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Novikoff, Alex Benjamin (*b*. Semyonevka, Ukraine, 28 February 1913; *d*. New York, NY, 9 January 1987), *histochemistry, cell biology*.

Among biologists Alex Novikoff is known foremost for his contributions to the discovery and characterization of several cell organelles—lysosomes, peroxisomes, microperoxisomes and the Golgi body—as well as helping to pioneer the field of cell biology. Among a wider audience, he is notable as a victim of the excesses of the anti-communist movement in mid-20th-century America. Novikoff's early associations with Marxism led to productive conceptual interpretations in biology, but also to him being targeted by political demagogues.

Growing into Academics and Political Activism

Alex was born in the Ukraine, then a republic with the Soviet Union. However, his family, hoping to escape poverty there, soon emigrated to the United States. They eventually settled in the Brownsville section of Brooklyn, New York, among other immigrants. Alex's father worked for his brother-in-law as a salesman in the garment industry [•Holmes, 10]. Alex excelled in school, even in his early years. At home he exhibited an interest in nature, keeping many small animals, skinning and dissecting the corpses, and even boiling a dead cat to study its skeleton. Alex eventually skipped four grades, graduating high school at age fourteen. The family, steeped in a Jewish heritage of valuing intellectual achievement, pinned its hopes (and its limited financial resources) on Alex pursuing a career in medicine. When he graduated Columbia College in 1931 (still age eighteen), however, new shifts in institutional sentiment limited opportunities for Jews. Despite promising credentials, Alex was not admitted to several medical schools. The experience left Alex bitter, and helped fuel an uncompromising advocacy for justice.

Following the advice of his mentors, Alex instead entered graduate school in Zoology in 1931, also at Columbia University. To finance his study, he began teaching at the newly formed Brooklyn College. For several years, Alex would commute twice daily between the two campuses and their respective contexts. So began a lifelong pattern, recognized by colleagues, of being "tirelessly and utterly devoted to his work" [• de Duve 1987]. At Columbia Alex pursued experimental embryology and, beginning in 1932, spent several summers doing research at Woods Hole Biological Laboratory. From Arthur Pollister he gained an enthusiasm for cells [• Novikoff & Holtzman 1970, iv]. In 1936, still only age twenty-three, he published his first scientific paper, followed in the next two years by three more. Meanwhile, at Brooklyn College, Alex did not take well to the stratification of junior and senior faculty. In 1935, he joined the growing Communist party, an expression of his progressive idealism, his interest in Marx's scientific perspectives towards society, and the party's focus on local labor issues. That simple act would haunt him for the next three decades. Soon he was helping to write and distribute the Communist newsletter on campus and defending the rights of younger staff. Alex was able to work on little sleep and he continued his prodigious efforts. As he commuted, he wrote up his thesis and in 1938 received his Ph.D.
[• Holmes, 1-44]

Weathering Repercussions

With his new degree, Novikoff was due for promotion at Brooklyn College. However, he had irritated many departmental colleagues and annoyed the administration with his activities for the teachers union. Novikoff's credentials, even with many additional letters lauding his scientific work, seemed insufficient. Only after a year of public politicking was the new position approved. Antagonism towards the union sharpened. [• Holmes, 44-54]

Novikoff married in 1939 and began to drift from party activities. His research continued and by 1940, for example, he had published nine papers [• pp.59,90]. That same year a wave of conservatism swept through the state, and legislative committees targeted the Communist affiliations of the teachers union. The new college president, no friend of the union, did not intervene. Novikoff was investigated. Ultimately, no action was taken. Still, seeds of doubt were sown — and preserved in filed reports. [• pp.62-79]

When the U.S. entered World War II, Novikoff wanted to serve in the military and sought a medical commission. Yet the mere suspicion of unspecified activities now dogged him. His application was denied, once in 1942 and again in 1943, due to vaguely documented doubts about his "loyalty" [• pp.82-86]. Later, in 1948, Novikoff was hired by the U.S. Army to consult on two films about enzymes and carbohydrate metabolism. Again, questions about his "loyalty" surfaced and, although his work was purely biological and largely already completed, his appointment was terminated [• pp.95-96].

After an exciting post-doctoral fellowship on cells and cancer at the University of Wisconsin (1946-1947)—and five more papers—Novikoff was hired for a permanent position at the University of Vermont Medical College. Over the next several years he successfully secured grants and continued active publication [• pp.95-98]. By 1953, however, the anti-communist movement had flared again. Novikoff's personal associations in the late 1930s again became the subject of scrutiny, now at the federal level. Ultimately, Novikoff invoked the Fifth Amendment to refrain from "naming names." Due to leverage by the governor of Vermont and public opinion inflamed by the press—and despite faculty recommendations to the contrary—Novikoff, age forty, was dismissed. He had failed, the official documents alleged, to exhibit "the qualities of responsibility, integrity and frankness that are fundamental requirements of a faculty member" [• *Rutland Herald*, 1979; Holmes, 214]. Ironically, thirty years later, in 1983, the university's president would salute Novikoff"s "integrity and courage" in acknowledging the incident and awarding him an honorary degree [• Holmes, 247].

