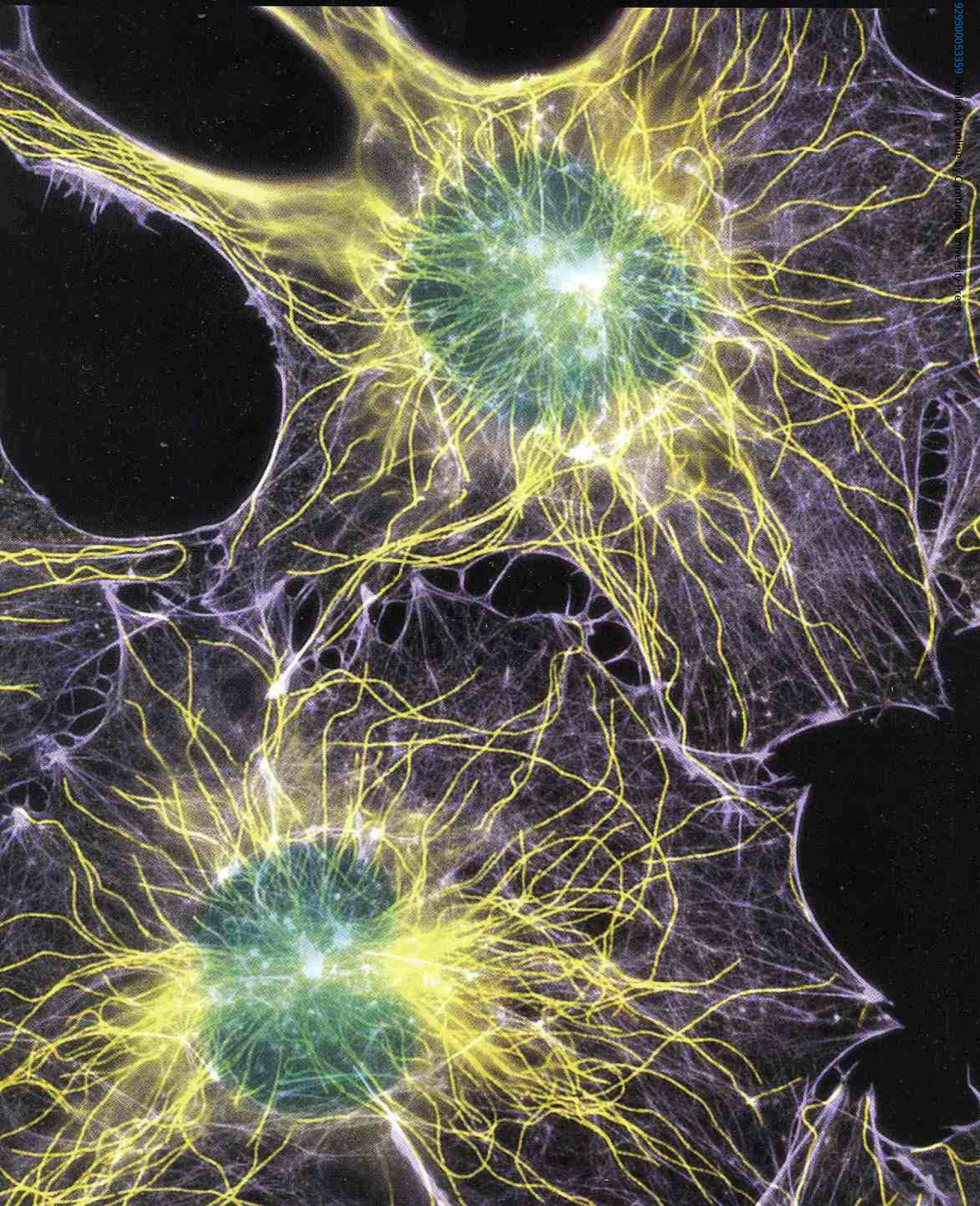


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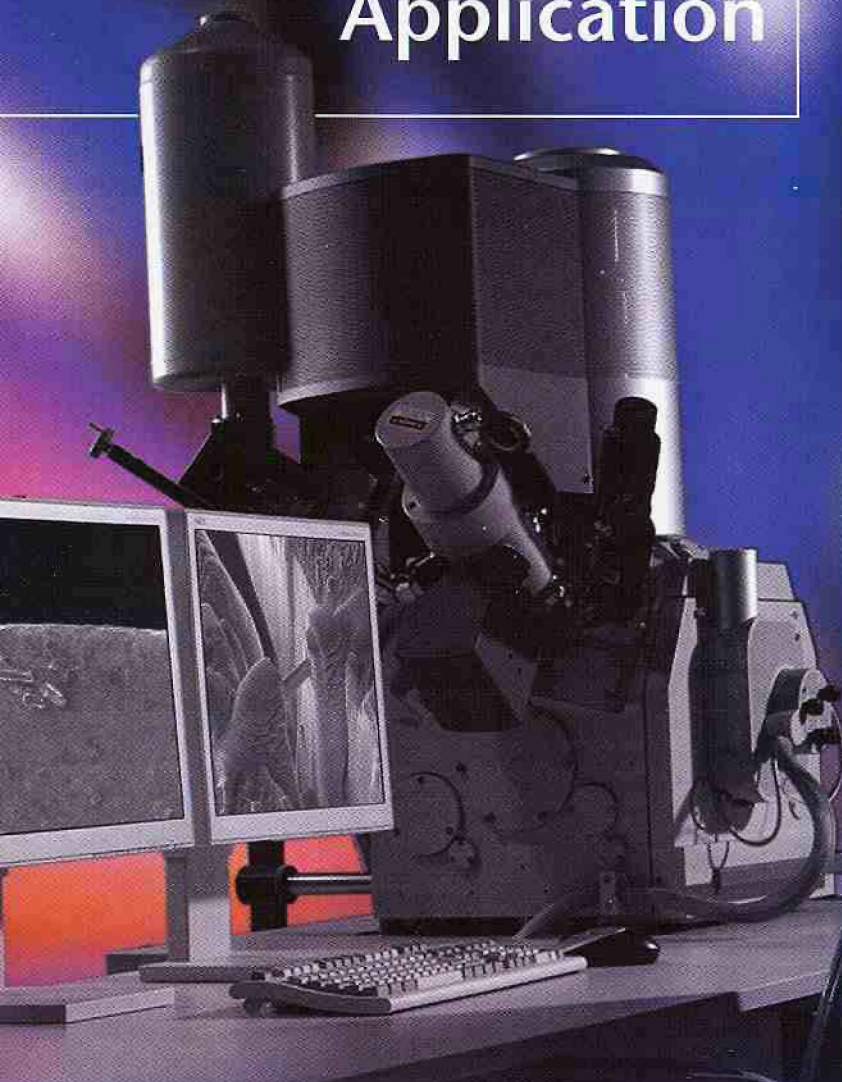
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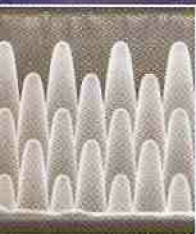
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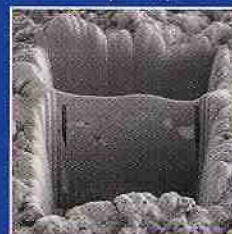
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Sub-Ångstrom Resolution

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Antoni van Leeuwenhoek showed the practical use of the light microscope in the 1600s after much effort to improve the quality of optical lenses. Pioneering microscopists such as Ernst Abbé, Hermann Ludwig Ferdinand von Helmholtz, Lord John Rayleigh, Carl Zeiss, and August Köhler then brought us to the brink of optimal performance of the light microscope approximately a century ago. Ernst Ruska and Max Knoll showed in the 1930s that high-energy electrons could be used in place of light, giving greatly improved resolution. In the 1970's Albert Crewe and co-workers developed the scanning transmission electron microscope (STEM) and used the Z-contrast method to improve resolution in the electron microscope by about a factor of two. The scanning probe (non-optical) microscopes aside, there hasn't been a significant advance in spatial resolution since.

It has been well appreciated that spherical and chromatic aberrations have limited resolution in transmission electron microscopes (TEM) as well as limiting the probe size in the STEM. Philip Batson, Niklas Dellby, and Ondrej Krivanek have greatly modified a commercially available VG Microscopes STEM to achieve a probe size of 0.74 Å and a consequent resolution of 0.76 Å², this is the best probe size ever reported for an electron microscope.

The microscope was modified to correct spherical aberration, and the STEM design was chosen since it is less sensitive to chromatic aberration. The heart of the aberration correction was the introduction of seven new sets of electromagnetic lenses (four

quadrupoles separated by three octupoles, with extremely stable computer-controlled current supplies) into the optical pathway. Detectors (television cameras) were placed in the far field behind the specimen. The software then corrects the detected aberrations, by introducing distortions to oppose existing aberrations, canceling them out.

