Ruffles and Flourishes

Each living organism has a characteristic way of moving. A man walks, a child toddles, a horse trots, a snake slithers, a bear shuffles. What about smaller organisms? Well, it seems that a cell "ruffles."

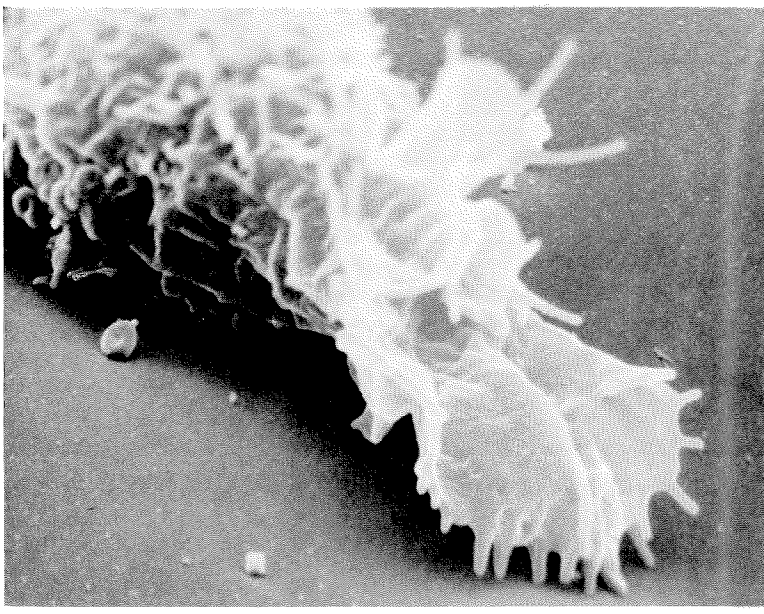
At least this is how Jean-Paul Revel, professor of biology, describes the carefully orchestrated process by which a cell uses a thin ruffled line of veil-like folds along its "front" edge to pull itself across a surface.

Our understanding of cell movement has been based on indirect evidence only. But Revel, using the newly acquired scanning electron microscope (SEM), has produced a series of detailed photographs that gives him a direct look at the ruffles. His spectacular close-ups are also among the first high-quality, high-resolution photographs ever taken of the ruffling mechanism in operation.

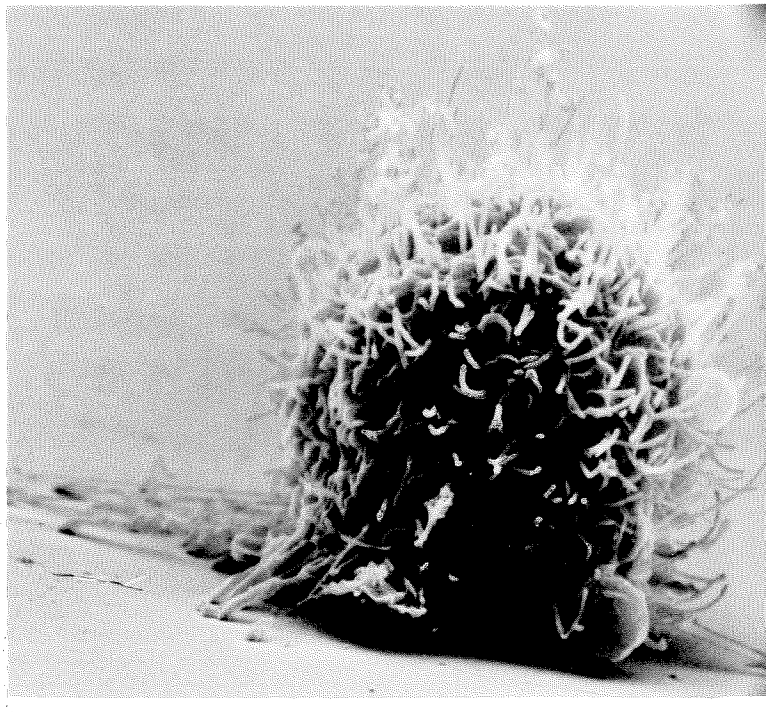
What seems to happen is that as a cell moves across a surface, ruffles can be seen on its forward edge. These ruffles grow upward, extend outward, and then drop to the surface, where they stick. The rest of the cell then flows into and over the ruffles at these attachment points. As the body of the cell moves over the first set of ruffles, another set appears near the new front edge. This second set attaches to the surface in turn, and the first set—now at the rear of the cell—disconnects.

