NATIONAL ACADEMY OF SCIENCES

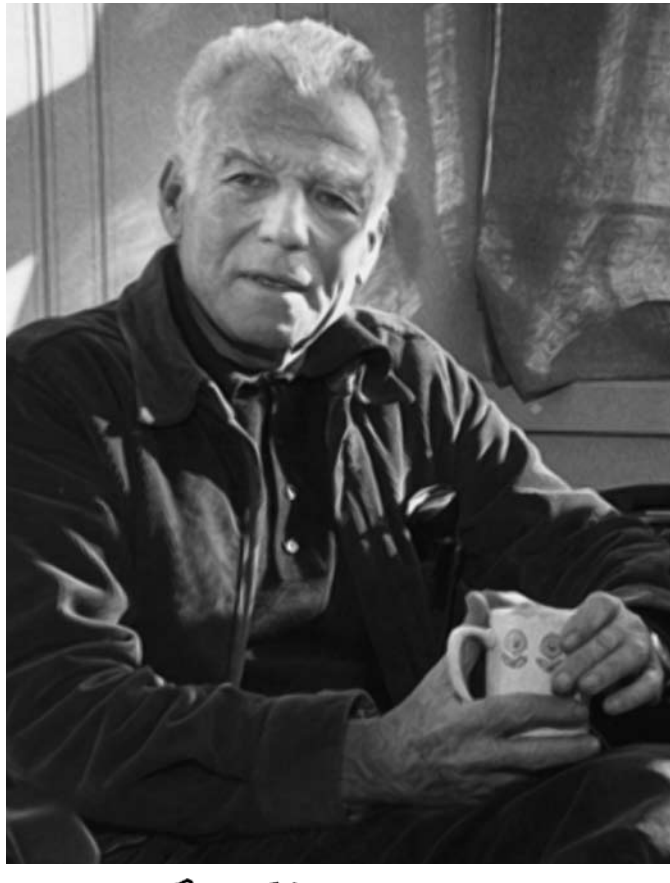
ROBERT MILTON SILVERSTEIN
1916–2007

A Biographical Memoir by

JAMES H. TUMLINSON AND DAVID L. WOOD

Any opinions expressed in this memoir are those of the authors and do not necessarily reflect the views of the National Academy of Sciences.

Biographical Memoir



R M Silverstein

ROBERT MILTON SILVERSTEIN

March 26, 1916–February 26, 2007

BY JAMES H. TUMLINSON AND DAVID L. WOOD

ROBERT MILTON SILVERSTEIN was born in Baltimore, Maryland, on March 26, 1916. His parents' families had both emigrated from Romania, where his mother had grown up in a *shtetl* straight out of *Fiddler on the Roof*. His grandfather was a Talmudic scholar, which meant he was honored but poor. To supplement his income he made and sold unlicensed liquor, which his daughters delivered in a baby carriage. After emigrating and meeting in the United States, Milt's parents eventually settled in the small town of Tottenville on Staten Island, where they owned a small general store.

As a child playing on the beaches and in the neighboring woods and ponds, Milt developed an abiding passion for the natural world. Additionally, Milt was an enthusiastic Boy Scout, eagerly learning how to tie sheepshank knots, pitch a pup tent, and fish for his dinner. Most significantly, in Tottenville he also met Olive Jorgenson, who was to become his lifelong partner and share his passions for both nature and science.

After high school, he attended the University of Pennsylvania but took time off in the summer of 1936 to travel to Hamburg on a freighter as a "wiper," a seafaring janitor. He liked to tell the story of the courageous Hamburg bookseller who discouraged him from buying books written by Nazi

leaders, directing him to some classics instead. He earned a B.S. in chemistry from the University of Pennsylvania in 1937 and an M.S. from New York University in 1941. This was followed shortly by receipt of a letter with the common salutation of the time: "The President sends you greetings."

Clutching his diploma, Milt reported to a medical battalion in the Sixth Armored Division, U.S. Army, and was stationed at Fort Sam Houston in San Antonio, Texas. Milt's handling of an incident that occurred during his training at the then segregated base in Texas illustrates an uncompromising insistence on fairness that he displayed throughout his life. White soldiers under his command rebelled when black soldiers wanted to use their facilities while the plumbing in the black soldiers' facilities was being repaired. Milt met with the first sergeant of the black company and worked out a schedule to accommodate both groups, then ordered his men to go along with the new arrangements, thus averting what could have become a serious conflict. After a period of service in the noncommissioned officer ranks, he received a direct commission in 1943, and promptly proposed to Olive Jorgenson by phone from San Antonio. She arrived after two days by train, and they were married on the same day in a chapel at Fort Sam Houston. Within two months Milt was shipped to a field hospital unit in the southwest Pacific. His final assignment was to set up and operate a medical laboratory in Leyte in the Philippines. Milt was discharged as a captain and arrived home on Christmas day in 1945, with very brown skin and yellow eyes after two and a half years on Atabrine—but no malaria.