Batson *et al.* pointed out four recent technical advances that made these improvements possible. First, computation of electron optical parameters is now possible, allowing practical designs to be devised. Second, there have been significant advances in mechanical fabrication tolerances. Third, the stability of electronic components has improved recently, allowing for exquisite control of currents within electromagnetic lenses. And fourth, the computing capabilities to provide real-time feedback between the detectors and lenses are now readily available.

Using this improved instrument with resolving power below the diameter of a hydrogen atom, Batson *et al.* are using it to image single atom defects in inorganic specimens. The usefulness of this instrument in monitoring nanofabrication was obvious. The potential of employing such a STEM in a manner somewhat similar to confocal light microscopy to image subcellular structure at the atomic level in biologic specimens is also very tantalizing. Nevertheless, Batson *et al.* have made the most significant breakthrough in optical microscopy in decades. I can hardly wait to see how this new, improved design will be put to use! ■

Footnotes

¹ The author gratefully acknowledges Dr. Philip Batson for reviewing this article.

² Batson, P.E., N. Dellby, and O.L. Krivanek, Sub-ångstrom resolution using aberration corrected electron optics, *Nature* 418:617-620, 2002.

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ABOUT THE COVER

Serum-Starved Mouse Fibroblasts

Fixed with glutaraldehyde in a microtubule-stabilizing buffer and processed for immunofluorescence with a tubulin antibody, fluorescently labeled phalloidin and a nuclear dye. Single channel images were acquired on a conventional epifluorescence microscope equipped with a grayscale 14-bit cooled CCD camera. In order to achieve maximal contrast and an image that is more pleasing to the eye than the usual RGB fluorescence micrographs, the individual grayscale channels were first mixed arithmetically before combining them into a color image. The final, false-colored image, highlights fine details of the cytoskeletal structure and microtubules appear in yellow, filamentous actin in blue and the cell nuclei in green. This fluorescence micrograph was acquired and processed by Dr. Torsten Wittmann, a postdoctoral fellow in the laboratory of Dr. Clare Waterman-Storer at the Scripps Research Institute in La Jolla, CA, and won first place in the 2003 Nikon International Small World Photomicrography contest.