The exact mechanism by which this ruffling takes place —or even if it is involved at all in cell movement—is not clearly understood, and two other possibilities are being examined. One is that the ruffles are the way the cell forms new membrane. The fact that this occurs while the cell is moving is coincidental. The other possibility is that the primary movement mechanism of the cell is internal and that the ruffles are just portions of the external cell surface that have been distorted by this process.

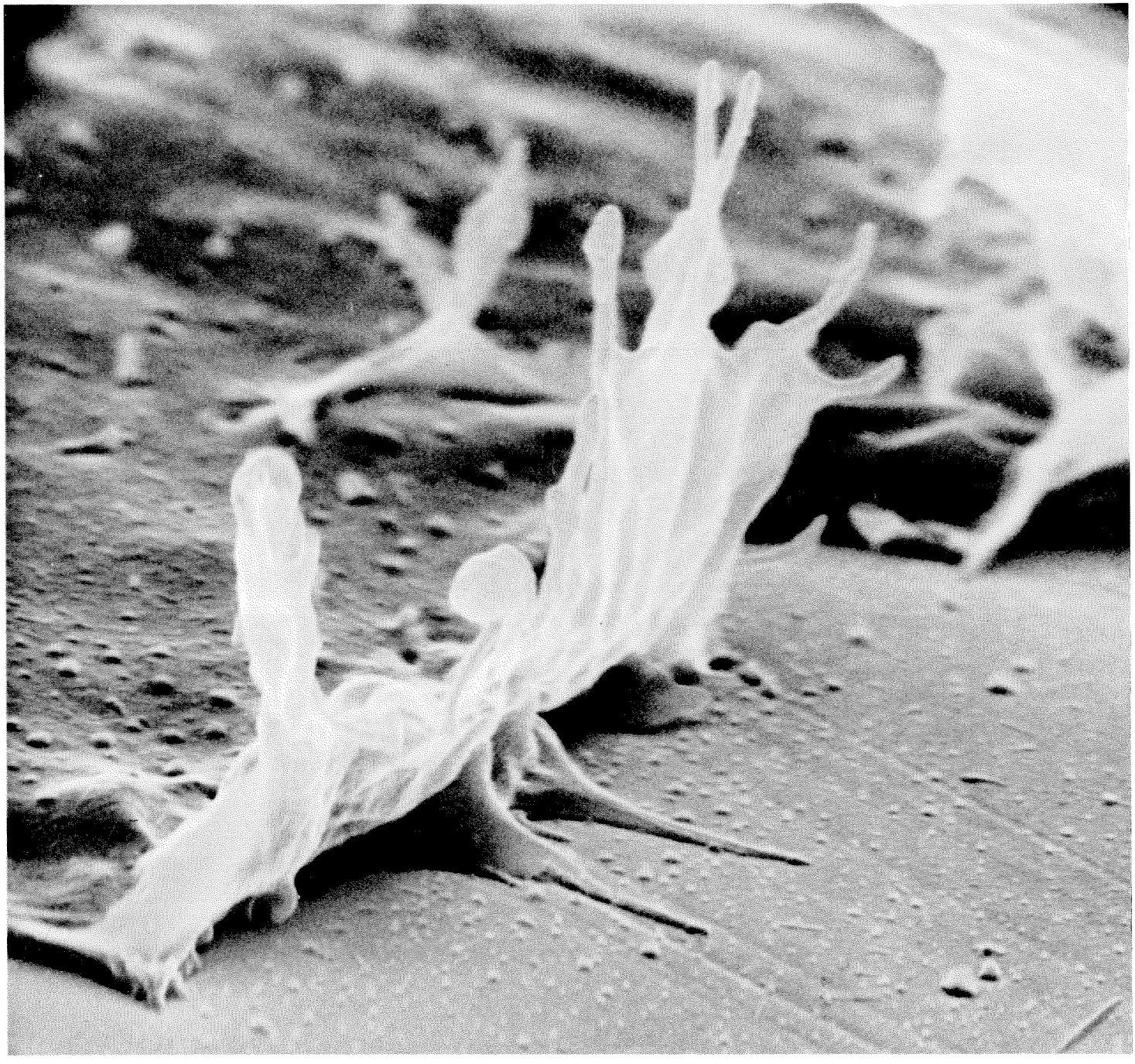
The key to the ruffling mechanism appears to lie in the nature of the cell membrane surface, so Revel and his co-investigators are looking at its detailed structure for useful information.



