Autobiography

"He can't even throw a baseball!" was the way my cousin Harvey greeted me soon after my birth on May 8, 1947. Looking forward to a fellow athlete, Harvey, age three, found me ill prepared for sports. I suspect the disappointment continued, as Harvey progressed to become one of the star little league players in Chicago. I did not.

Family history

Chicago is my hometown. My mother Mary Savit Horvitz was born in Chicago, and my father Oscar Horvitz was born in the neighboring town of Joliet. Both of my parents were first-generation Americans, the children of Jews who left Eastern Europe around the turn of the century. My maternal grandfather David Savit (Savitzky) was born in 1879 and came to Chicago in 1904 (via Liverpool, Halifax and Detroit) from Oster, Russia, in present-day Ukraine about 40 miles north of Kiev. He was the second oldest of ten children, and his widowed mother Malke Zolotar Savitzky and his eight younger siblings followed him to Chicago. David was a dress manufacturer and a grocer, but I remember him most reading, playing chess (sometimes with me) or standing at his newstand selling newspapers. The family held him in awe as a gentle and caring human being, and as a scholar.

My maternal grandmother Rose Bleiweiss Savit came to Chicago from Galicia, Austria, around 1902. She was from an area that was alternatingly Austrian and Polish, from a town that is now Debica, Poland, about 60 miles east of Cracow. I always thought of her as Polish. She was one of the lucky members of her family, as her father Hersch David Bleiweiss and at least three of her siblings were murdered by the Nazis. Rose married David Savit in 1908, and my mother Mary Savit was born in 1921, the youngest of four girls, after Ann, Sylvia and Esther. In the early 1950s, David and Rose moved to Miami because of Rose's ill health, but after David's death in 1957 Rose returned to Chicago. She lived with us from 1963 until her death in 1968. Like David, Rose played chess, but she enjoyed poker more and sometimes joined poker games with my friends and me. Before I left for college in 1964, I spent one year living with Rose and during this time heard many stories, most of them about Chicago speakeasies during the 1920s.

My father's parents were Samuel and Celia Horvitz. Sam's original name was Solomon ben Mikhail Gourevitch, but, like many other immigrants to the U.S., he found his name altered upon entry to the country. Sam was from a Jewish village called Shchedrin, located near Minsk, in what was then Russia and is now Belarus. Sam was from a wealthy Russian family. His father ran a lumber business but, being Jewish, was not allowed to own any land himself. Sam spoke Russian, Polish, Yiddish and German. He married his first wife (not my grandmother) in Poland in 1902 and went to Chicago to avoid the 1904-1905 Russo-Japanese War. Once in the U.S., Sam worked in the garment trade as a presser. In 1910, he was blacklisted for participating in the four-month long Hart, Schaffner and Marx labor strike. Hart, Schaffner and Marx was a giant clothing

manufacturer, the largest company in Chicago at that time. Employees were subjected to excessive work hours, miniscule wages and subhuman working conditions, and a strike at the company became the basis of a city-wide violent clash between businesses and the unions. Sam kept a hat with a bullet hole in it, a souvenir of a shot taken at him during a union rally. He became an insurance salesman, and it was because he was working for a Polish insurance company that from 1917 to 1920 he lived in Joliet, which had much industry, many steel mills and large numbers of Polish immigrants. Later, Sam operated a Chicago dry cleaning business, which I remember visiting once, just before he died in 1951.

