NEW WINDOWS ON THE BIOLOGICAL WORLD

Two new kinds of microscopes promise to further biomedical research

BY JOAN AREHART-TREICHEL

Since Anton van Leeuwenhoek developed the first light microscope in the 17th century, microscopes have revolutionized medical science. More than any other instruments, they offer fantastic glimpses into the lilliputian world of cells and subcellular structures.

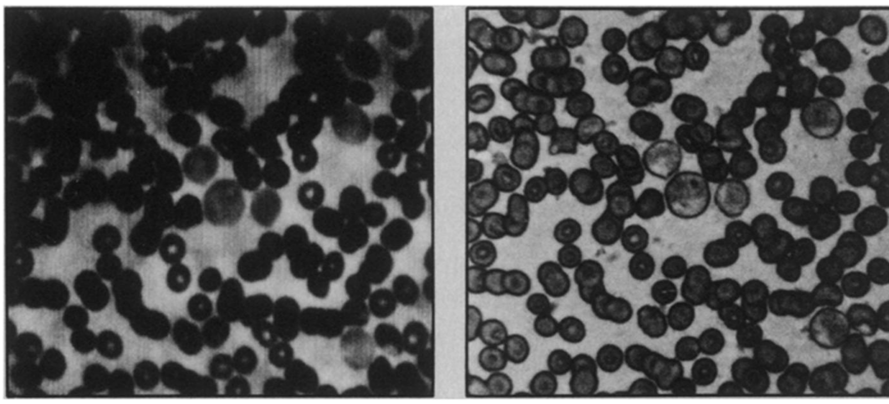
The microscopes that are accessible to biomedical scientists in the 20th century include the light microscope, the transmission electron microscope (available since the 1920's) and the scanning electron microscope (available since 1965). All the microscopes currently on the market use either light or electrons to make an image of a biological specimen. Now two new microscopes may become available to biomedical investigators within several years—an acoustic microscope and a scanning transmission ion microscope. Each promises to yield fresh insights, based on revolutionary techniques, into the murky cellular world.

The acoustic microscope, designed by Ross A. Lemons and Calvin F. Quate of Stanford University, uses acoustic energy to make images, according to a report in the May 30 SCIENCE. Incoming electromagnetic energy is converted to acoustic energy by a transducer on the surface of a crystal. The acoustic wave that is generated propagates through the crystal until it encounters a concave, spherical surface between the crystal and a small volume of water. At that interface the acoustic wave is refracted and focused to a point of about one micron (a thousandth of a millimeter) in diameter. The object is placed at that focal point. A fraction of the acoustic wave is transmitted through the object and is detected by a receiving element exactly like the transmitter.

Another crystal rod with a concave lens surface collects the energy diverging from the focus of the sample and transforms it back into an acoustic beam. Now the beam is propagated through the crystal rod until it hits a second transducer, which converts the acoustic wave back into an electromagnetic signal. The electromagnetic signal then is displayed on a cathode ray tube screen—similar to what is done with a scanning electron microscope—and an image of the biological specimen is produced.

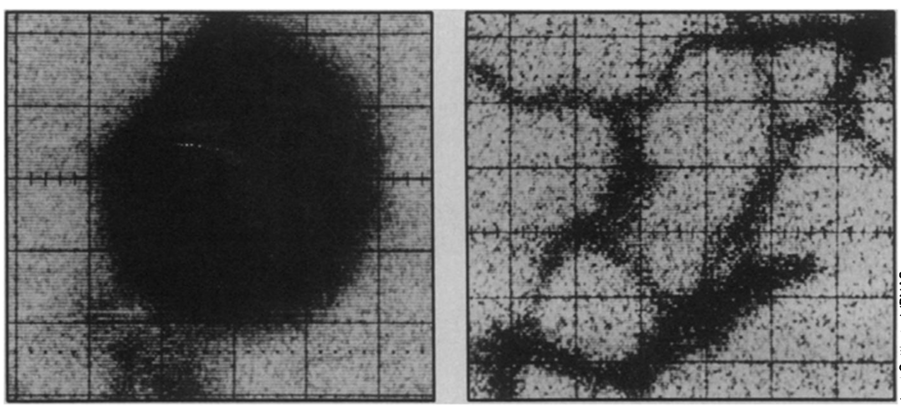
How does the acoustic microscope compare with those already available? Like the light microscope (and unlike the electron microscope), it can visualize living cells and tissues. Another advantage is that because the acoustic microscope uses a different source of energy, it can reveal information about the properties of elasticity and viscosity (fluidity) in cells and tissues. The acoustic microscope is expected to offer new insights into the contractile properties of muscle fibers, cellular cytoplasm during cell division and differences between diseased and healthy cells and tissues, as far as elasticity and viscosity are concerned.