On Staten Island he and Olive set up home in a house so small that to seat four people at the dining table, two had to sit on the porch. Their son Roy was born there, followed shortly by their daughter, Amy. The youngest, Paul, was born some years later after their move to California.

Milt returned to New York University and received his Ph.D. in chemistry in 1949. After NYU he was hired by the prestigious Stanford Research Institute, where he spent the next 21 years making significant contributions to the development of analytical methods and flavor and fragrance chemistry. While at SRI, Milt analyzed flavor constituents of many foods, including potato chips and coffee. A thorough analysis of the flavor constituents of coffee led him to concoct what he described as a terrible cup of coffee. Nevertheless, he was invited to Brazil to investigate methods to use large surpluses of coffee beans that existed at that time. He developed a large-scale method for extraction of caffeine from crushed beans. The caffeine was sold to drug companies and the residue used for cattle feed. His work on extraction of caffeine eventually contributed to the development of decaffeinated coffee. While at SRI he wrote (with the help of Clayton Bassler) his textbook *Spectrometric Identification of Organic Compounds*. This book has given several generations of students the intellectual tools to identify trace components of flavors, fragrances, and insect, tick, and other animal pheromones; the book is now in its seventh edition and has been translated into five languages.

While at SRI, Milt began his ground-breaking studies in chemical ecology. In 1962 he phoned the Department of Entomology and Parasitology at the University of California, Berkeley, to inquire about entomologists working on insect behavior. He was ahead of the times. He recognized the significance of Adolph Butenandt's landmark identification of the silkworm-moth sex attractant, a 16-carbon alcohol called "bombykol," in 1959. Butenandt had extracted 500,000 female silkworm-moth abdomens to obtain 12 mg of an ester derivative of the pure pheromone for identification. Milt reasoned that use of newly developing techniques in micro-analytical chemistry would facilitate identification of much smaller

quantities of natural compounds and make pheromone identification more practical. At this time synthetic organic pesticides were being used indiscriminately against insects, mites, and nematodes in the United States and throughout the world. As a consequence pest resistance, resurgence, and replacement with new pests became a central theme in pest control. In these early days Milt concluded that naturally occurring compounds that control insect behavior and development could be identified, and thus be made available to reduce pest-caused damage in an environmentally friendly way. He vigorously pursued this objective throughout his career, as can be seen from the long list of invertebrate pests that he investigated.

Milt's first foray into chemical ecology started with the bark beetle, *Ips paraconfusus* (*I. confusus*), in collaboration with Berkeley entomologist David Wood. Their objective was to isolate, identify, and synthesize the pheromone in the "frass" (composed of phloem and xylem fragments and fecal material) produced by the male beetle boring into ponderosa pine. The pheromone attracts large numbers of both male and female beetles, which overwhelm the tree. Chemical fractionation was monitored by a laboratory bioassay that depended on walking rather than flying beetles, a calculated risk in extrapolating to a field response. When the gas chromatographic fractionation proceeded to a certain stage, none of the fractions was active. This caused some dismay because the few previous studies on moth and honeybee pheromones had conditioned them to think in terms of a single active compound. They were quite surprised to find that the pheromone comprised three individually inactive compounds. This was the first beetle pheromone and the first multicomponent pheromone to be identified, and they were the first to demonstrate the importance of using a complete blend of pheromone components.

At the same time they (with Otto Rodin, a chemist at SRI) had made the first discovery of synergism in an insect pheromone, involving the three terpene alcohols isolated from 4.5 kg of the attractive substrate. They rushed to the field to test two of these compounds that together elicited an attractive response in the lab. Milt could be seen picking these little (3-4 mm) beetles out of the talcum-powderlike dust around the sticky trap and tossing them onto the trap. He was convinced that they were "near misses" and were, in fact, responding to that treatment. With or without the near misses the differences were obvious. But they had trapped a different species than the one producing the compounds that were being tested. They were all amazed by this unexpected result. When the third compound was added to the first two, they trapped the species that had produced them. At the same time, the catch of the cohabiting species (in the pine host) that had responded to the two-compound mixture was greatly reduced. They had discovered the interruption, or disruption, phenomenon that facilitates species separation, or isolation, and would later be used to reduce aggregation and mating of pestiferous species.