Sam's first wife died in 1908, and he and their two daughters moved in with cousins, where my paternal grandmother Celia Bolotin was a boarder. Celia was from Novgorad-Syovorsk, about 150 miles northeast of Kiev in Russia. Celia was generally called by her Hebrew name of Tzipporeh, which means "little bird." In Russia she had lived in a one-room house, which her family shared with the domestic animals, for mutual warmth. As a young girl, Celia was unusual. First, unlike most girls in her town, she learned to read. Second, she was rather stubborn and independently minded. Because in one of the books she had read a girl was cruelly mistreated by her step-mother, when young Celia's widowed father remarried and was loading a cart to take his family and possessions to another town to live with his new wife, Celia refused to go, and moved in with an aunt. Both a desire for knowledge and a strong will are family characteristics that have endured. In 1905, Celia, not yet 20 years old, was involved in the first Bolshevik uprising and was captured by the Czar's police. Knowing that they were executing people who knew how to read or write, she feigned illiteracy. They released her, but informed her if caught again she would be killed. Celia left Russia, traveling via Rotterdam to Chicago. She and Sam were married around 1909, and she raised Sam's two daughters (Faye and Bess) as well as two daughters (Pearl and Diana) and two sons (Mike and my father, Oscar) from their own marriage. My father, like my mother, was the youngest. My father's family moved a lot - about every three months - because landlords offered three months free rent to attract tenants. I never knew either of my father's parents very well, as Celia died before I was three and Sam when I was four. My father and Sam were not on good terms, both because Sam left Celia for another woman and because Sam failed to provide any support for the large family he deserted during the Depression. I think both Celia and Sam influenced me greatly through my father, who learned about responsibility from his mother and about the costs of irresponsibility from his father.

My father was born on November 3, 1918, just before the signing of the armistice ending World War I. His parents were delighted that the war was ending, and named him Oscar Freedom Horvitz. My father never liked and never used his middle name, signing things as Oscar F. or, more often, simply as Oscar. He grew up on the north side of Chicago, but nonetheless became an ardent fan of the south-side Chicago White Sox baseball team. Dad himself wanted to be a professional baseball player, but his eyes went bad when he was young (as did mine) and his family could not afford to buy eyeglasses. Eventually, one of his teachers purchased a pair of glasses for him. As a teenager, my father worked as a milkman's helper, and many weeks the family lived on the butter, eggs, milk and cottage cheese he was allowed to bring home from whatever was left over at the end of

the daily run. After my father finished high school, he went to work to support both his mother and himself. He took a job with an advertising agency, clipping ads from daily and weekly newspapers around the country. He found the job tediously dull, and to amuse himself he memorized the names of every town and its newspaper. He remembered these names throughout his life, and I think back fondly how years later people would express amazement that he knew not only the locations of their hometowns but also the names of their hometown newspapers.

My mother Mary Savit was born on June 5, 1921. Not given any middle name, she decided to adopt the middle initial "R," because it gave her the initials "MRS." She lived in a variety of neighborhoods in Chicago's north side. My parents met at a Christmas party in 1938, when my mother was 17 and my father 20. While in high school, my mother worked for 25 cents per hour as a sales clerk in a dimestore. In college, she had a part-time job as a bookkeeper and telephone switchboard operator at a company that made and sold uniforms for military officers. My mother obtained a teaching certificate in elementary education and then a B.A. in English from the Chicago Teacher's College. She began substitute teaching in the Chicago public schools. My father changed jobs, working next at a mail-order house, and attended night school to study chemistry, which he loved. However, he soon realized that he could not afford the continued schooling that would be needed to allow him to make a living as a chemist. He switched to accounting. In 1941, my father passed the civil service exam in accounting and was hired by the General Accounting Office of the U.S. Government for a job in Washington, D.C. To be together, he and my mother decided to get married. Because he could not afford and my mother did not want a diamond ring, my father bought a ring for my mother in a dimestore. He returned to Chicago for the wedding, which was on June 30, 1942. They lived in Washington until 1945, when they moved back to Chicago. While in Washington, shortly after my parent's marriage, my father was hit by a car, soon thereafter leaving him with a steel pin in his shoulder. He later told me that without this accident I might never have existed, as otherwise he would have been drafted into the army and who knows what would have happened to him if he had gone to war. In Chicago my father continued working with the General Accounting Office, while my mother continued the employment she had begun in Washington, D.C., with the Social Security Board of the U.S. Government.

