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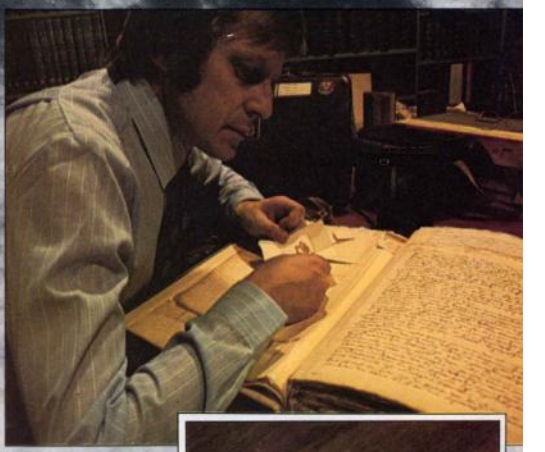


All photographs by Brian Ford

Left **A portrait of Anton van Leeuwenhoek who was born in 1632 and is said to be the father of microscopy. He made up to 500 tiny microscopes which had amazing resolution. His work must put him amongst the founders of microbiology. After 307 years a British scientist found nine of Leeuwenhoek's specimens** *(top right)* **folded inside small paper packets** *(bottom right)* **and sent to the Royal Society.**

A VISION REDISCOVERED

Microscopy has reached a high degree of sophistication, bringing an unseen world into sharp focus. And its origins are not so primitive as we thought

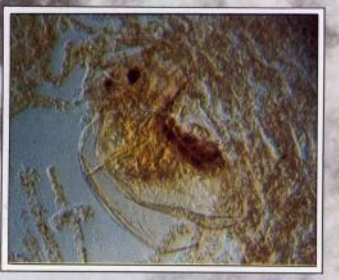
The pictures on this page (printed for the first time) are a unique glimpse straight across 300 years of history. Locked away and forgotten since the 1600s in the London headquarters of the Royal Society, nine of the world's oldest microscope specimens have been re-discovered by a British scientist, Brian Ford. The specimens tell the story of the birth of modern biology. They even include the very tissue in which it was first discovered that there were such things as cells. The find has been hailed as the most exciting discovery in the history of the microscope.

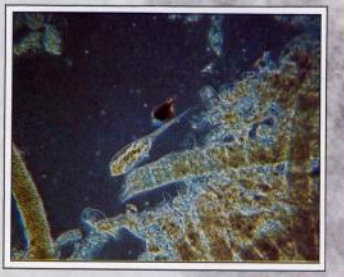
Anton van Leeuwenhoek was the inventive genius who first prepared the specimens. A draper by trade, he became interested in microscopes and the study of biological material in his late thirties. It was a brand new branch of science; the world's first known microscope dates from 1590. The word microscope was first coined in 1625, seven years before Leeuwenhoek's birth. His first serious work was done when he was 40, but he kept up his activities until he died at the age of 90 in 1722.

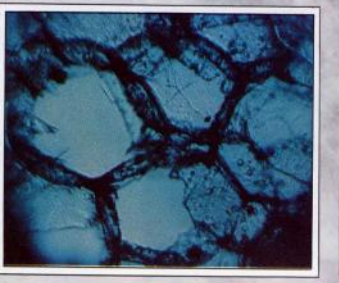
Micrographia

Leeuwenhoek seemed to have been inspired by an English book on the microscope written by Robert Hooke. He visited London just when Hooke's book, called 'Micrographia' was at the height of popularity. In it were engravings of familiar specimens – from lice and fleas to moulds and crystals – including some remarkable studies of cloth specimens. To the draper Leeuwenhoek this would have been enormously attractive, and after his return to Holland he began to make tiny microscopes.

