Revelation and the single lens

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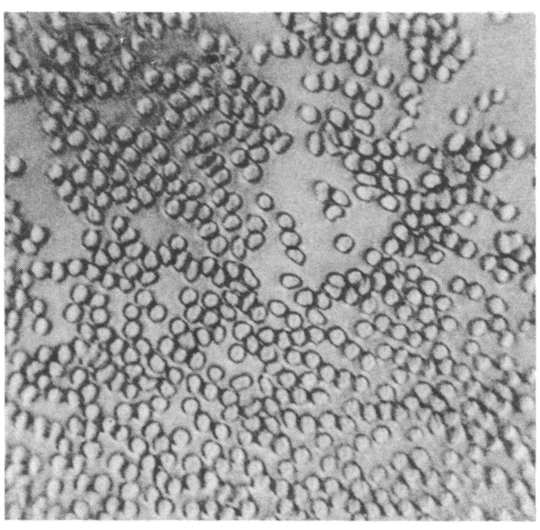
Perhaps the most misunderstood instrument in the history of medicine is the simple microscope. It is seen as an unsightly plaything, a single bead of glass or semi-precious mineral, generating hazy and multi-coloured images that were blurred and distorted.[1] I have reconstructed many of the pioneer experiments using microscopes from the period covering the late seventeenth century to the early nineteenth, and find that in practice the performance of these single-lensed instruments far exceeds such preconceptions. The images that can be obtained compare favourably with what we would expect to see today.

Antony van Leeuwenhoek

The simplest of these microscopes must be the type made by the great pioneer of microscopy, Antony van Leeuwenhoek. This year saw the 350th anniversary of his birth. Leeuwenhoek, who did not begin his half-century of devotion to the science of microscopy until he was nearly 40, made some 4-500 little microscopes by rivetting together rectangular plates of metal (often brass or silver) which he had perforated with an aperture in which the lens was "sandwiched". The specimen was usually held on a small metal pointer in place of a stage, and it could be moved into position and then focused by two screws set at right-angles to each other. The whole instrument was around 50 mm in length, and observations were made by holding the microscope close to the eye and illuminating it with a restricted cone of light. This would be a candle or a lamp-flame, or for daylight observations the light from a distant window. Leeuwenhoek understood the need to restrict the aperture of his illuminant in order to obtain a clearly defined image.



Unstained smear of author's erythrocytes imaged with Leeuwenhoek microscope in fig 1. View compares favourably with a modern microscope of medium power, and bacteria can be satisfactorily resolved by this lens, which dates from around 1700.

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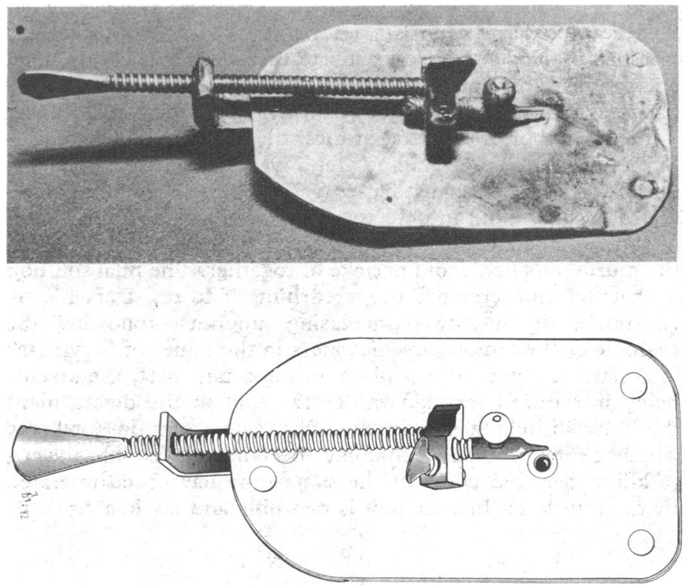


Photograph of original Leeuwenhoek microscope at the University of Utrecht and diagram showing its construction. Specimen was glued or impaled on point adjacent to single lens. Note positioning screws and small lens aperture immediately behind pointer. The entire assembly is less than 50 mm long.

