



Linda B. Buck

Science of Smell: Solving One of Biology's Greatest Puzzles

Linda Buck at the Fred Hutchinson Cancer Research Center in Seattle, May 2002. Behind her are molecules representing different scents. Photo: Meryl Schenker/SeattlePI.com/Polaris

In 2004, the Nobel Prize in Physiology or Medicine was awarded to Linda B. Buck, jointly with Richard Axel, for discoveries that transformed scientific understanding of one of the most mysterious human senses: olfaction, or the sense of smell. What began as a simple question—how do we smell?—became a lifelong intellectual pursuit that revealed deep connections between biology, perception, memory, and emotion. Buck's work not only uncovered the molecular and neural mechanisms underlying smell but also reshaped how scientists understand sensory perception itself.

Linda Brown Buck was born in Seattle, Washington, in 1947. Unlike many future scientists, Buck did not grow up with a clear ambition to pursue science as a career. Instead, she possessed something more fundamental: curiosity. Her father, an electrical engineer, and her mother, a homemaker, shared a love for puzzles, inventions, and problem-solving. This environment fostered a mindset that Buck would later recognize as central to scientific inquiry. As she would come to describe it, science is, at its core, “really puzzle-solving.”

Her parents encouraged exploration, independent thinking, and the expectation that she would ultimately do something meaningful with her life. Yet Buck's path toward science was far from linear. After enrolling at the University of Washington, she initially studied psychology, considering a future as a psychotherapist. Uncertain about this direction, she left university to travel and explore other possibilities, returning intermittently to take classes.

In 1975, at the age of 28—ten years after she first began her undergraduate education—Buck graduated with a Bachelor of Science degree in both microbiology and psychology. The combination would later prove uniquely valuable, bridging molecular biology with questions of perception and behavior.

Buck went on to earn a PhD in immunology at the University of Texas Southwestern Medical Center in Dallas. There, she learned the craft of research under the mentorship of Ellen Vitetta, whom Buck credits with teaching her not just experimental techniques, but how to think like a scientist: how to ask the right questions, design rigorous experiments, and persevere through uncertainty.

After completing her doctorate, Buck joined Columbia University, where she entered the laboratory of Richard Axel, a neuroscientist known for applying molecular biology techniques to the nervous system. Axel's lab was studying the molecular basis of neural signaling, including work on the nervous system of a sea snail. For Buck, this environment opened a new intellectual landscape.

She became fascinated by the extraordinary diversity of cell types in the brain and by the question of how molecular differences translate into complex sensory experiences. While reading a scientific paper on possible mechanisms of odor detection, Buck experienced what she later described as a life-changing moment. For the first time, she confronted the mystery of olfaction—an everyday human experience that science had barely begun to explain.

In 1988, Buck embarked on what would become one of the most important investigations in sensory biology: the search for odour receptors. At the time, scientists did not know how the nose recognized and differentiated between thousands of distinct smells. The prevailing theories were speculative, and no molecular mechanism had been firmly established.

Buck worked intensely for three years, applying molecular genetics techniques to identify the receptors responsible for odor detection. In 1991, she and Axel published a landmark paper revealing the existence of a large family of olfactory receptor genes.

Their discovery showed that mice possess around 1,000 different olfactory receptors, located in the olfactory epithelium at the back of the nose. These receptors are proteins embedded in the membranes of sensory neurons. Each receptor binds to specific odorant molecules, initiating a signal that travels to the brain. Humans, it turned out, have fewer receptors—around 350—but the basic mechanism is the same.

Solving the problem of odor detection only raised a deeper question: how does the brain interpret these signals to create the rich world of smells we experience? With only 350 receptors, how can humans distinguish among 10,000 or more different odors, many of which are chemically similar?

To answer this, Buck moved to Harvard University, where she continued her research as an assistant professor and later as a full professor. Her focus shifted from the nose to the brain—from reception to perception.

In 1999, Buck uncovered the solution: the olfactory system uses a combinatorial coding strategy. Rather than each receptor corresponding to a single smell, each receptor can respond to multiple odorants, and each odorant can activate multiple receptors. Together, these patterns of activation form a unique “odorant code” for each smell.

Buck’s research did not stop at decoding odor patterns. She wanted to understand how these signals are processed in the brain to influence memory, emotion, attraction, and aversion. Unlike other senses, smell has a direct and powerful connection to the brain regions involved in emotion and memory.

In 2001, Buck published studies showing how olfactory neurons are organized and mapped in the olfactory cortex. These findings revealed that the brain maintains spatial representations of odor information, transforming molecular signals into meaningful perceptions.

This work illuminated why smells can evoke vivid memories, trigger emotional responses, and influence behavior in profound ways. From the comforting scent of home to the warning signal of smoke, olfaction plays a crucial role in survival and identity.



(Fred Hutchinson Cancer Research Center | Science News Releases)

In 2004, Linda Buck and Richard Axel were awarded the Nobel Prize in Physiology or Medicine for their discoveries of odorant receptors and the organization of the olfactory system. The Nobel Committee recognized their work as a foundational contribution to neuroscience and molecular biology.

Two years earlier, in 2002, Buck had returned to her hometown of Seattle, where she established a laboratory at the Fred Hutchinson Cancer Research Center. There, she continued exploring the olfactory system, expanding her research into how smell influences physiology and behavior across species.

For Buck, the Nobel Prize was not an endpoint but a platform. She hoped that her recognition would send a message—particularly to young women—that science is open to them.

“As a woman in science,” she said, “I sincerely hope that my receiving a Nobel Prize will send a message to young women everywhere that the doors are open to them and that they should follow their dreams.”

Linda B. Buck’s work fundamentally changed how scientists understand the sense of smell, transforming it from a poorly understood phenomenon into a well-defined molecular and neural system. Her discoveries revealed how biology translates chemical signals into perception, memory, and emotion—processes that lie at the heart of what it means to be human. ♦

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—Linda Buck