Growing up

I was born in 1947 and given the name Howard Robert Horvitz. My first name, which started with an "H," was in memory of my great-grandfather Hersch, who had been shot a few years before by the Nazis. "Robert" my parents simply liked, in fact so much that they decided to call me "Bobby" and registered me for kindergarten as "Robert H." Later, when I went to university, I reverted to the name on my birth certificate and became known as "H. Robert." As I grew up my parents mostly called me "Bob," reserving "Robert" for times of disapproval and "Rob" or sometimes "Robin," by my father, as terms of love. I begged my parents for a baby sister, and, on October 5, 1950, my sister Carol Cecile was born. She was named for my grandmother Celia, who had died earlier that year. I remember awakening the day my sister was born, surprised to find myself in my parent's bed next to my Aunt Ann, my mother's oldest sister. Ann died of Alzheimer's

Disease many years later, one of a number of my personal reasons for becoming interested in neurodegenerative disorders.

Me, with The Great Pumpkin (1948).

We lived on the north side of Chicago, which led to my becoming a fan of the Chicago Cubs baseball team, unlike my father, whose loyalty to the White Sox continued. My parents saved their money and moved repeatedly to find better homes for themselves and their family. When I was born, we lived in a one-room kitchenette near Lake Michigan, and I slept behind a screen while they ate, entertained or slept. We moved some miles west in 1948 to a one bedroom, four-room apartment. After my sister Carol was born, we moved again a few blocks away to a five-room bungalow on Rockwell St. Sometimes at night Carol and I secretly crawled out through her window to play in the back yard with friends who lived next door. One of the great delights of my receiving the Nobel Prize was that I was contacted by many old friends with whom I had lost touch, including one of these next-door neighbors on Rockwell St.

The Rockwell St. house is where I feel that I grew up, living there from ages five through 12. The neighborhood at that time was a mix of 1920s bungalows and apartment buildings, and was mostly Jewish. Author Saul Bellow's father lived a few houses south of us. I was a member of a club we named the Epics, without having any idea what the word meant but simply because we liked its sound. The year after I moved out of Chicago, the Epics became the Commodores, a gang. Rockwell St. was also important for me because it was while living there I became good friends with Ira Zarov, who lived across the street and whose mother was my Den Mother in Cub Scouts. Ira and I remain very close, exchanging e-mails almost daily and spending a week of most summers with our families together at his family home along the south shore of Lake Michigan, near Chicago.

I went to the DeWitt Clinton Elementary School and got into trouble repeatedly for small misdemeanors, particularly in the third grade. One transgression was my insistence upon crossing in the middle of the street to walk to school with Ira. Another involved the fact that Ira and I had acquired vast quantities of gumballs as a consequence of having found a cardboard circle that could substitute for a penny in the gumball machine in the local candy store. A few years later Ira and I were stopped at knife point by a boy trying to rob

us. He was no bigger than we were. Ira and I moved apart and pointed out to our assailant that we had him outnumbered. He left.

In 1960, my family moved to the northern Chicago suburb of Skokie, because the schools were better. I attended eighth grade at East Prairie Grammar School. Because I had come from the Chicago school system, I was placed in the lowest of the three academic tracks for all of my classes. Within a few weeks, each of my teachers moved me to the highest track. The consequence was that I got to know, and become friends with, most of the eighth grade students very rapidly. My eighth grade English teacher, Marcia Wachs, is particularly memorable and engaged me in the reading of proper English literature. A year after I left her class, she sent me a book accompanied by a very nice note: "How many times I have thought of you and wondered how you were enjoying high school. ... You seem to have a talent for writing, and I thought you might profit from reading this book. It's a gem ... ." The book was "The Elements of Style" by Strunk and White. I still have both the book and her note, and I use the book to this day (particularly when I try to educate members of my laboratory concerning the usage of "which" and "that").