The figure on the left shows how good his lenses could be in practice. Erythrocytes are not easy structures to examine successfully, even using modern microscopes of high resolution. The specimen here was an unstained and unmounted finger-prick smear of my blood, imaged through the Leeuwenhoek microscope that is now in the collection of the University of Utrecht. This instrument has a magnification of $\times 266$[2] and a resolution approaching 1 μm. I have used a modern single-lens microscope to demonstrate living bacteria of the genus *Spirillum*,[3] and the Leeuwenhoek microscope at Utrecht shows bacilli, and the mixed bacterial populations of buccal mucosa smears, with ease. Little wonder that one worker has reportedly said that a comparison between this lens and a sophisticated Zeiss doublet lens of the second half of the nineteenth century (when lens grinding was at its height) showed the Leeuwenhoek lens to give better results.[4]

But Leeuwenhoek was not only a skilled instrument maker and observer. My investigation of his work led to the unexpected and invaluable revelation that the earliest of the specimens he sent to London in 1674 had survived to the present day,[3 5] and these have shown for the first time how expert Leeuwenhoek was as a technician. He could cut sections of plant material down to 15 μm and less, and the range of specimens he sent to the Royal Society between 1674 and 1687 show a wide-ranging ability to handle material.[3]

Where did he first come into contact with microscopy? The biographical accounts[6] suggest that he was entirely self-inspired and was making microscopes of his own design in the late 1660s. But Leeuwenhoek himself, and his friend the anatomist Reinier de Graaf, both wrote in 1673 that he had started making microscopes "recently"; Leeuwenhoek himself made a visit to London (his only one) around 1667 or 1668, when the second edition of Hooke's popular *Micrographia*[7] was at its height of popularity;

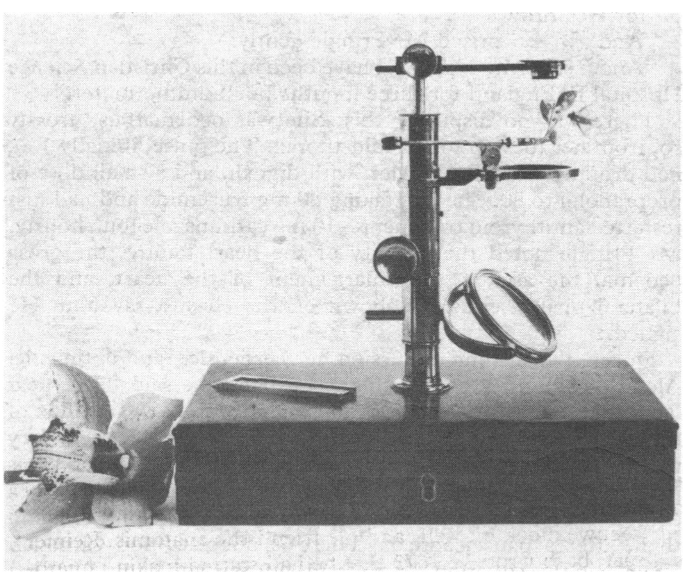
and the first subjects Leeuwenhoek wrote about in his letters to London were, in effect, responses to Hooke's observations.

Most interesting of all, however, are the facts that the specimens Leeuwenhoek first prepared—and which were among those he sent to the Royal Society—were sections of cork, elder pith, and writing quill; and these are referred to in similar words, and in the same order, in *Micrographia*. In addition, the design of the Leeuwenhoek microscope is clearly derived from Hooke's own description:

"Hence it is that if you take a very clear piece of a broken *Venice* Glass, and in a Lamp draw it out into very small hairs or threads, then holding the ends of these threads in a flame, till they melt and run into a small round Globule, or drop, which will hang at the end of the thread; and if further you stick several of these . . . and with a little Tripoly, rub them till they come to be very smooth; if one of these be fixt with a little soft Wax against a small needle hole, prick'd through a thin Plate of Brass, Lead, Pewter, or any other Metal, and an Object, plac'd very near, be look'd at through it, it will both magnifie and make some Objects more distinct than any of the great Microscopes."[8]