In searching for new options, Novikoff learned of plans for a new medical college to honor Albert Einstein: a Jewish institution that would in part accommodate those excluded from other schools. Novikoff wrote to Einstein. That led, in 1955, to his founding appointment at the new college, which became his home for the next three decades. In 1962, he received a lifetime career grant — $25,000 annually for twenty-five years — from the National Cancer Institute [pp.241,243]. Still, Novikoff was excluded from government review panels until 1972 [p.245]. He was elected to the National Academy of Sciences in 1974. His FBI file, closed by then, contained 822 pages.

Discovering Lysosomes

Ironically perhaps, the last research Novikoff published before his dismissal at the University of Vermont was to be among his most significant. Novikoff and "his girls" (as he fondly called his assistants) had analyzed enzymatic activity in different parts of the cell. At the time, cells were typically broken and the parts separated by weight by centrifuging them at successively higher speeds and collecting each fraction. The standard protocol generated four fractions. Novikoff created ten, allowing for a more fine-scaled analysis. He measured the level of seven strategically selected enzymes in each fraction. He was then able to modify his fractions into six groups, effectively sorted by particle size and corresponding enzyme activity. As would become clear much later, Novikoff had mapped characteristic markers to six major cell organelles — two not yet known.

Novikoff's work came to the notice of Christian de Duve at the University of Louvain, who was particularly interested in one fraction. While investigating the effect of insulin on the enzyme glucose-6-phosphatase in rat liver cells, de Duve had encountered puzzling changes in the level of acid phosphatase activity. He had then isolated the effect to one fraction of the cell, and in 1952 proposed that it signaled an unknown membrane-bound particle. Novikoff's 1953 work on acid phosphatase seemed to confirm that interpretation. The two met in New York City and discussed their results in Central Park. By 1955, de Duve had identified five other enzymes in the same fraction. All broke molecules apart and so he called the prospective new organelles *lysosomes* (for *lyse*, to cleave).

De Duve's proposal was unusual because previously all organelles had first been identified visually. Perhaps his biochemical data did not reflect a real particle? De Duve thus invited Novikoff to collaborate towards generating micrographic evidence. Novikoff spent six weeks in Belgium the summer before he was to begin work at Albert Einstein Medical College. De Duve's lab provided the cell fractions, but had no electron microscope. As a result, at the end of each day Novikoff took the samples, iced in a thermos bottle, from Louvain to Paris by train and worked late into the night to produce the images, returning the next day to repeat the routine. The stunning results were announced the following spring: they had successfully visualized lysosomes — and thereby credibly demonstrated their existence.

Werner Strauss, working independently at the same time, further established a primary enzymatic role of lysosomes as intracellular digestion. De Duve continued for many years to characterize how lysosomes functioned. Novikoff adapted a lead-based stain for use with acid phosphatase, which helped critically in further visualizing and interpreting lysosomes. His synoptic chapter on lysosomes in a 1961 textbook was instrumental in establishing their relevance among a wider audience. Novikoff went on to study the form of the lysosome in diverse cell types and tissues and in pathological conditions (such as in fatty liver, tumors, or nephrosis): this relatively unglamourous work importantly revealed context. (The cells included an induced hepatoma, now named for Novikoff.) "It is largely due to Novikoff's bold and imaginative use of morphological techniques," de Duve noted later, "that lysosomes have come to be recognized in a broader biological context." [• de Duve 1969, 11] Novikoff's detailed scrutiny also revealed a close relationship between the lysosome and other organelles: the Golgi apparatus and endoplasmic reticulum (ER). He named the special hybrid structure GERL. It gave clues to how lysosomes formed. De Duve shared a Nobel Prize for his work in 1974 and Novikoff, overlooked in the award, wrote generously about de Duve's achievements for *Science* magazine.