The SEM enables Jean-Paul Revel to record cell movements in 3-D, at 50 times greater magnification and with 10 to 20 times finer detail than is possible with a light microscope. Magnified 15,000 times, a fibroblast cell from the connective tissue of a mouse (above) unfolds an elaborate ruffle on its "forward" edge, which appears to serve as a kind of leg for moving across surfaces. When treated with the enzyme trypsin to detach it from the substrate, the cell contracts into a ball (below), and bubbles develop on its membrane. The magnification is 10,000 times actual size.



The scanning electron microscope reveals how a cell moves



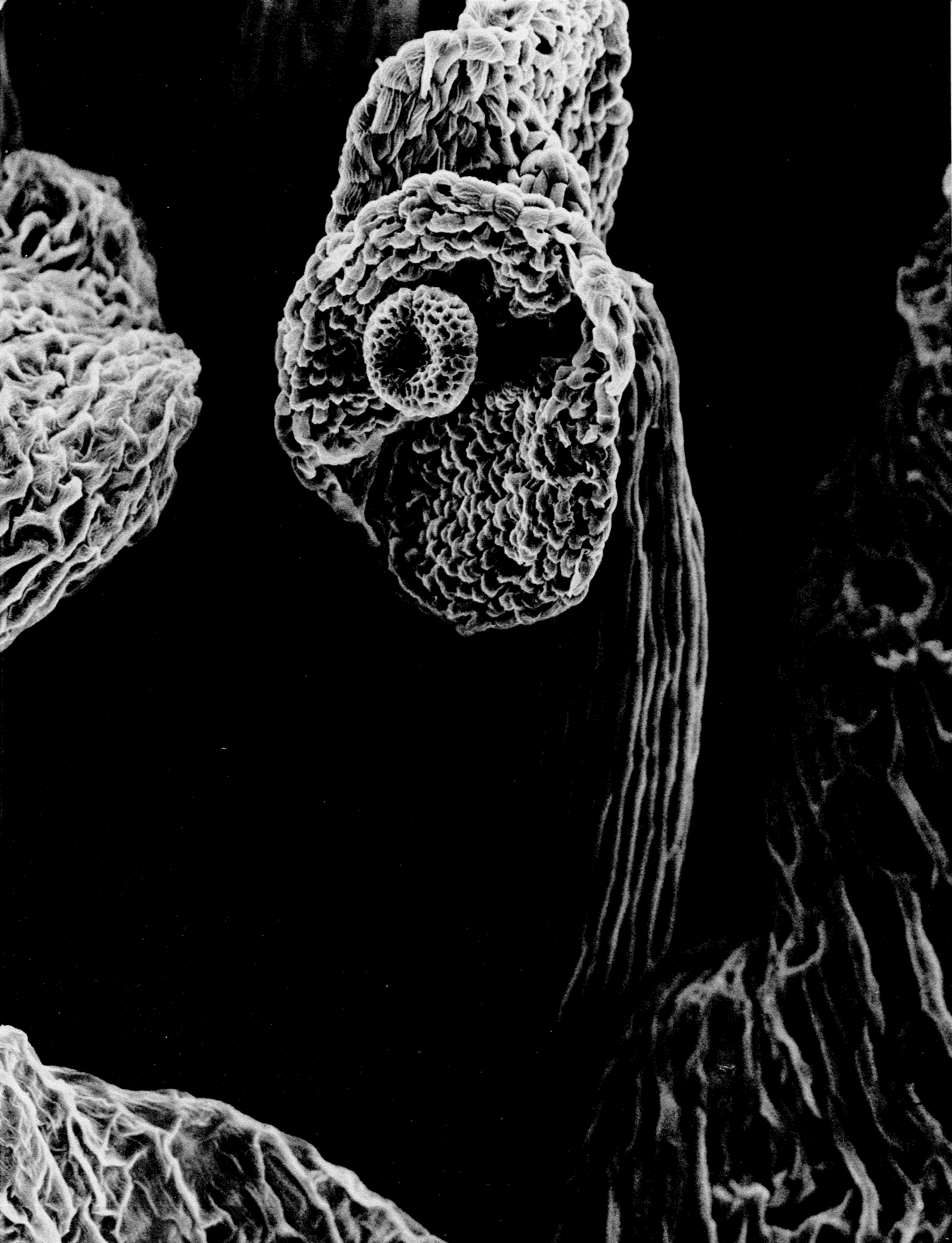
Dried, thinly coated with gold, and photographed by an SEM, a baby hamster's kidney cell is caught in the act of ruffling its way across a petri dish. The magnification—15,000 times actual size—makes it possible to show the cell's newest set of ruffles forming and moving over an older set. The ruffling mechanism seems to be triggered by the proximity of the cell membrane to the surface it is traversing and by the movement of older sets of ruffles toward the back of the cell.

