartz, 2011). The newest advances in physics and optics are helping to close the gap between the limit of resolving power of the light microscope and electron microscopy. Scientists are beginning to use the renewed power and versatility of light microscopy to explore, *in-situ* and in real-time, how proteins and other cellular components function and interact within their natural environment.

References

Abbe, E (1873) Beiträge zur Theorie des Mikroskops and der mikroskopischen Wahrnehmung. *Archiv für Mikroskopische Anatomie* 9: 413- 468.

Bracegirdle, B (1986) Famous microscopists: Antoni van Leeuwenhoek, 1632-1723 *Proceedings of the Royal Microscopical Society* 21/6: 367-373.

Bracegirdle, B (1987) Famous microscopists: Joseph Jackson Lister, 1786-1869. *Proceedings of the Royal Microscopical Society* 22/5: 273-297.

Gerth, K & Wimmer, W (2005) *Ernst Abbe (1840-1905): scientist, entrepeneur, social reformer.* Bussert & Stadeler, Jena. ISBN 3-932906-57-8

Hartley, GW (1993) *The Light Microscope: its use & development*, Senecio, Oxford. Chapter 1, pages 1-6.

Haselmann, H (1993) One Hundredth Anniversary of Köhler illumination. *Proceedings of the Royal Microscopical Society* 28/4: 186-188.

Köhler, A (1893) Gedanken zu einem neuen Beleuchtungsverfahren für mikrophotographische Zwecke *Zeitschrift für wissenschaftliche Mikroskopie* 10: 433-440. A reprint translated into English of Köhler's original paper: *A new system of illumination for photomicrographic purposes*, is in: *Proceedings of the Royal Microscopical Society* (1993) 28/4: 181-186.

Lippincott-Schwartz, J (2011) Bridging structure and process in developmental biology through new imaging processes. *Dev. Cell* 21/1: 5-10.

Lister, JJ (1830) On some properties in achromatic object-glasses applicable to the improvement of the microscope. *Phil. Trans. R. Soc. Lond*. 120: 187-200.

Volkmann, H (1966) Ernst Abbe and his work. *Applied Optics* 5/11: 1720-1731.

Further Reading

Amos, B (2000) Lessons from the history of Light Microscopy *Nature Cell Biology* 2/8: E151-E152

Bracegirdle, B (1978) The performance of seventeenth- and eighteenth-century microscopes. *Medical History* 22/2: 187-195.

Bracegirdle, B (ed) *Beads of Glass: Leeuwenhoek and the early microscope*. Catalogue of an exhibition in the Museum Boerhaave Nov 1982-May 1983 and in the Science Museum May-Oct 1983.

Bradbury, S (1967) The quality of the image produced by the compound microscope: 1700-1840. *Proceedings of the Royal Microscopical Society* 2/1: 151-173.

Bradbury, S (1996) The reception of Abbe's Theory in England. *Proceedings of the Royal Microscopical Society* 31/4: 293-299.

Bradbury, S (2001) Ernst Abbe's theories and his letters to English Microscopists *Quekett Journal of Microscopy* 39/2: 139-161

Dobell, C (1960) Antony van Leeuwenhoek and his 'Little Animals', Dover, New York.
Unabridged reprint of Dobell, C (1932), Constable, London.

Fripp, HE trans. (1874-1875) Abbe, E. A contribution to the theory of the microscope, and the nature of microscopic vision. *Proceedings of the Bristol Naturalists' Society* **I** pt. II: 200-261.

Fripp, HE (1876-1877) On Professor Abbe's experimental demonstration of diffraction spectra in the microscope. *Proceedings of theBristol Naturalists' Society* **II** pt. I: 24-38.

Journal of Microscopy, volume 155 part 3, September 1989
(In celebration of the 150th anniversary of the Royal Microscopical Society). Including:

Bennett, JA (1989) Social history of the microscope, pages 267-280
Bradbury, S (1989) Landmarks in biological light microscopy, pages 281-305
Bracegirdle, B (1989) Development of preparative techniques, pages 307-318
Hartley, WG (1989) Triumphs and conflicts in microscopy, pages 319-326

Piston, DW (2009) The impact of technology on light microscopy *Nature Milestones* S23-S24

Turner, G L'E (1990) 1590 and all that. *Proceedings of the Royal Microscopical Society* 25/6: 423-424