[• Novikoff 1973, 1974; Novikoff et al 1953; Novikoff et al 1956; de Duve 1969, 1987, 2005; Bechtel, 254-56; Essner 1987]

Pioneering Cell Biology

Novikoff contributed substantially to the early development of cell biology in other ways, as well. For example, his 1953 cellular enzyme analysis included urate oxidase (uricase), which seemed to fractionate with acid phosphatase. De Duve [•2005] thus began including it in his own studies. However, it was John F. Thomson and Florence J. Klipfel, in 1957, who observed that it sedimented with the familiar enzyme catalase, which breaks down hydrogen peroxide. By the mid-1960s du Duve's lab had characterized them both as part of a second suite of enzymes in yet another new organelle: the *peroxisome*. Soon, it was linked to structures (named microbodies) already identified microscopically in kidney cells by Johannes Rhodin in 1954. More extensive study of peroxisomes was facilitated by a stain (alkaline diaminobenzidine, or DAB) co-developed by Novikoff and Sidney Goldfischer in 1969, which effectively visualized the activity of catalase in electron micrographs. Novikoff systematically surveyed peroxisomes as he had lysosomes, and in 1972, working with his second wife (and former lab technician) Phyllis, discovered a unique type, the *microperoxisome*.

Novikoff's most enduring contributions were technical and critical, not conceptual. As noted, he developed important stains for studying lysosomes and peroxisomes. Another important stain, developed in 1961, also with Goldfischer, was for nucleosidediphosphatase, an important marker for the organelle, the Golgi body. This also provided the first information about that organelle's enzymatic properties. Novikoff was equally adept at finding flaws in widely used techniques. His important critiques included the Wachstein-Meisel procedures (1967), the interference of enzymes by lead in the Gomori technique (1970); and diffusion artifacts from diaminobenzidine cytochemistry (1972, 1980). He was an active participant in debates, strongly probative, yet also gracious and conceding when shown to be wrong.

Novikoff summarized his expansive knowledge in a 1970 textbook, *Cells and Organelles*, co-authored with Eric Holtzman, a former student. It was intended in part to present the achievements of cell biology, the understanding of the parts of the cell, as a complement to the molecular bias of James Watson's 1965 *Molecular Biology of the Gene*. The text was framed by opening and closing chapters on research methods and history, aimed towards encouraging others into research. One reviewer described it as "extraordinarily fine" and "at once exciting, scholarly, concise, and penetrating" [• Barr 1971, p. 174]. It was used extensively and went through two subsequent editions.

Finally, Novikoff assumed many leadership roles. Among them, he was second President of the American Society for Cell Biology [• CV, Bechtel 273]. He also served on several editorial boards, most notably for the *Journal of Histochemistry and Cytochemistry* from 1955 into the 1980s.

[• Novikoff 1973, 1974; Novikoff et al 1953; Novikoff & Novikoff 1972; de Duve 1969, 1987, 1996; Essner 1987]

Working with a Marxist Perspective

Novikoff's brief participation in the Communist Party, as noted above, adversely affected his career. But his exposure to Marxism also helped contribute productively to the content and practice of his science. His conceptual outlook, interpretations of evidence and professional conduct were all shaped in part by Marxist perspectives.

The traces are perhaps clearest in several publications from 1945. After not publishing anything for nearly four years, Novikoff wrote a synoptic theoretical paper on "The Concept of

Integrative Levels and Biology" for *Science*. It was a programmatic call against the extremes of both vitalism and mechanistic reductionism. Biologists, he claimed, needed to understand both parts and wholes. In particular, Novikoff rejected vague organizing principles at higher levels of organization, stressing instead "the material interrelationships" of different levels [• p.215a]. Also, in denying privilege to either atomism or organicism, he advocated a "dialectical approach" [•215a]. Here he echoed the explicit Marxist language of "dialectical materialism."

Accordingly, Novikoff profiled biochemistry as both essential to and limited in understanding cells. Likewise, he underscored how development transformed simple cell functions, at one level, into physiology at another level. But the ultimate aim of Novikoff's analysis was human society. He criticized thinkers, like Herbert Spencer, who appealed to a misleading organism-society analogy that biologized culture, and he cautioned that conflating levels of organization led to "erroneous and dangerous social conclusions" [•213b, +212a, 214a, 214b]. He pointedly targeted the justification of fascists (namely, the Nazis), who alleged that "man's biology decides his social behavior" [•214b]. Novikoff claimed that we needed to understand distinctly sociological principles to keep society "free and democratic" [•214b]. He further referred, in a Marxist vein, to "the economic basis of social relations"[•213b] and to the technological (materialist) roots of change [•211b]. Here, in essence, was a biological framework, guided by Marxist principles, for interpreting social political action.

