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Bob Horvitz

Howard Robert "Bob" Horvitz grew up with a love for numbers. His father was a CPA and the treasurer of a trucking company in Chicago. "Numbers were his friends," Horvitz recalls. Oscar Horvitz taught his son how to make games out of thinking about numbers, and Bob seriously considered becoming a mathematician. Horvitz's family moved from Chicago ("North side, Chicago Cubs") to suburban Skokie while he was in the eighth grade.

Horvitz's first exposure to experimental biology came in 1961 when he attempted to replicate Gregor Mendel's 3:1 and 9:3:3:1 inheritance ratios using Drosophila for a ninth-grade science fair project. His mother, Mary Horvitz, who was then teaching seventh and eighth grade mathematics and science, gave up her bathroom so he could breed flies. "There were flies all over the house," Horvitz remembers, "and the bathroom smelled awful." Still, the crosses worked, and he won a prize. "Growing up," Horvitz recalls appreciatively, "the entire mentality at home was that learning about things in general and particularly about things related to science was fun." Horvitz's early experiences with biology were not all rosy, however. In the same year as his Drosophila experiment, Horvitz and a friend were collecting insects when they were mugged in Chicago's Humbolt Park. "I lost my butterfly net and 39 cents," he laments. In addition, Horvitz found ninth grade biology "rather boring." The unpleasant smell of formaldehyde is his most prominent memory. Since his teacher was allergic to formaldehyde and did not stay in the classroom during dissections, Horvitz's intellectual stimulation was mostly limited to the games of dots he played with his laboratory partner.

Undecided between mathematics and chemistry, Horvitz went to MIT for college. There he became involved in the student newspaper and student government, and was elected President of the undergraduate student body. His major was theoretical mathematics, and he accumulated enough credits to graduate in three years. "But I was having too much fun," he said, so he took a fourth year to also earn a degree in economics. His undergraduate thesis was a mathematical modeling of the utilization of exhaustible resources (e.g., minerals), and was written under the tutelage of Robert Solow, who later won the Nobel Prize in Economics. ("Not because of my work," Horvitz points out.)

Horvitz was persuaded by a roommate, Al Singer (now at the National Cancer Institute), who was a biology major, that biology had progressed beyond formaldehyde. As a senior, Horvitz registered for the introductory biology course taught by Cy Leventhal. After six weeks, Horvitz went to Leventhal and said, "I think I'm interested in graduate school in biology, but I know nothing about it and am getting degrees in mathematics and economics. Am I crazy?" Leventhal responded, "I have degrees in physics and economics, and I'm teaching your course!" Still, Horvitz was uncertain and obtained applications to graduate schools in mathematics, economics, business, law, medicine, and biology. He claims that because he knew least about biology, he enrolled in 1968 as a graduate student in the Department of Biology at Harvard. Al Singer says that Horvitz was a "brilliant student," but he was still "surprised when Bob made the switch to biology so quickly."

At Harvard, Horvitz worked in the laboratory jointly run by Jim Watson, Wally Gilbert and Klaus Weber. "The synergism among these three scientists was phenomenal," Horvitz notes, "and the training they offered was superb. Jim had a great biological intuition, Wally could find the pitfalls in the interpretation of any experiment, while Klaus knew precisely how to make experiments work."

Horvitz's goal in entering the field of biology was a small one - to elucidate the mechanistic basis of consciousness. He hoped that his knowledge of mathematics would somehow prove useful. (He is still hoping.) Believing that a solid training in experimental thinking would provide a basis for later more difficult pursuits, Horvitz analyzed modifications made by bacteriophage T4 to the Escherichia coli RNA polymerase. His studies helped reveal the mechanisms responsible for the changes in transcription that drove T4 development. Recognizing that this effort was a far cry from analyzing the mind, and by then having become enamored with the approaches of genetics, Horvitz in 1974 took a postdoctoral position with Sydney Brenner to study the nematode Caenorhabditis elegans at the Medical Research Council Laboratory of Molecular Biology in Cambridge, England. Little was known about C. elegans at the time, and Horvitz's applications for postdoctoral funding had but one reference to the organism, "S. Ward, personal communication." As a postdoctoral scientist, Horvitz hoped to use biochemistry ("I had just spent six years in a cold room"), molecular biology and, in particular, genetics to explore the nervous system. Horvitz acknowledges that "I wasn't convinced I could use C. elegans to study consciousness, but given its small size, cellular simplicity and spectacular genetics I believed I could use C. elegans to see how a simple nervous system forms and processes information. Those are basics that should help us to take the next step toward an understanding of more complicated structures and processes."