In 1947, the year I was born, my father became a Certified Public Accountant. His professional life thereafter was that of an accountant. My father loved numbers, a love I learned from him. Eventually, he became the Vice President and Treasurer of a major trucking company based in Chicago. Whenever we went on family trips, Carol and I always watched for Spector trucks, sometimes reminded by my father that the stock he had purchased for us was almost enough to say that we owned one of the tires on the truck. He was President of the Motor Carriers Accountants Society of Chicago. I was always very proud of the fact that he had published a book, which was an income tax guide for farmers. He also authored a chapter in a book about data processing. Published in 1957 and focused on the accounting machines and punched cards of the era, his chapter noted, "Long-range studies of electronic computers are being made at the present time." In 1989, my father died from amyotrophic lateral sclerosis (ALS). His illness moved me to become actively involved in research involving this horrific neurodegenerative disease.

A sense of my father is reflected in a dedication written by my sister and me to an ALS Resource Book, the publication and distribution of which we funded. We wrote: "Dad was a humanitarian, not only in his values, but also in the actions of his everyday life. He cared deeply about people and always had the time to listen and provide insight. He was happiest when he was making someone else happy. In our family, Dad created an environment filled with a love of knowledge and the joy of inquiry and discovery about the world around us. Not a day went by without his learning something new and our learning something from him. So many things interested him: foreign languages, exotic places, history, new words, opera, baseball, people. He was equally excited by an exchange of smiles with little children as by a beautiful piece of music or by some scientific discovery. He also had a way with languages and often surprised people by speaking with them in their native tongue or talking with them about some detail of their country that few would know about. He once dreamed of being a major-league catcher, and then of being a research chemist. Numbers were his friends, and he chose accounting

as his profession. However, his love of science continued and was infectious, giving both of us the opportunity and encouragement to study and lead lives dedicated to scientific inquiry. Dad was a wonderful mentor. He always strove to do his best, and he always brought out the best in those around him."

My father's illness and death were an immeasurable loss to me. My father was a major cornerstone of my life. It was my father who came to talk with the elementary school principal with me after my more serious infringements. It was my father who - after at age 15 I had attempted unsuccessfully to drive the family car using a "borrowed" key and knocked down a wall of the garage - convinced me over the telephone not to run away from home and who then came home from work not to punish me but rather to console and comfort me. It was my father who would sit with me and amaze me as he solved diagramless crossword puzzles and double acrostics by simply reading the clues and writing in the answers to each as he read them. It was my father who, throughout my adult life, prepared my income tax returns and who, once ill and dying, taught me how to prepare them myself. I think it was when my father died that I really grew up. I also became more introspective and much closer to both my sister and my mother during his illness. This closeness has continued.

My mother began working as an elementary school teacher in 1948, stopped in 1950 when my sister was born, and then resumed teaching in 1955. She first taught in the third grade and then progressed through the grades with me until she stopped as a seventh and eighth grade teacher of math and science. Her training was in English, and her interest in science and her desire to be a good teacher led her to take part in a program supported by the National Science Foundation in which she spent a summer studying astronomy. Later she returned to school and obtained an M.A. in guidance and counseling, after which she worked as an elementary school guidance counselor. My mother retired in 1988. My mother has been a wonderful model for the professional woman - a loving mother dedicated to both her family and her work. She inspired me, made me proud and developed in me an enormous respect for women in general. My mother chose teaching as a profession in part because it would allow her to be home with her children as they grew up. Nonetheless, to this day, she asks me if she ruined my life by returning to work too soon after my birth. I tell her I do not believe that I turned out so badly.

I could always depend on my mother. She is capable, organized, practical, logical and absolutely reliable. Although she is a worrier, my mother never loses her sense of purpose or her ability to deal with difficult situations. When I was hit in the eye with a baseball, it was my mother who took me for stitches (after leaving my father the succinct note: "Took Bob to the hospital. Don't worry."). When friends and I rode our bicycles to O'Hare Airport (a trip far beyond the confines we were supposed to traverse) and one of the others got a flat tire, it was my mother who came and brought us home. It was also my mother, with her interest and knowledge as a science teacher, who encouraged my first experiences with experimental science. My sixth grade science project, which I think was her idea, was entitled "Electricity Produces Light through Heat" and won a third prize. My ninth grade project, in which I used the fruit fly *Drosophila melanogaster* to replicate Gregor Mendel's famed 3:1 and 9:3:3:1 inheritance ratios, required my mother

to relinquish her bathroom for my breeding experiments. She helped me prepare the fly food, which smelled awful, and tolerated the fact that to anesthetize the flies I used ether, which smelled worse. This project also won a prize, and earned me a trip to the Illinois State Science Fair, in Champaign-Urbana. My mother saved the (written) project intact, and when the announcement was made that I had received the 2002 Nobel Prize in Physiology or Medicine, my mother showed a local reporter my 1961 science fair poster, one panel of which was then reproduced in the Chicago Sun-Times on October 8, 2002 (next to my high school graduation photograph).

