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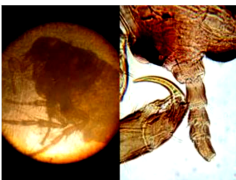
News

Early microscopes offered sharp vision

Images from the first microscopes were clearer than was once believed.

Phillip Ball

The first microscopes were a lot better than they are usually given credit for. That's the claim of microscopist Brian Ford, a specialist in the history and development of these instruments based at the University of Cambridge, UK.



A flea, as seen through an eighteenth-century microscope used poorly (left) and correctly (right).

Wh.0080, Whipple Museum of the History of Science, University of Cambridge / B. Ford

Ford says it is often suggested that the microscopes used by seventeenth-century pioneers such as Robert Hooke and Antony van Leeuwenhoek gave a blurry view of biological structures such as cells and microorganisms. Hooke was the first to record cells, seen in thin slices of cork, while Leeuwenhoek described tiny 'animalcules', invisible to the naked eye, in rain water in 1676.

The implication is that these breakthroughs involved more than a little guesswork and invention. But Ford has looked again at the capabilities of some of Leeuwenhoek's microscopes, and says the results were "breathtaking", and comparable to those obtained with a modern light microscope. He describes his studies in *Microscopy and Analysis*¹.

Inept modern reconstructions have given seventeenth-century instruments a bad name, says Ford. In contrast to the hazy images shown in some museums and television documentaries, the right lighting and focusing can produce micrographs of startling clarity using original microscopes or modern replicas ([see slideshow](#)).

"Ford is the world's leading expert on the topic, and what he has to say here makes a good deal of sense," says Catherine Wilson, a historian of microscopy at the University of Aberdeen, UK.

Wonderful spectacle

Ford made some of these improvements when he was granted access to one of Leeuwenhoek's original microscopes owned by the Utrecht University Museum in the Netherlands. Leeuwenhoek, a linen merchant living in Delft, made his own instruments using a single lens — a tiny bead of glass mounted in a metal frame. These simple microscopes were harder to make and use than the more familiar two-lens compound microscope, but offered greater resolution.

Hooke popularized microscopy in his 1665 masterpiece *Micrographia*, which included stunning engravings of fleas, mites and the compound eyes of flies. The diarist Samuel Pepys judged it "the most ingenious book that I ever read in my life". Ford's findings show that Hooke was not, as some have suggested, embellishing his drawings from imagination, but should genuinely have been able to see such things as the tiny hairs on the flea's legs.

Even Hooke was temporarily foxed, however, when he was tasked with reproducing Leeuwenhoek's results. It took him more than a year before he could see these animalcules, whereupon he wrote: "I was very much surprised at this so wonderful a spectacle, having never seen any living creature comparable to these for smallness."

"The abilities of those pioneer microscopists were so much greater than has been recognized," says Ford. He attributes the misconception to a recent decline in the teaching of microscopy.

References

1. Ford, B. *Microsc. Anal.* (in the press).

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Excellent article on early microscopes. #18618

Here are details of genesis and growth of Microscopy.

The rise of modern light microscopy

The first detailed account of the interior construction of living tissue based on the use of a microscope did not appear until 1644, in Giambattista Odierna's L'occhio della mosca, or The Fly's Eye.

It was not until the 1660s and 1670s that the microscope was used extensively for research in Italy, Holland and England. Marcelo Malpighi in Italy began the analysis of biological structures beginning with the lungs. Robert Hooke's Micrographia had a huge impact, largely because of its impressive illustrations. The greatest contribution came from Antoni van Leeuwenhoek who discovered red blood cells and spermatozoa and helped popularise microscopy as a technique. On 9 October 1676, Leeuwenhoek reported the discovery of micro-organisms.

In 1893 August Köhler developed a key technique for sample illumination, Köhler illumination, which is central to modern light microscopy. This method of sample illumination gives rise to extremely even lighting and overcomes many limitations of older techniques of sample illumination. Further developments in sample illumination came from Fritz Zernike in 1953 and George Nomarski 1955 for their development of phase contrast and differential interference contrast illumination which allow imaging of transparent samples.

Electron microscopy

In the early 1900s a significant alternative to light microscopy was developed, using electrons rather than light to generate the image. Ernst Ruska started development of the first electron microscope in 1931 which was the transmission electron microscope (TEM). The transmission electron microscope works on the same principle as an optical microscope but uses electrons in the place of light and electromagnets in the place of glass lenses. Use of electrons instead of light allows a much higher resolution. Development of the transmission electron microscope was quickly followed in 1935 by the development of the scanning electron microscope by Max Knoll.

Electron microscopes quickly became popular, following the Second World War Ernst Ruska, working at Siemens developed the first commercial transmission electron microscope and major scientific conferences on electron microscopy started being held in the 1950s. In 1965 the first commercial scanning electron microscope was developed by Professor Sir Charles Oatley and his postgraduate student Gary Stewart and marketed by the Cambridge Instrument Company as the "Stereoscan".

Scanning probe microscopy

The 1980s saw the development of the first scanning probe microscopes. The first was the scanning tunneling microscope in 1981, developed by Gerd Binnig and Heinrich Rohrer. This was closely followed in 1986 with Gerd Binnig, Quate, and Gerber's invention of the atomic force microscope.