During experiments in 1965 near Yosemite National Park, Milt learned the rigors of field research. When he and William Bedard, a USDA Forest Service entomologist, arrived at the field site, they soon realized that they had forgotten the release devices. Milt offered to stay behind and watch over the traps. Milt lay down in the tall grass to take a nap. Suddenly he was awakened by an order to stand up slowly and identify himself. As he opened his eyes he stared up at the barrel of a sawed-off shotgun aimed at his head by a deputy sheriff from Madera County. He said what went through his head was, "I am a chemist employed by the Stanford Research Institute in Menlo Park, California, and that I am in this brush field testing bark beetle pheromones. …

No!…He will never believe this story!" Milt's employee card saved the day.

In 1969 Milt and his family moved to Syracuse, New York, where he was appointed professor of chemical ecology at the State University of New York, College of Environmental Science and Forestry (ESF), the first position of its kind in the world. One of his first research projects was isolation, identification, and synthesis of the sex pheromone of the elm bark beetle. At that time Dutch elm disease, transmitted by the beetle, was wreaking havoc on the stately elm trees that shaded the streets of many U.S. cities. John Peacock, an entomologist with USDA Forest Service, and Gerald Lanier, an entomologist at ESF, joined the research and tens of thousands of the beetles were reared from logs cut from infested elms and the females separated before they had a chance to mate. Milt's students collected the volatiles given off by the virgin females boring into elm logs by passing a stream of air over the insects and then through an adsorbent trap. The collected volatiles were fractionated, monitored by a bioassay, and the pheromones were purified and identified by spectroscopic methods. Here again they found that no single compound was active alone but that compounds produced by the beetles were synergized by volatiles produced by the trees to give maximum attraction to the males and females. Subsequently, Gerald Lanier and collaborators developed methods to trap the beetles, and several cities employed the synthetic pheromone blend to protect their elms.

At ESF Milt focused on developing the field of chemical ecology, publishing more than 200 research papers and 7 books over his career. He also wrote the definitive papers on the role of chirality in insect pheromones. He continued his collaboration with David Wood and established new collaborations with biologists all over the world. These collaborations, encompassing a wide range of biological systems, had

a tremendous impact on expanding the scope of chemical ecology in the early stages. He and his colleagues demonstrated the importance of host tree compounds in synergizing bark beetle pheromones and identified and synthesized the pheromones of over 20 species of beetles, several ticks, and moths. Working with John Moser of the U.S. Forest Service, he and his students made the first identification of an ant trail pheromone from the species *Atta texana*. With Dietland Muller-Schwarze they completed the first isolation and identification of mammalian pheromones from deer and the pronghorn antelope. His pioneering work on pheromones provided the knowledge and tools for successful monitoring and control programs for insect pests of forests, stored products, and agricultural crops. As an example, he played a critical role in identifying the pink bollworm-moth sex pheromone which has been used successfully for control of this important pest of cotton, thus avoiding the use of pesticides on thousands of acres.

Soon after moving to ESF, Milt began planning for a journal that would provide a home for all the papers that were beginning to be published in the area of chemical ecology but were scattered throughout the biological and chemical literature. In 1974 he and John Simeone led the efforts to establish the *Journal of Chemical Ecology*. Together Milt and John edited the journal for 20 years, until 1994. Milt and John also helped to establish the International Society of Chemical Ecology, which was incorporated on September 12, 1983. The society's Silverstein-Simeone Lecture Award was established in honor of the enormous contribution made to the field of chemical ecology by Milt and John. The award is normally given in recognition of outstanding recent or current work at the frontiers of chemical ecology.

Throughout his career Milt was at the forefront of his field and was in much demand as an invited lecturer. He

accepted an invitation to attend a meeting in France only to learn that all lectures must be given in French. Although he spoke no French, he was not dismayed. He wrote his lecture and found a colleague who could translate it into French. Then he spent weeks in his office memorizing and practicing it. He related with his typical sense of humor that at the end of his talk all the questions were in English, indicating that perhaps his French was not as good as he had hoped.