My mother's strength and independence became clearest to me as she nursed my father during his illness and as she has coped with and redefined her life after his death. My mother, now age 81, is impressively active and completely engaged in the events of the world. She regularly takes brisk walks for exercise and particularly enjoys walking at a nearby botanical garden. She is a bridge player, and loves the theater, the symphony, movies and art. She has long been politically active, and for some years has supported local and national actions of the National Council of Jewish Women. My mother has many friends, some of whom, albeit sadly a diminishing number, she has had for decades. My parents traveled together extensively, and my mother has continued her travels on her own, for example touring Australia, New Zealand and China. She also has visited Greece, Turkey and Costa Rica with my sister Carol. Their descriptions of the trip to Costa Rica, to see one of Carol's field stations in the tropical rainforest, were somewhat divergent. Whereas Carol described the site as the Hilton of field stations, my mother emphasized the primitive conditions that she had experienced. Carol never told my mother that each night before going to sleep she would check my mother's bedding for deadly snakes and spiders. After my father died, my mother for 10 years taught English as a second language on a volunteer basis to immigrants from all over the world. She also has taken countless adult education courses, on topics as diverse as international relations, world religions, poetry, music appreciation and money management. She has very recently obtained and begun to learn to use a computer. My mother is highly organized, and both her home and her person are well-kempt. She has been described as "an elegant woman." She is constantly sending me newspaper clippings, sometimes about the world but more often with advice about foods, health, finance or child-rearing. Generally, the advice is very good.

My father and my mother were a team, in raising my sister and me and in life in general. Together they instilled in me a sense of responsibility, of commitment, of determination, of fairness, of pride, of ambition, of optimism and of love. People, particularly family, came first. Knowledge and learning were revered. We were all always expected to do our best. Prejudice was unacceptable and attributed to ignorance. Time together and family vacations were important, and we traveled together extensively within the U.S. Without doubt, my parents defined the priorities and many of the interests that came to be central in my life.

Growing up with my sister Carol was a special delight, except perhaps during a few of my teenage years when I regarded her at best as an intrusion. When little we would play together, and I would make up long stories of flying horses and imaginary friends. Carol

voiced progressive views at an early age. When she was about five, she was listening to a conversation between my father and me. After he told me "Everything is made of atoms," she immediately cried in response, "That's not fair! Isn't anything made of Eves?" Carol and I were quite divergent in our interests, with her gravitating toward the artistic and poetic aspects of life, whereas I was more focused on math, science and schemes to make money. Carol also was more rebellious, first against our quite secular home - she adapted the orthodox Jewish custom of lighting candles and saying prayers on Friday nights and went to a Hebrew overnight camp - and later politically, leaving Barnard College (at Columbia University) with the plan of becoming a left-wing political activist. Our parents intervened, and she registered at highly liberal Antioch College in Ohio, which because of its workstudy program allowed her to be almost any place but Ohio. While she was a student at Antioch, Carol spent time in Colombia, South America, and developed her passion for botany, Spanish and Latin culture. During this period Carol was rescued rather dramatically and against her will by our parents from a nearly fatal disease and an ill-fated engagement to a Colombian merchant marine, after which she stayed briefly in Chicago. I invited her to come to Boston, and she moved in with me, living on a front porch that we insulated for her and working at the Harvard Herbarium. Carol then went back to school and obtained a Ph.D. degree in biology, just like me. It is amazing, given our backgrounds and interests, that we both became biologists. Carol married Randy Nutt, an artist also from Chicago, and the two of them now live in Miami, Florida, where Carol is on the faculty of the University of Miami. Carol has spent much of her life in the tropical rainforests of Mexico, Central and South America. I believe we have always been close and mutually supportive, and I often think about the different view of life held by those who are not lucky enough to have siblings.