Fluorescence and light microscopy

The most recent developments in light microscope largely centre on the rise of fluorescence microscopy in biology. During the last decades of the 20th century, particularly in the post-genomic era, many techniques for fluorescent labeling of cellular structures were developed. The main groups of techniques are small chemical staining of cellular structures, for example DAPI to label DNA, use of antibodies conjugated to fluorescent reporters, see immunofluorescence, and fluorescent proteins, such as green fluorescent protein. These techniques use these different fluorophores for analysis of cell structure at a molecular level in both live and fixed samples. The rise of fluorescence microscopy drove the development of a major modern microscope design, the confocal microscope. The principle was patented in 1957 by Marvin Minsky, although laser technology limited practical application of the technique. It was not until 1978 when Thomas and Christoph Cremer developed the first practical confocal laser scanning microscope and the technique rapidly gained popularity through the 1980s. Much current research (in the early 21st century) on optical microscope techniques is focused on development of superresolution analysis of fluorescently labeled samples. Structured illumination can improve resolution by around two to four times and techniques like stimulated Emission Depletion microscopy are approaching the resolution of electron microscopes.

Types of microscopes

Microscopes can be separated into several different classes. One grouping is based on what interacts with the sample to generate the image, i.e., light (optical microscopes), electrons (electron microscopes) or a probe (scanning probe microscopes). Alternatively microscopes can be classed on whether they analyse the sample via a scanning point (confocal optical microscopes, scanning electron microscopes and scanning probe microscopes) or analyze the sample all at once (wide field optical microscope and transmission electron microscopes).

The wide field optical microscope and transmission electron microscope use the theory of lenses (optics for light microscopes and electromagnet lenses for electron microscopes) in order to magnify the image generated by the passage of a wave through the sample, or reflected by the sample. The waves used are electromagnetic (in optical microscopes) or electron beams (in electron microscopes). Resolution in these microscopes is limited by the wavelength of the radiation used to image the sample, shorter wavelengths allow a higher resolution.

Scanning optical and electron microscopes, like the confocal microscope and scanning electron microscope, use lenses to focus a spot of light/electrons onto the sample then analyze the reflected and/or transmitted waves. The point is then scanned over the sample to analyze a rectangular region. Magnification of the image is achieved by displaying the data from scanning a small sample area on a large screen. These microscopes have the same resolution limit as wide field optical and electron microscopes.

Scanning probe microscopes also analyze a single point in the sample and then scan the probe over a rectangular sample region to build up an image. As these microscopes do not use electromagnetic or electron radiation for imaging they are not subject to the same resolution limit as the optical and electron microscopes described above.

Optical

The most common type of microscope is the first invented is the optical microscope. This is an optical instrument containing one or more lenses producing an enlarged image of an sample placed in the focal plane. Optical microscopes have refractive glass and occasionally plastic or quartz, to focus light into the eye or another light detector. Mirror-based optical microscopes operate in the same manner. Typical magnification of a light microscope, assuming visible range light, is up to 1500x with a theoretical resolution limit of around 0.2 micrometres or 200 nanometers. Specialized techniques (e.g., scanning confocal microscopy, Vertico SMI) may exceed this magnification but the resolution is diffraction limited. The use of shorter wavelengths of light, such as the ultraviolet, is one way to improve the spatial resolution of the optical microscope, as are devices such as the near-field scanning optical microscope.

Sarfus, a recent optical technique increases the sensitivity of standard optical microscope to a point it becomes possible to directly visualize nanometric films (down to 0.3 nanometer) and isolated nano-objects (down to 2 nm-diameter). The technique is based on the use of non-reflecting substrates for cross-polarized reflected light microscopy. Ultraviolet light enables the resolution of microscopic features, as well as to image samples that are transparent to the eye. Near infrared light images circuitry embedded in bonded silicon devices, as silicon is transparent in this region. Many wavelengths of light, ranging from the ultraviolet to the visible are used to excite fluorescence emission from objects for viewing by eye or with sensitive cameras.

Phase contrast microscopy is an optical microscopy illumination technique in which small phase shifts in the light passing through a transparent specimen are converted into amplitude or contrast changes in the image. A phase contrast microscope does not require staining to view the slide. This microscope made it possible to study the cell cycle.

The traditional optical microscope has recently been modified into a digital microscope, where, instead of directly viewing the object, a charge-coupled device (CCD) is used to record the image, which is then displayed on a computer monitor(Source:Wikipedia).

Dr.A.Jagadeesh Nellore (AP), India

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2011-03-05 05:49:49 AM

Posted by: **Anumakonda Jagadeesh** |

Anumakonda Jagadeesh

#18652

Thank you for an excellently informative extension to the interesting primary article, here.

Martin Woodhouse

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2011-03-07 06:14:37 AM

Posted by: **Martin Woodhouse** |

This is an excellent article. I love it very much.

#18848

As a student of systematics I appreciate good microscopy. Unfortunately, as the article points out in the last sentence, the teaching of microscopy skills has recently declined. Some may argue this is not the case, that people are using larger and fancier scopes now more than ever. However, larger and fancier does not mean the person using the scope is more skilled, especially in general light microscopy, where resolution is limited to ~1000x or less within the means of most any student. The skill of the user means so much towards seeing a high quality image, but such things are seldom taught anymore. I'm referring to simple techniques such as Kohler illumination, which is crucial to getting good color images in a compound light microscope, or adjustment of the aperture to change the depth of field, etcetera.

I honestly wish there were microscopists willing to take apprentices, so I could learn the old skills no one else seems to know.

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2011-03-14 06:22:57 AM

Posted by: **Zachary Burington** |

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