

Bringing Biology into Focus

In 1957, Marvin Minsky patented a "microscopy apparatus" that described the use of a pinhole to limit the light reaching the objective to only that which is in focus—making it the first description of a confocal system. We can be fairly certain that he could not have foreseen how this simple and elegant idea would be modified and refined into a technique that would revolutionize the field of microscopy. Some of this certainty comes from the fact that at the time his invention was patented, the technology was not yet even available to build it.

Confocality, which essentially describes the quality of light as being in the same focal plane, allows for the scanning of a sample to generate optical sections. Reconstruction of these individual images produces a sharp 2-D or 3-D final rendering, a boon for researchers seeking to visualize detail, especially in thick sections or even entire small organisms.

It took another few decades before a working version of Minsky's design was actually realized (unfortunately for Minsky, this was after the patent had already expired). Among other things, the field had to wait for the development of reliable and powerful lasers that could excite fluorophores at a variety of wavelengths, necessary for visualizing cells and subcellular structures. But it was not always smooth sailing for confocal microscopy. Image acquisition speed was in constant tension with detection sensitivity, and increases in either of these degraded resolution. These ongoing challenges can be represented by the so-called Eternal Triangle, with speed, resolution, and sensitivity at its apexes (see main poster). Generally speaking, pulling on one point of the triangle negatively impacts the others. So an increase in resolution invariably means slower image acquisition and/or decreased sensitivity.

Researchers and microscope makers alike are constantly striving to push the boundaries of sensitivity, resolution, and speed. Their determination has produced a steady stream of advances in microscope technology, and researchers armed with these ever-improving tools and techniques are squeezing ever more and better data out of their samples. This poster, created by the *Science*/AAAS Custom Publishing Office and sponsored by ZEISS, leads the reader through the past, present, and future of confocal microscopy. Additionally, you can go online to find an interactive version of the poster with additional information and graphics (posters.sciencemag.org/confocal).

It is our hope that readers will find this poster both engaging and informative. In a field that is moving and growing so quickly, we are providing just a snapshot of where we are today and a glimpse at where we might be in the future. If the past is anything to go by, that future looks quite luminous.

Sean Sanders, Ph.D., Commercial Editor, *Science*

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Background: Confocal image of mouse brain cortex | Courtesy of Yi Zuo, Molecular, Cell and Developmental Biology (MCPB) department, University of California Santa Cruz.

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Publication date: 31 October, 2014

Produced by the
Science/AAAS Custom
Publishing Office



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