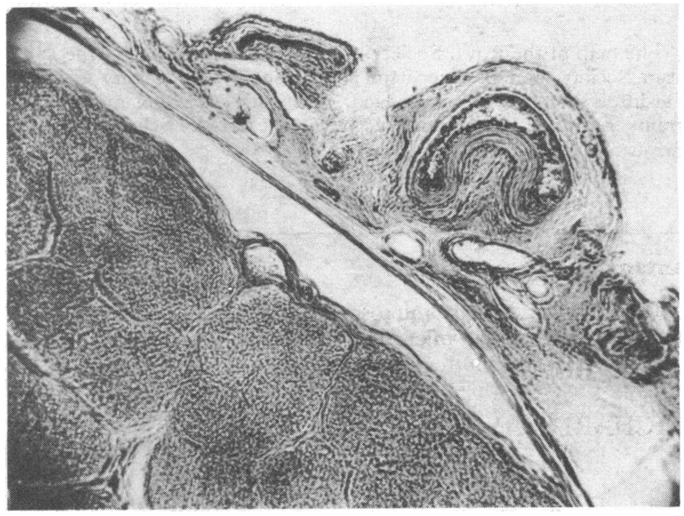
Brown and the Bancks microscope

The reason why simple microscopes were not more popular had nothing to do with the quality of the image they produced, but was because—in Hooke's own words[8]—they "are yet very troublesome to be us'd, because of their smallness, and the nearness of the Object." Over the next two centuries, simple microscopes became progressively more complex and the instruments of the first half of the nineteenth century were usually fitted with a double-sided mirror and focusing controls. By 1830 some form of fine-adjustment was often incorporated into the design. One leading manufacturer in Britain (who has been all but ignored in the standard works) was Robert Bancks. His design was owned by Darwin, and by many biologists of the early 1800s. The Bancks microscope owned by Robert Brown, and with which he made his pioneering observations on Brownian movement and the cell nucleus, is now in the collections of the Linnean Society. It was mounted on the lid of a mahogany box and was fitted with a rack and pinion focusing control near the midpoint of the main pillar. A second control allowed the lens arm to be tracked across the specimen, and the single lenses (mounted in brass cups each about 20-25 mm diameter) ranged in magnification from ×6 to ×170.



Simple microscope of Robert Brown, FRS, now at the Linnean Society. It was with this instrument that Brown observed the nucleus in orchid epidermis, so naming a structure fundamental to modern medicine.

Though Leeuwenhoek observed cell nuclei, and figured them in his studies of frog erythrocytes, Brown first noted them as an "areola, or nucleus" in the epidermal cells of orchids and their allies and in this manner gave science one of its most familiar terms. The cytoplasmic streaming within the cells of the flowers from *Tradescantia virginiana* was first described by Brown using this form of microscope, and recently, to commemorate the 150th



A Victorian section of human optic nerve viewed through No 3 lens of Brown's microscope, with a magnification of ×32·5 (Brown's most powerful lens magnifies ×170). Optic artery, epineurium, and perineurium are well displayed by this modest lens.

anniversary of Brown's naming of the nucleus, I repeated his original experiments.[9] For all routine laboratory purposes where low or conventional high magnifications are used (though obviously excluding oil-immersion microscopy) I am convinced that the simple microscope would be of value today. For histological use, cellular structures, nuclei, larger cell inclusions (such as the nucleolus) can be seen with ease, and stained preparations of bacteria can be adequately resolved. With a modern single lens magnifying ×395 (which is probably less than Leeuwenhoek's best lenses) I have obtained satisfactory micrographs of human metaphase chromosome plates.

A useful ally

The convenient conclusion that the simple microscope preceded its compound counterpart historically is without foundation. The first microscopes (which predated by several decades the birth of Leeuwenhoek) were compound, and so were the microscopes used by Hooke for his research work almost a decade before Leeuwenhoek entered the field. Even in the mid-nineteenth century, when brass compound microscopes abounded and the principle of achromatism had made them optically superior, simple microscopes were popular. As late as 1854 the Society of Arts awarded a prize for the design of a simple microscope for field use, but from then on the device was seen more as a dissecting microscope, and the achromatic compound instrument came into its own.

Perhaps the mechanical intricacy of the compound microscope made it more attractive and prestigious. Contemporaneous accounts tend to refer to the simple microscope in condescending terms,[10] and the most complex of the compound microscopes, such as the Ross Radial or the Powell and Lealand No 1 of the mid-1800s, were replete with devices that most users must have found decorative rather than useful. One is put in mind of the costly and over-elaborate hi-fi consoles and cameras of today, which seem to reveal more of the aspirations of the owner than anything else.

