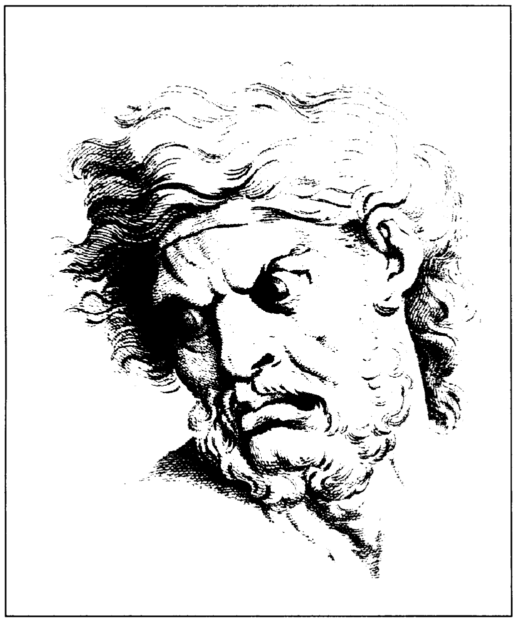

WELLCOME INSTITUTE FOR THE HISTORY OF MEDICINE

Man in a state of anger. The studies of expression by Charles Le Brun were engraved and widely reprinted in the 18th century. (From Deanna Petherbridge and Ludmilla Jordanova's *The Quick and the Dead: Artists and Anatomy*, published by the Hayward Gallery and the University of California Press, 1997.)

nervous system" may be a combination of the preparation of the body for fight or flight, and the use of visible signs of those involuntary reactions as guarantees to skeptical perceivers that our threats and promises are not bluffs and double-crosses.

Expression is a captivating book. From questionnaires Darwin had furnished to missionaries and explorers, he reports that many of our familiar expressions are also found among "Hindoos, Kafirs, Negroes, wild Malays, Esquimaux, New Zealanders, Abyssinians, the Dyaks of Borneo, and Indians of North America," which led him to the strikingly modern conclusion that "the several races [are] descended from a single parent-stock, which must have been almost completely human in structure, and to a large extent in mind, before the period at which the races diverged from each other" (p. 355). The universality of these expressions—and the appearance of many of them in infants, animals, and the congenitally blind—also convinced Darwin that these attributes are innate. He enriched his arguments with hundreds of insightful observations (many with the pathos and humor of great literature), as when he describes the terror of a man being led to his execution, the comical dejection of his dog as soon as it sensed that a walk was coming to an end, and the movement of the eyeballs of nursing infants that "gives to them an absurd appearance of ecstatic delight." Equally riveting are the macabre photographs of an institutionalized man literally shocked into exaggerated expressions by electrodes placed on his face.

The "bonus tracks" (including a fascinating essay by Phillip Prodger on the dawn of scientific photography) are excellent. Ekman explains why the book went unnoticed for most of this century—largely because of behaviorism, which outlawed discussion of mental states, and a prevailing dogma that denied the existence of human nature. He reviews recent literature on topics Darwin discussed, much of it from his own groundbreaking research, which he places in historical context. These insertions of contemporary commentary might be seen as marring the "definitive" version of a classic, but I found them quite appropriate. Ekman is a fitting heir of the Darwin of *Expression*, having catalogued the major facial expressions, documented their anatomy and physiology, and shown their universality across cultures in the teeth of fierce opposition (in Ekman's case, from relativist anthropologists such as Margaret Mead). Indeed, Ekman's additions pay the book the ultimate compliment. This edition has the feel not of a lovingly restored museum piece but of a seminal work that needed only minor updating. It is as fresh and provocative today as it was 125 years ago.

BOOKS: HISTORY

Focusing Cell Biology

Peter Satir

In the years after World War II, the biological sciences experienced a dramatic explosion. Increasing governmental support and new methodologies created entirely new fields of inquiry—molecular biology, cell biology, and biophysics—with their attendant institutions—new scientific societies and new journals. This was the time of Watson and Crick's DNA double helix, tobacco mosaic virus and bacteriophage, polio virus and the Salk vaccine. We found that lipids self assemble into membranes, that proteins self assemble into structures as complex as ribosomes, and that cells have fine structure in their cytoplasm. These dramatic achievements contributed to the optimistic belief that we would come to understand critical medical problems rationally, in terms of molecular processes within the cells.