The design he favoured was described by Hooke in the Preface to 'Micrographia'. Hooke explained how to melt a tiny bead of glass, to polish it using jewellers' abrasives, and then mount it against a hole punched in a small metal plate. Leeuwenhoek's finest lenses probably gave him a magnification of up to 500 times. His best surviving lens, locked away in the University of Utrecht, magnifies 266 times, and is good enough to







Brian Ford, who discovered Leeuwenhoek's original preparations, flew with them to Holland where he viewed them using one of the original tiny microscopes *(far right)*. **The microscope was simplicity itself: a tiny bead of polished glass, the lens, mounted over a hole in a metal plate, was held up to the eye and focused using a screw which altered the distance between the specimen and the lens. Three of Leeuwenhoek's original preparations show just how carefully he worked. After 300 years, instantly recognizable, a water flea stares out at us** *(top right)*; **another slide shows a long-tailed rotifer** *(centre)* **and a third shows a section through plant tissue** *(bottom)*. **When compared with the view through a modern phase-contrast microscope it is surprising how well the original tiny lens performs. Also, Leeuwenhoek had devised surprisingly sophisticated techniques for preparing specimens.**

study bacteria with ease. It is amazing to realize that these tiny and primitive microscopes gave the same sort of magnification and definition as the highly engineered optical instruments of today.

Leeuwenhoek became an obsessive observer of living things. He carried lice around with him, hidden on his body, to study their development. The drawers and cupboards of his home were filled with dry and decaying specimens of animal tissues for study with his tiny microscopes.

Despite his lack of any scientific training, Leeuwenhoek was indeed the founder of modern biology. His studies of corpuscles, bacteria, pond life, spermatozoa and the structure of living creatures set in train the modern era of microscopy. He even observed nuclei inside living cells.

Leeuwenhoek's career was effectively launched in 1673 when he was introduced to the Royal Society through a letter written by a compatriot, Reinier de Graaf. Leeuwenhoek began to send specimens to the Royal Society of material he had prepared for inspection with his microscope. One letter he despatched said, 'I have sent you and your curious friends some small particles, cut off with a sharp razor, cork, the pith of elder and the white of a quill'. The specimens were stored on squares of paper, each folded over four times to make a small packet.

It was these very specimens that Ford discovered 307 years later, still attached to the original letter. Leeuwenhoek sent over many other preparations including some sections of the optic nerve of a cow and some dried pond material that contained many species of microbes he had discovered. All the specimens uncovered by Ford proved to be in remarkably good condition.

A legend

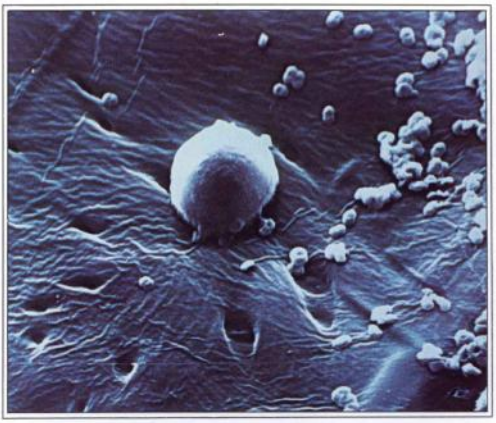
Leeuwenhoek became something of a legend in his own time. He was elected to Fellowship of the Royal Society and received visits from such distinguished people as Peter the Great, Czar of Russia and the English Queen Mary II. Despite all his activity as a lay scientist of international acclaim Leeuwenhoek could only speak Dutch. He had to rely on friends to translate scientific papers written in French and English in order to keep abreast of developments in the field of microscopy.

Just how fine Leeuwenhoek's specimens actually were emerged when Ford prepared the sections of elder pith and cork for analysis in a modern electron scanning microscope in the Department of Zoology at Cardiff University. Coated with a fine layer of gold, to make them electrically conducting, the specimens were displayed with three-dimensional clarity. Each was cut as fine as would be the case if they had been prepared in a modern botany laboratory. The regular edges showed how perfectly sharp Leeuwenhoek's razor edge had been.