The SEM Looks into a Flower

With an eye for beauty, a natural curiosity, and an SEM, Jean-Paul Revel made these spectacular photographs of an insignificant-looking plant that grows at the main entrance of the Church Laboratory of Chemical Biology. An ordinary photograph (top) of the polygonum, or knotweed, shows the sturdy structure of the fingernail-sized flower. But increasingly powerful magnification reveals a hidden beauty. The SEM photographs of the anther and pollen grains of *one* blossoms are—from left to right—magnified 38, 145, and 650 times.

The instrument that allows them to do this, the scanning electron microscope, is rapidly becoming at least as useful as the standard transmission electron microscope (TEM), which for years has been an invaluable tool in genetics, molecular biology, and virology. While the TEM allows magnification up to 250,000 times, it is only able to record two-dimensional "shadowgraphs" of three-dimensional objects through which electrons are passed. Scientists try to overcome this drawback by slicing their specimens very thin, taking TEM "shadowgraphs" of each of them, and then reconstructing a three-dimensional image from the slices.

The SEM makes this tedious process unnecessary by bouncing electrons off—rather than passing them through—specimens under observation. The secondary electrons that are bounced back are collected and accelerated against a scintillator, which transforms them into bursts of light. These light impulses are amplified to provide a display that can either be viewed directly like television, or photographed. Caltech's SEM can magnify objects up to 100,000 times, and has attachments that allow manipulation of a specimen so that it can be viewed from almost every direction—that is, in three dimensions.



This nightmare is a Hemipteran (alias "bug") magnified 400 times. Revel found it on one of his African violet plants. The honeycombed objects on its antennae are pollen grains from the violet's blossoms.

SEMS have been used in industry for about ten years, but only in the last few years have the quality and resolution of imaging improved enough for them to be useful in basic scientific research. The Caltech SEM is about eight months old, and Revel and many of his colleagues are still getting acquainted with its capabilities. In addition to scanning cells, it has been used to look at the way amoebae aggregate to form slime molds, the appearance of normal and cancerous cells, the origin of nerve cells, the development of chicken embryos, the detailed surface structure of fruit-fly mutants, and the microscopic substructure of various materials like rocket propellants, the "teeth" of mollusks, and bits of meteorites.

"With the scanning electron microscope we can 'fly' around a specimen at high altitude and look at it from all angles," Revel says. "If we find something interesting, we can swoop down for a closer look. If there is something *really* interesting, we can 'land,' walk up to it, and stick our noses inside to see what's going on. □