Picture Control
The Electron Microscope and the Transformation of Biology in America, 1940–1960
by Nicolas Rasmussen
Stanford University Press, Stanford, CA, 1997. 356 pp. $55. ISBN 0-8047-28372.

In *Picture Control*, Nicolas Rasmussen explores the impact of one of the most productive of the new technologies, electron microscopy, on the biological sciences. By recounting the history of electron microscopy, particularly as practiced in the United States and Canada, he explores a more general question: how a new technology becomes established in, and useful for, science. The title is apt, for electron microscopy produced pictures with a resolution that had never been seen before. With this new view of the cell, we had to learn to see what was in the picture, and how to interpret what we saw. As every electron microscopist knows, those who control these factors, control the field.

The history Rasmussen relates is a fascinating one. Because the cast of characters was small, the roots of our present understanding are readily exposed. From about 1940 to the end of the 1950s, electron microscopes were expensive, hard to come by, and hard to use effectively with biologic materials. Only a few major centers developed where practitioners flourished: the University of Pennsylvania, the Rockefeller Institute for Medical Research, the Karolinska Institute, MIT, and Berkeley. Each of these groups was headed by one or a few individuals, whose philosophy and skills shaped their laboratories. Shaping the new field were Stuart Mudd at Penn, who used the microscope to study bacterial structure; Keith R. Porter and George E. Palade, the founders of cell biology (whose laboratory at Rockefeller I joined in 1956); Fritiof Sjöstrand, their European counterpart; Francis Schmitt at MIT, a founder of biophysics; and Robley Williams and Wendell Stanley, molecular virologists who built programs at Michigan and Berkeley. These researchers were responsible for the novel images and advances with the microscope, and for picture control in parts of the emerging fields.

The story Rasmussen tells begins in 1938, when Vladimir Zworykin, then head of electronics research at RCA and later famous in the United States as the "father of television," convinced his company to build an electron microscope in Camden, New Jersey, for possible commercial production. By 1940, Zworykin had recruited James Hillier from Toronto to build the workable model B, and Stuart Mudd, head of medical microbiology at

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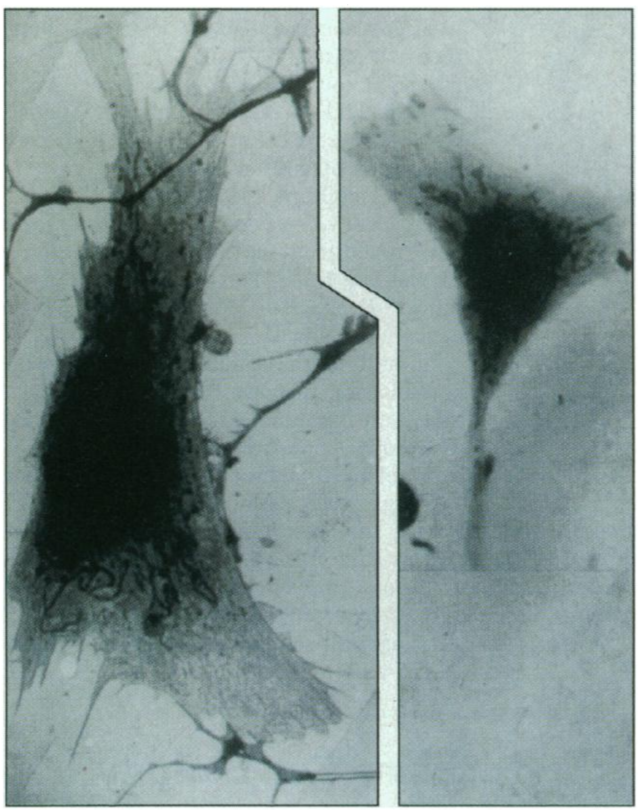
Penn, to oversee the biological use of the instrument. In two developments fateful for the field, Mudd was joined by his friend Wendell Stanley (who brought his plant viruses to RCA for imaging) and, with Zworykin, they chose Tom Anderson as the postdoctoral researcher to take electron micrographs of bacteria and viruses. Although I was aware of Anderson's important contributions to the field, particularly his introduction of the "critical point" method for drying specimens, I had not realized that he was, at least in Rasmussen's portrayal, electron microscopy's Robert Hooke. Paralleling the effects of Hooke's discovery of "cells" in cork, Anderson's images excited his contemporaries to explore the capabilities of the new microscope.