So it is fitting that we should rehabilitate the reputation of the simple microscope. Through its diminutive lens were discovered the nucleus, bacteria, and a host of cellular structures that had widespread effects on the progress of medicine and biology. We owe it respect; and it might prove to be a useful ally for student use in the increasingly cost-effective era into which we are moving.

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A health hazard

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Mr John Pringle, MS, FRCS, parked his car with dexterity—it had power-steering—and ignored the parking meter. At 5 30 pm it was worth the risk; the wardens would be on their way home, he hoped. He was as eminent a surgeon as one could be in a non-eminent society. He approved of this. The stage had undergone the same metamorphosis as medicine. Now there were fewer stars in the theatre and more generally good flexible actors and actresses. Gone were the days of the Lords Lister and Moynihan, just as there were now fewer Cowards, Lunts, and Thorndykes. In general, he reflected, the change had been for the good. The overall standard across the country had been raised and there were fewer pontificating gods. The growth of medical knowledge had made omniscience impossible.

As he stepped on to the pavement Mr Pringle discreetly dropped his cigarette end down the grated drain-cover in the road. Quite unconsciously he coughed as he climbed the six shallow steps to the main doors of the hospital.

Emerging from the lift on the fourth floor, the chequered garish carpet lining the hall and extended corridor made him feel slightly dizzy. Its tastelessness did not impinge further as he greeted Dr Fowler, occupied at the nurses' station. Mr Pringle liked Dr Fowler, though he did not know him well. A general practitioner, aged about 40, with an FRCS and an MRCGP, who had been a senior surgical registrar, was a comparative rarity.

"Mrs Nolan," Fowler explained about the patient they were about to see, "is aged 45. She asked me to see her for the first time yesterday. She comes from Dallas and is a Christian Scientist." He paused to let the significance of this last remark sink in. "She developed thyrotoxicosis two years ago. After six months, when she was very ill and had lost a lot of weight, her husband, who is not a Christian Scientist, persuaded her to see a doctor. She started taking an antithyroid drug and within three months was immeasurably better. Now . . ."

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"Don't tell me," said Pringle, "let me find out the rest for myself."

Mrs Nolan was propped up in bed. She was jaundiced and emaciated. Her animation and her prominent eyes contrasted with her thinness and extreme dyspnoea that made talking difficult. Even in illness she was elegant and attractive. From the side of the bed Pringle could not fail to notice the prominence of her neck veins. The pulsation in her jugulars extended to her ear lobes which pulsated regularly with each right ventricular contraction. "Surprising," he thought, "that she is still in sinus rhythm and has not developed atrial fibrillation."

"Yes," Mrs Nolan said in answer to his question, "I improved greatly with the doctor's treatment, but I am a Christian Scientist so I came to England to receive Christian Science treatment."

"My wife promised to continue taking the tablets our doctor in Dallas prescribed," interjected her husband, grey with concern, "but she threw them away, down the lavatory, as her plane took off for Heathrow."

"And . . . ?," prised Mr Pringle gently.

"And," said Mrs Nolan, "I have been in this Christian Science Hospital in England for three months but I am no better."

There was no disputing this. She was oedematous, grossly so, from her toes up to her mid-thorax. The pulse, initially 130, had dropped, said Dr Fowler, with digoxin and a small dose of propranolol to 80. She was taking 80 mg frusemide and had just restarted antithyroid treatment—10 mg carbimazole four-hourly. Mr Pringle noted the severity of the heart failure, the gross oedema, the ascites, the enlargement of the heart, and the bilateral pleural effusions shown on the chest *x*-ray film. He sighed.

During the ensuing discussion he was gentle—and optimistic. Alone outside the room with the husband, he said "The next week is likely to be critical. Your wife's jaundice is an index of the severity, of the gravity, of the heart failure which is secondary to her thyrotoxicosis. If she gets better over the next few days it is probable that with proper medical treatment she will make a complete recovery." He emphasised the word "proper" and then, after a pause, added "There is no place for Christian Science in this situation, I am afraid, but this you know." "It is a health hazard" replied Mr Nolan. "Indeed," reiterated Pringle quietly, "a health hazard."