For the first time in history, a leading scientist of today was able to inspect specimens from the earliest days of microscopy. But this was not the most exciting experiment Ford planned. He flew with selected sections to Holland, and with the assistance of the head of the University Museum in Utrecht, Dr. Peter Kylstra, carefully mounted

Chris Lyon

The original Leeuwenhoek microscope *(left)* **when compared to the high precision instruments of today** *(below)* **was tiny and primitive. Today's microscopes have internal light sources, high quality lenses and phase-contrast systems. Leeuwenhoek's had a glass bead as a lens, yet the magnifying power and definition compare very well with modern light microscopes. His best surviving lens could magnify specimens over 250 times, enough to see bacteria clearly.**



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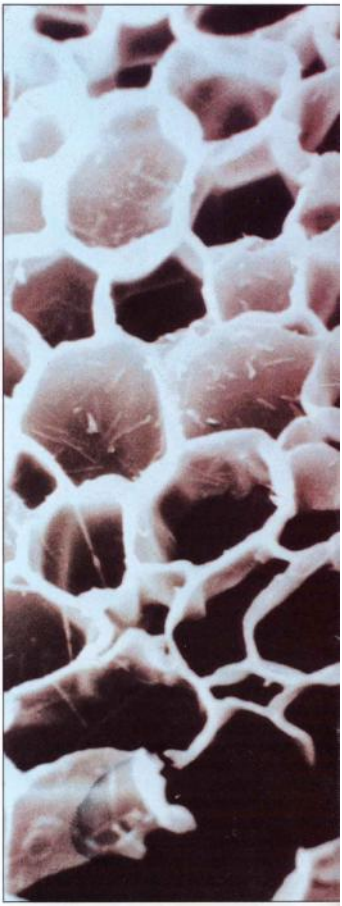
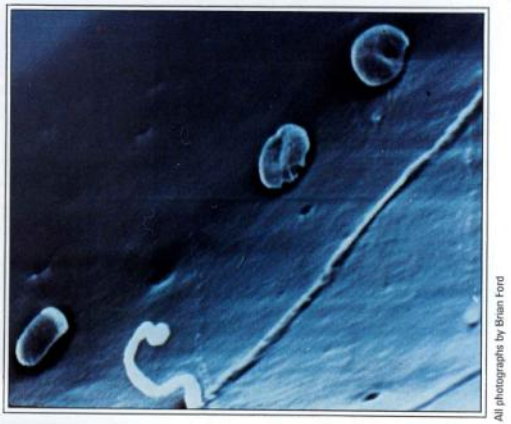


the original Leeuwenhoek microscope onto a specially modified stand he had designed for the purpose. With this contraption a section of cork and later, elder pith, was meticulously brought into focus through the lens made over 300 years ago. The amount of detail revealed was unexpected. Even fine white fungal threads that had grown in the specimens over three centuries in storage could clearly be seen. It was a triumph for the tiny pin-head-sized lens.

Difficult experiment

For comparison, the identical cells were later located under a modern Leitz microscope fitted with phase-contrast optics, and a comparative view obtained. This experiment revealed that Leeuwenhoek's view was surprisingly close to the image generated by the best modern lenses. Finally, in a delicate and difficult experiment, the same cells were captured under a scanning electron microscope, one of the world's most advanced microscopes. These experiments together spanned the entire history of the microscope, from its humble beginnings to its high-tech present form, and revolutionize our understanding of the beginnings of microscopy. Gone is the previously accepted view that (in the words of one historian) Leeuwenhoek did little more than 'tear apart' specimens for examination. On the contrary, he took great care with specimen preparation, cutting very fine clean sections. This revelation puts back the origins of microtomy (the preparation of sections for microscopic examination) by as much as two centuries.