If Anderson was the field's Hooke, then the group at the Rockefeller Institute provided both its Leeuwenhoek and its Virchow. The Porter-Palade team moved the practice of biological electron microscopy from scrutiny of bits and pieces of cells, through whole mounts, to standardized thin-section practice and interpretation for cells and tissues. With the new microscopy, they used cell fractionation to meld histology and biochemistry, and linked both to Darwinian evolution through comparative studies. Rasmussen discusses the advances carefully, but he does not know—or fails to convey—how important the "thick-thin section" technique used by this laboratory was in convincing people that the structures seen with the electron microscope were meaningful. In that technique, a thick-section of the specimen cut for the light microscope was used to orient the serially-cut thin sections for electron microscopy. Rasmussen does appreciate that Porter used a variation of this method to compare light and electron micrographs in his famous 1945 paper, which contained the first electron microscope image of a whole eukaryotic cell. (This is among the many historically famous micrographs reproduced in *Picture Control*.) The battles between the Porter-Palade laboratory and the Sjöstrand group over nomenclature and interpretation, especially of mitochondrial structure, are well recounted by Rasmussen. The Rockefeller school's victories were important in developing the discipline of cell biology it left as its legacy.



Congruent pictures. Chicken fibroblast cells grown in tissue culture, in electron **(left)** and light **(right)** micrographs. These images taken by Keith Porter and Albert Claude were convincing visual evidence that the electron microscopy procedures represented the same entities as traditional methods and introduced no drastic artifacts.

J. EXP. MED. 81, 233 (1945)/ROCKEFELLER UNIVERSITY PRESS

In the postwar period, electron microscopy—a field where physics, engineering, and life sciences co-mingle—was especially attractive to physicists looking to apply physical methods to biological structures. F. O. Schmitt led these efforts, which focused on collagen, on myelin and biological membranes, and on muscle structure. In contrast to the concerns of the Rockefeller school, these ventures (for example, "biophysical cytology") address macromolecular arrangements. The triumphs of this approach are recorded in *Picture Control*. Especially impressive were Jean Hanson and Hugh Huxley's elegant studies, which led to the sliding filament theory of muscle contraction.

A point to ponder while reading this chapter on Schmitt's biophysics is that molecular analysis is where electron microscopy currently makes its major impact. Having incorporated earlier findings from the electron microscope (on organelle structure, evolution, placement, and composition), cell biology now has largely abandoned the instrument, even when its use would seem essential. In its place, immunolocalization is used with light microscopes, and one hardly ever finds electron micrographs of cell cytoplasm in current issues of *Journal of Cell Biology* or *Cell*. On the other hand, for molecular analysis—especially cryomicroscopy of structures such as actin filaments interacting with myosin heads—electron microscopy remains highly significant.

The major chapters of *Picture Control* are very valuable to working scientists and students of science history interested in how the play of science proceeds. Rasmussen also includes discussions addressed to philosophers and sociologists of science. I found these sections, which open and close the book, more difficult and more forced. Nevertheless, there is an intriguing and vital question behind his approach: Rasmussen asks why some competitors in biological electron microscopy left minimal impressions, while others left major legacies. His answer, with which I agree in part, is that the advance of science depends on preconceptions (which are rooted in universal sensory experience) and sotto voce on the ability to raise and mobilize funding. Less emphasized by Rasmussen—but equally important in my view—are heuristic value and the play of individual personality (which is, of course, a major factor in the funding equation). A way of thinking also tends to survive better when bolstered by institutionalization, because this suggests that there are a sufficient number of people (a school) sharing similar views. The *Journal of Biophysical and Biochemical Cytology* (later the *Journal of Cell Biology*), the American Society for Cell Biology, the Electron Microscopy Society of America (later just the MSA), the Biophysical Society, the *Journal of Ultrastructure Research* (later the *Journal of Structural Biology*) are among the products of this institutionalization of electron microscopy and the success of its penetration into biology.

When I was a graduate student, I devoured *Biophysical Science – A Study Program*, a 1959 book edited by the biochemist J. L. Oncley that embodied the experimental approaches and methodological concerns discussed by Rasmussen. *Picture Control* allowed me to revisit that era. Its lessons for today are how the threads of the past influence or hinder the ways by which we learn in science to see with a fresh eye.