Milt disdained paperwork. On one occasion when he was out of town a secretary searched his office for information on a grant proposal he was preparing. She returned empty handed, exclaiming, "He keeps nothing in his filing cabinets. They are empty!"

Milt was a true gentleman who knew so much but was so humble. He will be remembered by his students, friends, and colleagues for his enthusiasm and fascination with chemical ecology and his skillful application of chemical techniques to solve complex biological problems. He will also be remembered for his sense of fairness, his wonderful and understated sense of humor, integrity, loyalty, courage, and his friendship. This is perhaps best illustrated by his own words, written on his election to the National Academy of Sciences,

> I can look with pleasure on the contributing factors: a most competent group of graduate students and postdocs, and an incredible selection of collaborators in chemistry and biology. The timing for the development of chemical ecology was perfect, depending in large part on the rapid evolution of capillary gas chromatography, HPLC, EAG, mass spectrometry, and NMR. My first comprehension of the "index of hydrogen deficiency" in mass spectrometry and of a "first-order spectrum" in NMR were indeed revelations. But, above all, were the friendships that evolved from the collaborative investigations that were breaking new ground. We all learned much from one another.

Thank you, Milt, and in his understated words of praise, "Good show."

HONORS AND DISTINCTIONS

Sigma Xi (Syracuse) award, 1977
American Chemical Society (Syracuse) award, 1978
J. E. Bussart Memorial Award, Entomological Society of America, 1978
Freshwater Biological Research Foundation Award, 1980
Medal of the Royal Swedish Academy of Agriculture, 1983
Silver Medal of the International Society of Chemical Ecology, 1986
Honorary member, International Society of Chemical Ecology, 1994
Silverstein-Simeone Award for Outstanding Student, sponsored by Plenum Press/ISCE, 1995
Festschrift issue of the *Journal of Chemical Ecology*, 1995
Member, National Academy of Sciences, 2000

SELECTED BIBLIOGRAPHY

1963-1998

With various coauthors. *Spectrometric Identification of Organic Compounds*, 7 editions. New York: Wiley.

1966

With O. J. Rodin and D. L. Wood. Sex attractants in frass produced by male *Ips confusus* in ponderosa pine. *Science* 154:509-510.

1967

With D. L. Wood, R. W. Stark, and J. O. Rodin. Unique synergistic effects produced by the principal sex attractant compounds of *Ips confusus* (LeConte). *Nature.* 215:206.

1968

With R. G. Brownlee, T. E. Bellas, D. L. Wood, and L. E. Browne. Brevicomin: Principal sex attractant of the Western pine beetle, *Dendroctonus brevicomis. Science* 159:889.

1969

With R. G. Brownlee, D. Muller-Schwarze, and A. G. Singer. Isolation, identification, and function of the chief component of the male tarsal scent of the black-tail deer. *Nature* 221:284.

With W. D. Bedard, P. E. Tilden, D. L. Wood, R. G. Brownlee, and J. O. Rodin. Western pine beetle: Field response to its sex pheromone and a synergistic host terpene, myrcene. *Science* 164:1284-1285.

With J. O. Rodin, R. M., Burkholder, and J. E. Gorman. Sex attractant of female dermestid beetle, *Trogoderma inclusum* Le Conte. *Science* 165:904-906.

1970

With D. L. Wood and M. Nakajima, eds. *Control of Insect Behavior by Natural Products.* New York: Academic Press.

1971

With J. H. Tumlinson, J. C. Moser, R. G. Brownlee, and J. M. Ruth. Identification of the trail pheromone of a leaf-cutting ant, *Atta texana. Nature* 234:348.

With U. E. Brady, J. H. Tumlinson, and R. G. Brownlee. Sex stimulant and attractant in the Indian meal moth and in the almond moth. *Science* 171:802-804.

1973

With H. E. Hummel, L. K. Gaston, H. H. Shorey, R. S. Kae, and K. J. Byrne. Clarification of the chemical status of the pink bollworm sex pheromone. *Science* 181:873.

1974

With D. Muller-Schwarze, C. Muller-Schwarze, and A. G. Singer. Mammalian pheromone: Identification of active component in the subauricular scent of the male pronghorn. *Science* 183:860.

With R. G. Riley and J. C. Moser. Biological response of *Atta texana* to its alarm pheromone and the enantiomer of the pheromone. *Science* 183:760.

1975

With W. E. Gore and G. T. Pearce. Relative stereochemistry of multistriatin (2,4-dimethyl-5-ethyl-6,8-dioxabicyclo[3.2.1]octane). *J. Org. Chem.* 40:1705-1708.