In later experiments, the dried specimens of pond microbes were examined by an electron microscope. Ford wished to see how they would have looked to Leeuwenhoek when they had been freshly gathered. To do this Ford reconstituted the specimens, using sterilized pond water. They were allowed to soak for two days before being submitted to optical microscopy, using a phase-contrast system of lenses. The reconstituted cells had a remarkably life-like appearance. Some of the algae Leeuwenhoek had described revealed detailed cellular structures. Even microscopic animals – such as the tiny rotifers



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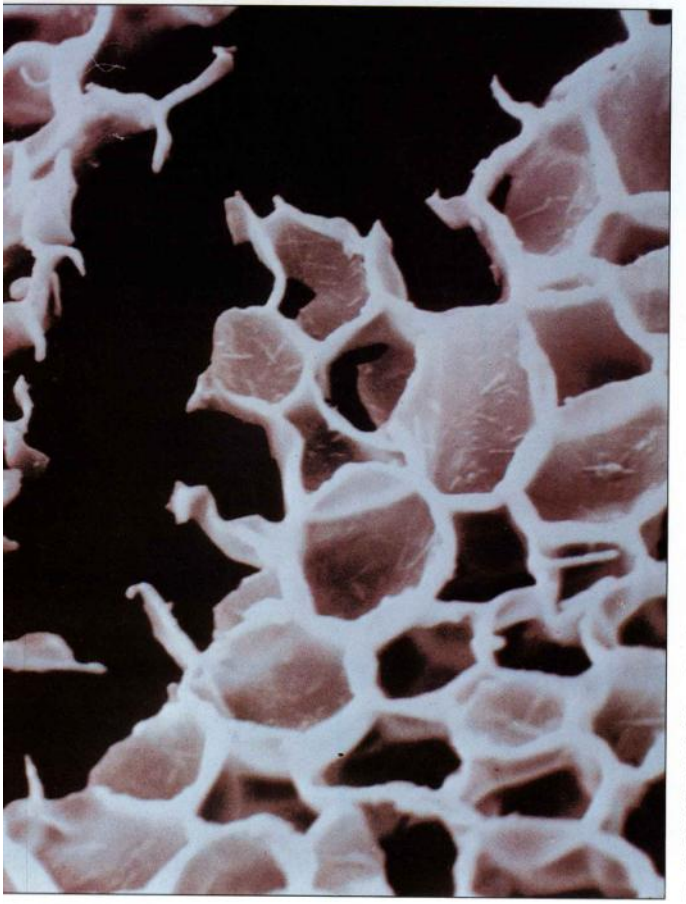

Some of Leeuwenhoek's preparations were found to have traces of the man himself left on them. One intriguing slide had a white blood cell deposited on it. This cell, which was probably produced by coughing, was surrounded by bacteria which had been actively growing at the time (*top left*). **It is thought that Leeuwenhoek had a throat infection when making this preparation. Another slide shows traces of red blood cells** (*above*). **He probably used a shaving razor to cut the sections for this slide and red corpuscles would have been transferred from the blade onto the sections. His preparations often showed tiny animals never before seen by Man, like this tiny mite** (*centre*). **Some of the original material was studied using a scanning electron microscope. The quality is amazing** (*left*), **still displaying a remarkable three-dimensional clarity.**

Leeuwenhoek discovered – could be easily recognized.

Most intriguing of all were the microscopic traces left by Leeuwenhoek himself. Ford located some red corpuscles (erythrocytes), their edges partially eroded with time, probably left behind when Leeuwenhoek's shaving razor was used to cut sections. Later, a white corpuscle was seen surrounded by bacteria that had been actively growing at the time they were deposited, probably by coughing. Did Leeuwenhoek have an infected throat at the time he prepared these specimens?

Nine survivors

It is thought that Leeuwenhoek made about 500 microscopes in his lifetime, of which just nine are known to have survived to the present day. The discovery of an equal number of specimens completes this picture of a truly remarkable man who founded modern microbiology, a science that is increasing in importance today with the emphasis on biotechnology taking over as the new technology.

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