The acoustic microscope has another property which can be an advantage in some cases, but a disadvantage in others.



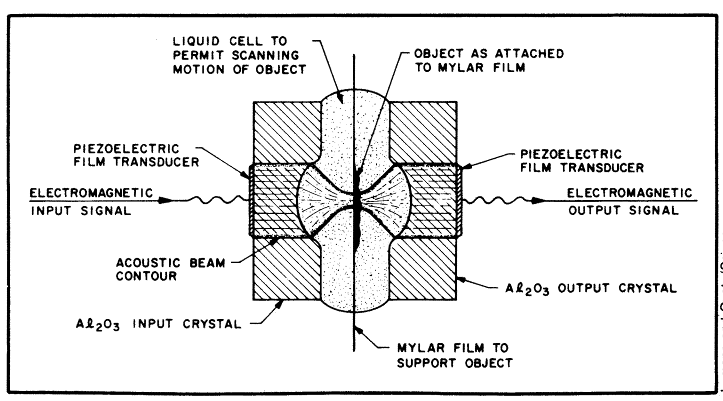
Lemons and Quate/Science

Acoustic image of bone marrow (left) and optical image of the same biological specimen.



Levi-Setti et al/PNAS

Scanning transmission ion photos of a lymphocyte nucleus (left) and a chromosome.



Lemons and Quate/Science

Diagram of the acoustic microscope system showing the lens configuration.

Its depth of field is significantly less than that of the scanning microscope and more like the light microscope. This is because a slender beam is focused from a long distance, like a very fine pencil, so information is equally focused at all points. In contrast, the acoustic microscope uses a highly convergent beam so that there is a steeply converging cone. If a sample is put in the vicinity of the focus, only that part of the sample at the narrowest part of the cone will be in sharp focus. So the acoustic microscope would be good for localizing a particular region of a specimen, obscuring the fraction of the specimen above or below. The scanning electron microscope is better for visualizing the total specimen.

And the acoustic microscope has a patent disadvantage. It will probably never approach the resolution of the electron microscopes, which is several thousands times greater. So, says Lemons, "We are shooting more toward the goal of seeing with the same fine detail as through a light microscope."

Stanford University has licensed the acoustic microscope (of which only four prototype machines exist) to the American Optical Corp. for development. The microscope, Lemons anticipates, should be on the market in the next several years. "It is simply," he says, "a matter of engineering the thing for simplicity of use."

The scanning transmission ion microscope was designed by University of Chicago physicists Riccardo Levi-Setti, W. H. Escovitz and T. R. Fox. As reported in the May PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, ion beams are focused down to a very small spot, then scanned across a specimen, and the ions sent through the specimen are displayed on a cathode ray tube screen. An image is produced. The depth of field of the scanning transmission ion microscope approximates that of the standard transmission electron microscope, providing images that look two-dimensional rather than three-dimensional.

The most revolutionary features of this microscope are several contrast mechanisms, based on the interaction of fast ions with matter, which should complement, in a unique fashion, the information obtained with the electron microscopes. The disadvantage of this microscope, as with the electron microscopes, is that cells and tissues must be killed, chemically fixed and thin-sliced before they can be visualized. Also, in its present stage of development, the ion microscope has a resolution slightly better than the light microscope, but not nearly as good as the electron microscopes.

The Chicago physicists are attempting to improve the resolution and expect progress this year. But it will be a few years before a high-resolution scanning transmission ion microscope will be available to biomedical researchers. ☐