1976

With G. T. Pearce and W. E. Gore. Synthesis and absolute configuration of multistriatin. *J. Org. Chem.* 41:2797-2803.

With D. E. Sonenshine, E. Plummer, J. R. West, and T. McCullough. 2,6-Dichlorophenol, the sex pheromone of the Rocky Mountain wood tick, *Dermacentor andersoni* Stiles, and the American dog tick, *Dermacentor variabilis* (Say). *J. Chem. Ecol.* 2:201-209.

1977

With W. E. Gore, G. T. Pearce, G. N. Lanier, J. B. Simeone, J. W. Peacock, and R. A. Cuthbert. Aggregation attractant of European elm bark beetle, *Scolytus multistriatus* (Coleoptera, Scolytidae): Production of individual components and related aggregation behavior. *J. Chem. Ecol.* 3:429-446.

With J. G. MacConnell, J. H. Borden, and E. Stokkink. Isolation and tentative identification of lineatin, a pheromone from frass of *Trypodendron lineatum* (Coleoptera, Scolytidae). *J. Chem. Ecol.* 3:549-561.

1978

With U. Ravid and L. R. Smith. Synthesis of enantiomers of 4-substituted gamma-lactones with known absolute-configuration. *Tetrahedron* 34:1449-1452.

1979

With J. H. Cross, R. C. Byler, U. Ravid, S. W. Robinson, P. M. Baker, J. S. de Oliveira, A. R. Jutsum, and J. M. Cherrett. Major component of the trail pheromone of the leaf-cutting ant, *Atta sexdens rubropilosa* Forel: 3-Ethyl-2,5-dimethylpyrazine. *J. Chem. Ecol.* 5:187-203.

1980

With J. H. Bordon, J. R. Handley, J. A. McLean, L. Chong, K. N. Slessor, B. D. Johnston, and H. R. Schuler. Enantiomer-based specificity in pheromone communication by two sympatric (*Gnathotrichus*) species (Coleoptera, Scolytidae). *J. Chem. Ecol.* 6:445-456.

With W. D. Bedard, D. L. Wood, P. E. Tilden, K. Q. Lindahl, and J. O. Rodin. Field responses of the western pine-beetle (Coleoptera, Scolytidae) and one of its predators to host-produced and beetle-produced compounds. *J. Chem. Ecol.* 6:625-641.

With G. N. Lanier, A. Claesson, T. Stewart, and J. T. Piston. *Ips pini*: The basis for interpopulational differences in pheromone biology. *J. Chem. Ecol.* 6:677-687.

With M. C. Birch, D. M. Light, D. L. Wood, L. E. Browne, B. J. Bergot, J. R. Ohloff, and J. C. Young. Pheromonal attraction and allomonal interruption of *Ips pini* in California by the two enantiomers of ipsdienol. *J. Chem. Ecol.* 6:703-717.

With R. F. Cassidy, W. E. Burkholder, T. Shapas, H. Z. Levinson, and K. Mori. Perception by *Trogoderma* species of chirality and methyl branching at a site far removed from a functional group in a pheromone component. *J. Chem. Ecol.* 6:911-917.

1981

With H. J. Williams, W. E. Burkholder, and A. Khorramshahi. Dominicalure-1 and dominicalure-2: Components of aggregation pheromone from male lesser grain borer, *Rhyzopertha dominica* (F) (Coleoptera, Bostrichidae). *J. Chem. Ecol.* 7:759-780.

Pheromones: Background and potential for use in insect pest-control. *Science* 213:1326-1332.

1983

With D. C. Booth, T. W. Phillips, A. Claesson, G. M. Lanier, and J. R. West. Aggregation pheromone components of two species of *Pissodes*-weevils (Coleoptera, Curculionidae): Isolation, identification, and field activity. *J. Chem. Ecol.* 9:1-12.

1987

With D. Crump, H. J. Williams, and T. D. Fitzgerald. Identification of the trail pheromone of the larva of the eastern tent caterpillar *Malacosoma americanum*. *J. Chem. Ecol.* 13:397-402.

1988

Chirality in insect communication. *J. Chem. Ecol.* 14:1981-2004.

1989

With G. N. Lanier, Y.-T. Qi, J. R. West, S. C. Park, and F. X. Webster. Identification of the sex pheromone of three *Matsucoccus* pine bast scales. *J. Chem. Ecol.* 15:1645-1659.