Once at the MRC-LMB, Horvitz's interest in development, in part based upon his fascination with the complex anatomy of the nervous system and in part derived from his graduate studies of T4, blossomed. He encountered John Sulston, an organic chemist who had begun to examine the neurochemistry of C.

elegans. Together these two novices in developmental biology did studies of C. elegans development that led to the first and to date only complete description of the cell lineage of an animal. Horvitz joined the Department of Biology at MIT in 1978 and became an Investigator of the Howard Hughes Medical Institute in 1988. He has taught, and enjoyed teaching, a variety of undergraduate and graduate courses, most with an emphasis on genetics. His research has continued to focus on C. elegans and has involved a wide range of biological problems: cell lineage, cell division, cell migration, cell-fate determination, signal transduction, programmed cell death, nervous system development and behavior. Horvitz reflects that when he started out in this line of research some scientists were skeptical, in part because worm genes could not be cloned.

Nevertheless, he persevered, focusing his major efforts on applying genetics to problems in development and behavior. Later, the cloning of worm genes became straightforward and in fact the worm genome project has very much proved a pilot for the human genome project. Horvitz's laboratory has discovered and cloned a wide variety of worm genes ("one of my graduate students recently told me we've cloned 58 worm genes defined by mutation to date"), and in the process identified and named such protein families such as the POU, LIM, and RGS families. Richard Hynes, his MIT colleague and former chairman, says Horvitz's "identification and cloning of worm genes really gave the clues that made it possible to make the major advances that have been made in the field." Hynes, who calls Horvitz a good friend, also says he "can always be counted on to pull his weight in the department." Of late, Horvitz has been particularly interested in programmed cell death and how it occurs. Horvitz says, "from our initial studies of cell lineage done in collaboration with John Sulston, it was clear that certain cells die as a normal part of worm development. So we asked how." Hynes says Horvitz's work on programmed cell death is "spectacular" and that his laboratory was responsible for "opening up the field and identifying cell death as an important issue."

Horvitz has also devoted long-term collaborative effort to a human disease that involves nervous system cell death: Amyotrophic Lateral Sclerosis (ALS), more commonly known as Lou Gehrig's disease. Horvitz's father died from ALS, and it was his father's illness that led Horvitz to become involved in this effort. This multi-laboratory collaboration resulted in the discovery that mutations in a gene that encodes the enzyme Cu/Zn superoxide dismutase are responsible for one inherited form of the disease. Horvitz has also worked for many years as an advisor to the Hereditary Disease Foundation, helping its efforts to understand Huntington's Disease, another human neurodegenerative disease.

Horvitz is also very involved with scientific societies. He was on the Board of Directors of the Genetics Society of America for six years and served as its President in 1995. He became a member of the ASCB in 1988, noting that "cell biology has always been close to my heart." Since 1993 he has been active with ASCB public policy activities including the Joint Steering Committee for Public Policy, an organization that was formed to advocate for biomedical research funding from the perspective of the bench scientist. Some of Horvitz's earlier work with the World Health Organization in Geneva led to his involvement with ASCB public policy activities: the WHO was attempting to quantify the economic return of research, a discussion for which Horvitz was well prepared given his background in economics and biology. This same issue was highly relevant as biomedical scientists were attempting to develop economic arguments for why the U.S. government should support basic research. Horvitz feels that "Congress and the public have a right to know what is being done with their funds." He also believes that scientists should make the case for why these funds are needed and why they are good investments for society as a whole. He says, "I believe that public policy efforts by scientists are extremely important. Scientists have a responsibility to communicate why research is important clearly and compellingly to non-scientists." Horvitz's former roommate, Al Singer, notes, "Bob has always had a deep social conscience." One way Horvitz has contributed to current public policy efforts was by coming to Washington last fall to brief the Congressional Biomedical Research Caucus on All Creatures Great and Small: The Universality of Genes, about how studies of non-human organisms can prove important for the understanding, prevention and cure of human disease.

Horvitz's wife, Martha Constantine Paton, is a neurobiologist at Yale. Their daughter, Alexandra, is four-and-a-half ("going on 20"). The family maintains two homes, one in Newton, Massachusetts, where Bob lives during the week, and one in Hamden, Connecticut. They spend weekends, and when possible extended weekends, together in one home or the other. While they have found this life manageable, it isn't easy.

Horvitz has remained close to his sole sibling, Carol Horvitz Nutt, a tropical ecologist at the University of Miami. "She has spent much of her time on her hands and knees in the jungle looking at plants and ants," he observes with admiration. He thinks that becoming a scientist was as much of a fluke for her as it was for him: her interest in language landed her in Colombia to learn Spanish. There she became intrigued by botany and jungle ecology. Horvitz believes one message of both their professional lives is "don't be afraid of doing something new."

Horvitz feels that his life as a scientist has been richly rewarding, sometimes in surprising ways. "I love to travel," he says, "and when I began as a biologist I had no idea that my professional life would take me all over the world." Horvitz has taught courses as far away as Japan and China, and has visited every continent except Antarctica, ("and I'm still hoping"). "But my biggest thrills," he states with enthusiasm, "have been helping students develop into innovative and successful scientists and, of course, discovering something fundamentally new about how life works."