In addition to my family, there was another constant presence in my young life that I believe influenced me greatly. At age two and a half, I acquired asthma. For many years thereafter, nights (in particular) could plague me with a shortness of breath that made me feel (and occasionally wish) that I was dying. When I was small, my father would carry me in his arms through the night. Later I would just lie in bed, waiting for the dawn and hoping for the relief that often came with daybreak. I had tests, medications, and shots. The asthma continued and affected my life in many ways. Most sports seemed precluded. At age 10, I insisted upon going away to Camp Chi, an overnight camp in nearby Wisconsin, and spent almost the entire two weeks in the infirmary, with an adrenaline inhalator next to my bed. Despite these stresses, instead of becoming increasingly afraid of life, I think I became more and more determined to experience and conquer it. Nothing, I thought, could be worse than what I had already suffered. I became fearless, unafraid to go anywhere and try anything and determined to persevere, even when my shortness of breath made my physical suffering so great I could barely force myself to move.

In retrospect, I think back to growing up in Chicago with the impression that I had far more freedom and independence than I would allow a child today. After school, my friends and I wandered the neighborhood, which was assumed to be and probably was safe. For a while, Ira and I went house-to-house selling magazine subscriptions, hoping to earn all sorts of wonderful prizes. We rang every doorbell within the distance we could

walk between school and dinner. We never sold a single subscription, but we did meet and talk with lots of people. For greater distances, my bicycle was my major source of transportation. Bicycle explorations went far beyond my local neighborhood and as often as possible into unknown areas. These adventures perhaps helped kindle the wanderlust that stays with me today.

In high school, the means of my explorations progressed from bicycles to cars. Before I could drive, I hitch-hiked through Chicago, simply going wherever the drivers were headed. Once the first of my friends turned age 16, we had access to cars, and a much greater world was opened. We went north to the expansive Lake Michigan beaches of wealthy Chicago suburbs and once even to Wisconsin (discovering in the process how fast a station wagon could go). We went south into the heart of the Chicago slums. 14th and Peoria, reportedly the site of various houses of ill-repute (we never got out of the car, so I never ascertained if that was true), was a favorite target.

As a high school student I did well academically. My introduction to biology was in the ninth grade, when I did my *Drosophila* breeding experiments. The class consisted almost entirely of dissections of formaldehyde-preserved animal corpses. The teacher was allergic to formaldehyde (or so he told us), and left us on our own each day. Mostly, I played dots with my laboratory partner. Based upon this experience, I never would have guessed that I would later become a professional biologist. For a project for this class, I made an extensive insect collection, which the school kept and displayed. While collecting insects in Chicago's Humboldt Park, Ira and I were mugged by two older boys. They put their arms around our necks, and one said, "Your money or your lives." Ira and I laughed, which was the wrong response. They squeezed more tightly, and I relinquished my butterfly net and thirty-nine cents.

As a sophomore, I received my first B, which was for one quarter of a summer school World History class. It was traumatic. I had been encouraged at home to have high expectations. Later B's were less upsetting. I tended to work reasonably hard and developed a method of study that consisted of my trying to think of every possible question the teacher could ask followed by my writing both the question and the answer to the question on paper, which then allowed me to review both easily. This approach took some time and presumably reinforced the various facts I was supposed to be learning. I was the Assistant Editor-in-Chief of the school newspaper, The Nilehilite, which was my main extracurricular activity.