Novikoff's portrayal of evolution also reflected Marx's views on history and progress through a series of revolutions. Even the opening sentence stated, "the concept of integrative levels of organization is a general description of the evolution of matter through successive and higher orders of complexity and integration." [•209a] At the same time, Novikoff warned against assumptions of an ill-defined progressive organizing trend, again echoing Marxist materialism. Novikoff noted the special features of humans, such as their ability to control their environment [•214a] and thus, in a sense, to guide their own destiny. He also alluded to the plasticity of human intelligence [•213a], implying the potential for cultural change. The explicit lesson was that "social progress rests upon the planned activity of men" [•214a], not nature. He quoted fellow biologist Julian Huxley: "Purposes in life are made, not found"[•214b]. Finally, Novikoff noted that "man possesses a unique head and hand," invoking Marx's view of the parity of intellectual and manual labor [•211b]. In all, Novikoff presented a view of the levels of biological organization — and its implications — that was strongly guided by Marxist principles of social change and scientific humanism [•214b].

In the same year, 1945, Novikoff wrote his first of two books for children. Writing about science for a young audience was largely unprecedented, and it became an innovative landmark in children's literature. Writing the book itself thus expressed a kind of socialist outlook that deemed all ages as equally important audiences, and it was published by a Communist press in New York City.

Novikoff's topic was evolution. The central theme, *Climbing Our Family Tree*, presented life's history as largely progressive. The bulk of the book explained and celebrated major evolutionary innovations, such as the transition to land or homeothermy, again commensurate with Marx's view of progress through revolutions. The culminating section, "Man's Freedom," described the same concepts about social organization that appeared in the "Integrative Levels" paper in *Science*: human independence from the environment and the roles of tools and of planning in social change. It closed poetically with a socialist ideal: "Men, working with each other, can become ever more free — ever more human." [• p.93]

Novikoff's second book for children, *From Head to Foot*, described human physiology. In addition to surveying the major systems, it introduced some great scientists and their historical discoveries and books, giving a sense of science as an active, exciting—and human—endeavor. Novikoff again closed portraying socialist ideals: "Man's complicated brain and nervous system, his body which can adapt itself so easily to different surroundings, his ability to plan, work, and use tools, give him a chance to work together with his fellows and deliberately improve his society until it suits him, until it gives everybody a good life." [• p.95]

The perspectives so evident in these early writings persisted as a context in Novikoff's later work. First, Novikoff was sensitized to look for differences and complexity among the parts, even in well integrated structures. For example, in his 1953 study of cell fractions, he stressed the "heterogeneity" of enzyme activity in the different parts of the cell. Initially, he interpreted those differences as variations in the known organelles, the mitochondria and microsomes (ribosomes). Later, with more data, he accepted de Duve's claim that the unusual distributions indicated instead a new, undocumented organelle. The theme of heterogeneity reappeared in a 1959 paper, where Novikoff profiled how the cells in a section of liver tissue, always assumed to be uniform, exhibited significant variation. Novikoff also clearly appreciated that the "less prominent" organelles, such as the lysosome or peroxisome (that he studied so thoroughly), were just as significant as any other, when viewed as part of the integrated whole.

Second, Novikoff continued to balance reductionist and more holistic perspectives. Much of his work involved the reductionist's aim of localizing biochemical functions to parts within cells. But he also did not lose sight of context. He studied how lysosomes and peroxisomes (as units) differed in widely various cellular conditions. In a similar way, he cautioned others about how cells differed in context: in tissue cultures versus in organic tissue [• Bechtel 148]. Parts and wholes were on a par. In his 1970 text, for example, after describing the many cell *organelles* (parts), he gave just as much coverage to the many *cell types* made from recombining them into different wholes.

Marxist and ocialist perspectives also seemed to shape how Novikoff practiced science. He shared credit generously. When invited to comment on his 1961 *PNAS* paper as a "citation classic," for example, he acknowledged the key contributions of six others in a brief half-page article [• Novikoff 1985]. Novikoff was utterly without pretension [• de Duve 1987; Holtzman 1987]. Once when interns and residents at Albert Einstein Medical College went on strike, he joined the picket lines. Viewing science as a community of equals, he engaged in conversation—or debate—with any colleague, regardless of stature, to the pleasant surprise of many students. His posture of valuing "dialectics" promoted the critical analysis of ideas.

Novikoff's science was richly—and fruitfully—influenced by Marxist perspectives. Ironically, such real, but hardly subversive influences were never the focus of the those who targeted Novikoff for "Communist" activities. Ultimately, Novikoff's career, as one colleague noted, indicated that a passion for social justice and for one's own work need not be inconsistent with good science. [• Holtzman 1987]

[• Novikoff 1945a, 1945b, 1946; Holtzman 1987; Holmes 90-92]

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Works about Novikoff

David R. Holmes, *Stalking the Academic Communist: Intellectual Freedom and the Firing of Alex Novikoff*. Hanover, VT: University Press of New England, 1989.

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Novikoff's complete papers (c.1930-1985) are archived at the University of Vermont, University Archives, Record Group 74, Boxes 197-224.

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