MAGNIFYING POWER

New microscopes are revealing sights that have never been seen before. *Nature* profiles five machines that are changing how biologists view the world.

Close-ups of cork, lice and fly's eyes do not inspire the rhapsodies that they did more than 300 years ago when Robert Hooke first observed them under a microscope. But other pictures do — the boughs and twigs of a branching neuron in its forest; the scuttle of vesicles delivering molecular loads; the endless thrill of a cell carving itself in two again — and again, and again — as an embryo buds into being. Now, as then, microscopy is central to the understanding of living systems. In this special section, *Nature* reporters look at five microscopes that are resolving aspects of life in stunning new ways.

Microscopes today still do the job that Hooke asked of his: gathering information on details that the human eye cannot resolve and magnifying them to a size that it can.

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The microscopes that greet undergraduate biologists in university teaching labs are remarkably similar to those that Carl Zeiss developed in the nineteenth century. On that basis of continuity, one might think that the technology was mature. But although the laws of optics have not changed, the ways they are applied are in constant flux.

Part of the flux is due to the ingenuity of engineers and scientists. Applying the laws of optics to electrons, rather than to light, was possibly the greatest development in microscopy of the twentieth century — and it is still yielding dividends in the twenty first, as the ultrahigh-voltage electron microscope at Osaka demonstrates (page 634). Recently some of that ingenuity has explored the possibility of doing with electronics what used to be done with carefully crafted glass, producing technologies that do away with lenses altogether. The microscope-on-a-chip featured here could turn microscopes into a disposable commodity (page 632).

But perhaps the greatest potential for progress is not so much in the engineering of microscopes, as in the engineering of what can be seen with them. Hooke and his successors used the microscope to see the world as it was, revealing seemingly miraculous detail at scales far too fine for human craft — powerful evidence, so it seemed, for the infinite superiority of divine craftsmanship.

Today's microscopes are used more and more to look at systems that are carefully prepared to make their workings visible. The dramatic fruits of this transformation can be seen in the green-fluorescent-protein revolution of the past decades, which has made it possible to engineer appropriate illumination into organisms under study. Its full impact will only be realized when microscopes can capture everything that these organisms can reveal.

This is why there is so much excitement around the arrival of the stimulated emission depletion (STED) microscope (page 638) and other 'super-resolution' techniques that are allowing light microscopy to resolve details on the nanometre scale, something once thought impossible. And the unassuming single plane illumination microscope (SPIM) microscope, with its way of imaging life without killing it, could herald an era of 'systems microscopy' (page 630). New ways of manipulating life will supply — and indeed demand — new ways of seeing what is going on. At the same time, there will also be those who prefer to make observations without the interference of labels. For those researchers, there are improved ways to identify molecules by their intrinsic chemical properties, such as the stimulated Raman scattering microscope sitting in a Harvard basement (page 636).

All these developments share one thing in common: computers. As tools for the construction, manipulation and distribution of images, whether moving or still, in two-dimensions or three, computers are almost as central to the microscope now as the lens. The startled eye at the eyepiece, as rendered on our cover, may be increasingly a thing of the past, as all that microscopes show comes to be seen on screen. The shock of new discovery, though, will remain — and perhaps, even, intensify — for as long as the workings of life become ever more variously and acutely examined. ■

See Editorial, page 615, Essay, page 642 and online at http://tinyurl.com/microspecial.