

Three Hundred Years After Hooke and Van Leeuwenhoek: Optical Microscopy in the Twenty-First Century

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We are always trying to extend our vision through the four senses of sight, sound, touch and smell. The microscopy devised by Hooke and Van Leeuwenhoek more than three centuries ago are examples of methods used to extend our visible vision. In fact, instrument designers since then have constructed microscopes using each one of our senses to give us peeks into the microworld. When Robert Hooke took some scrapings from his teeth and viewed the bacteria in these scrapings in his primitive microscope,¹ a whole new view of the world ensued. It would, however, have been difficult to predict how microscopy would evolve in the following centuries.

I am asked how to make similar predictions. Where will optical microscopy be in a decade? In order to even attempt to answer this question with some sense of validity we must look at the prehistory and hope it allows us to extend into the future. However, insofar as technology is concerned, history has shown that (except for perhaps Jules Verne²), we are inadequate at making predictions. For example, think of the technology around in the '70's compared to what is actually being used today. Having said this, it should be noted that between quantum jumps in conception, instrument development improves at an incremental pace. Consider, for example, that optical microscopes used two centuries after Hooke and Van Leeuwenhoek were not much different than their 17th century counter parts. It was the elucidation of modern optics principles by Abbe and then by Zernicke³ that allowed for the design of most present day conventional optical microscopes and revolutionized the microscopes of their day.

After that revolution, the laws of physics appeared to forbid imaging structures significantly smaller than the wavelength, λ , of the light used. This therefore led to the search for other methods to increase resolution - for

example, the use of electrons. This revolution (e.g., ref. 4) led to the electron microscope and its ensuing progeny. Again the conventional electron microscopes of the '80's were not much different from those in the '40's. The development of scanning beam methods and field emission sources led to the imaging of atoms in the '70's⁵ and that avenue has been refined and perfected.

The same sequence of events has and will happen in optical microscopy. The rediscovery of near-field optics (e.g., reference 6) after its initial conception by Syngge in 1928⁷ has led to an explosion of new interest in the development of near field technology. I would surmise that this will now mature into a phase of more evolution as people try this form of microscopy with a different angle. By the next century, near field imaging should be available at close to nm spatial resolution using visible light.

In addition, offshoots of technology in other areas will be more frequently applied to optical imaging. A case in point is "video microscopy" (e.g., ref. 8) in which electronic imaging has allowed increased contrast of optical images after-the-fact. Coupled with advanced computational technology this has led to real optical tomography. As electronic recording media improve so will our ability to acquire photographic quality pictures (i.e., lots of pixels) and this will, in turn, allow for further revolutions in TV recording.

Other technologies will also find their way into optical microscopy. For example, the development of intense laser sources led to the use of "threshold" effects for less destructive optical microscopy. The "two proton" microscopy developed by Strickler and Webb⁹ enables us now to produce a focal spot extremely constrained in two directions.

Finally, because computational technology has proceeded and will continue to proceed at a rapid pace, rapid computations will be able to be performed on optical images to allow quasi-real time three dimensional imaging. This will allow much more definitive experiments to be performed as the algorithms get faster and more efficient.

In short, we are at the beginning of a renaissance in optical microscopy and about the only thing of which I am relatively sure is that this renaissance will continue into the next century. ■

1. Robert Hook, *Micrographia*, 1662.
2. Jules Verne, *Twenty Thousand Leagues Under the Sea*.
3. M. Born and E. Wolf, *Principles of Optics*, Pergamon Press, London, 6th ed. (1980).
4. Ernst Ruska, *Z. Physik*, 87, (1934) 580.
5. M. Isaacson, et al., *Proc. Nat. Acad. Sci. USA*, 74 (1977) 1802.
6. M. Isaacson, ed., *Proc. of the 2nd International Conference on Near Field Optics*, Raleigh, North Carolina (1994, in press)
7. E.H. Syngge, *Philosophical Magazine*, 6, (1928) 356.
8. S. Inoue, *Video Microscopy*, Plenum Press, New York and London, 1986.
9. J. Strickler and W.W. Webb, *Proceedings of SPIE*, vol. 1398, CAN-AM Eastern '90

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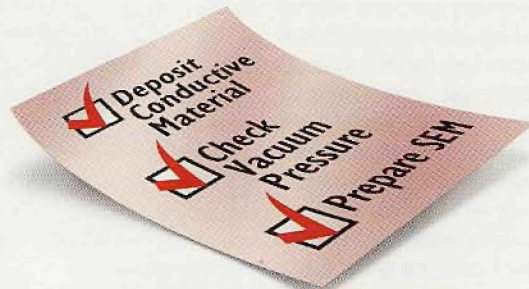
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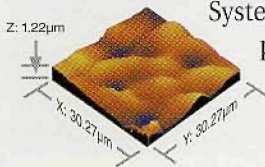
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