While I was in high school, my parents became convinced I would later become an entrepreneurial businessman. I had a variety of money-making plans. I published a magazine that I called Brigand (again, I simply liked the sound of the word), using a mimeograph machine for mass production. I sold advertisements for Brigand to local merchants and sold the magazines to friends, neighbors and relatives - mostly relatives. In another scheme, a shipment of sweatshirts had been damaged in one of the trucks from the trucking company at which my father worked. The trucking company had to buy the sweatshirts, which I purchased and resold at a profit. I also had a number of part-time jobs. For a while, I worked at an insurance company, looking at a handwritten number on

a new insurance application and stamping that number onto the upper righthand corner of the first page the application. My most memorable job was at the large discount house E. J. Korvette's, where I was employed in the record department and was able to buy records at wholesale prices. My boss was a bit of an eccentric, and every day after the store oficially closed he would play at maximal volume his favorite album, "The War Whoops of the North American Indians."

I did not have a clear idea about either where I wanted to go to college or what I wanted to study. I enjoyed science, particularly math and chemistry, but I also liked English and working on the school newspaper. It seemed likely that I, like most of my classmates who chose to continue their education, would attend the University of Illinois in Champaign-Urbana. Alternatively, some of the best students went a bit further away, to the University of Michigan in Ann Arbor. I applied to both schools. However, a guidance counselor insisted that I also apply to "some school in the East." I said that I would be happy to do so and that she should pick the school. She picked MIT, and I applied. I visited the University of Michigan the weekend of a Michigan vs. Michigan State football game, and the beer and partying convinced me this was not where I wanted to be. I was scheduled to visit the University of Illinois one weekend in November, but on Friday, November 22, President John F. Kennedy was assassinated, and my trip and much of the rest of what was happening in the U.S., were cancelled. The upshot was that when I was accepted to MIT, I saw no reason not to go there (except for the pleas from my English teacher, who warned me that my intellectual development would cease if I went to such a technical school).

The assassination of JFK for me, as for so many others, was an enormously deep shock. I was 16 years old and simply could not believe such things could happen in the country in which I lived. This event was one of a small number that no doubt are etched deeply in the minds of many, causing us all to remember precisely where we were at the time. In this case, I was in my high school cafeteria. Five years later, when JFK's brother Bobby was shot, I learned the news from the radio upon awakening in my apartment in Brighton, Massachusetts. Much more recently, on September 11, 2001, I was at a meeting of the Howard Hughes Medical Institute in Chevy Chase, Maryland, sitting next to the HHMI President, Tom Cech, when Tom was called outside to be told what was soon to be announced to the entire group about the attacks on New York City and Washington, D.C.

MIT, the first time

I flew from Chicago to Boston to begin life as an undergraduate student at MIT in September, 1964. At the freshman orientation, Dean Fred Fassett (whom I later got to know better after getting into some trouble) said "Look to your left. Look to your right. One of you won't be here when the rest of you graduate." My undergraduate years were a mix of academics and extracurricular activities, more of the latter than the former. I became Features and then Managing Editor of the MIT student newspaper, The Tech, and had the great excitement of scooping the Boston daily newspapers in getting a story and the paper out the morning after the great blackout in the northeast in 1965. I was very active in student government and was a member of a variety of committees and councils. When I became a candidate for student body president, I learned the names, hometowns,

faces and majors of all approximately 3500 undergraduates. I spent full-time campaigning, met lots of people, and won the election. The next year I lived in a three-piece suit and had endless meetings with MIT administrators and, less often, with students. I talked with James Killian (President Eisenhower's Science Advisor), Jerry Wiesner (President Kennedy's Science Advisor), Jay Forrester (the inventor of magnetic core storage) and other MIT luminaries. Professor Forrester offered the view that everyone should change professions every seven years, a comment I have thought about many times since. I felt that I was grooming myself for a career in law and politics or possibly in business.

My coursework probably suffered, not in my grades, particularly, but in what I was learning. Mostly I would wait until the night before an examination, stay up all night, and learn what I needed to know to answer the questions the next day. For some courses I did nothing whatsoever until the week before the final examination. When one of my professors penalized me for turning in all of my problem sets at the end of the course, I thought he was being quite unreasonable. I majored in mathematics, with an emphasis on its theoretical as opposed to its applied aspects. However, I knew that in contrast to some of my classmates, I was not a mathematician in my soul. I had sufficient credits to graduate after three years, but did not want to do so, in part so that I could continue with my extracurricular activities and in part because I was simply having too much fun to want to leave. I decided to earn a second undergraduate degree, in economics. I then had the enormous good fortune to be able to write my undergraduate thesis under the tutelage of Bob Solow of the Economics Department. Bob was amazing. I would struggle for two weeks, get stuck, go talk with him for 30 minutes, and be set back on course for the next two weeks. The title of my thesis was "The Profit-Maximizing Utilization of Exhaustible Resources," and in short what it said was that left to their own devices with a profit motive as the only goal, businesses would deplete natural resources (such as oil, timber or minerals) as rapidly as possible, with no reason for or thoughts of conservation for the future. I enjoyed this project very much, and thought about becoming an economist. My minors, which were called something different, were computer science and psychology.

My computer background was enhanced by my undergraduate summers, when I worked for IBM. My first summer (1964) I spent wiring panels for accounting machines. A friend of my father's had arranged the job, and I was employed by the IBM Chicago Transportation Office. Weekly business meetings were held at 7:30 a.m. Monday mornings, and the office was over an hour's drive from my home in Skokie. Business attire was suit and white shirt, with socks and tie that matched each other in color. The second summer I wrote computer programs for an IBM 1440 computer. There was lots of spare time, and I wrote a program that would randomize a virtual deck of cards and deal bridge hands. (I had started playing in duplicate bridge tournaments with my friend Ira.) The summer of 1966 I taught computer programming in the language Autocoder to business executives at the IBM Chicago Education Office in downtown Chicago. I still wonder what these high-level executives felt when they entered their first class and saw a 19 year-old standing in the front of the room. One special aspect of these summers was driving between Skokie and Chicago each day with my father. (The day I forgot to fill the gas tank and ran out of gas on the expressway during rush hour was particularly

memorable.) My last summer in college, I stayed in Boston and worked at the IBM Boston Programming Center helping to develop CPS (Conversational Programming System), an early timesharing system that used the first computer language that looked more like English than algebra. CPS was never released, but I had a great time and many good lunches.

It was that last summer in Boston that I met Joe Schwarz, one of my closest friends. A year later, Joe and I became roommates, as I began graduate school and he continued his graduate studies of astrophysics. Despite the fact that Joe and his family lead complicated two-city lives - splitting their time between Munich, Germany, and Milan, Italy - we see each other often and have shared family vacations on Cape Cod a number of times.

During those summers in Chicago, my friends and I continued a tradition we had started in high school - Saturday night poker. A group of us would gather at Ira Zarov's house - Ira had been my closest friend since third grade - to play poker, whether Ira was there or not. (Often he was not.) My father's accounting approaches had taken root in me by then, and I kept a detailed log of my winnings each night, to the penny. (During this same period, I also kept a log of the precise time I went to bed and woke up each day, to the minute.) I say winnings, because there never was a night that I lost. I had studied the odds and poker strategy, and I was disciplined and cautious. In fact, after a year or two, I became obsessed with winning and distressed by the possibility of losing on a single night. I altered my play toward the end of evenings to ensure that I would be ahead when we finished. I realized that this state of mind was not healthy, and one day I decided that the next time I played I would lose, no matter what. I did so, and after that I sometimes won and sometimes lost when I played what I believe was both a better and a more enjoyable game of poker. Ira, as I recall, lost more often but may well have won more overall, and later became a successful professional poker player for a period of time. Marty Chalfie, long a friend and later a colleague in the *C. elegans* field, sometimes joined the game.

Typically during these games we would break for a while so that someone could pick up pizza. During one such break, those of us who had stayed behind started talking about how we were wasting time. Each Saturday we sat playing cards and trading our money back and forth. We should be able to come up with something more productive to do. We sat, and we thought. Then I had an idea. When our pizza-buying group returned, they were surprised to find the rest of us reading telephone directories. The idea was simple. The Chicago Daily News was running a contest called "The Wizard of Odds." Each day during the week the newspaper published a one-digit number. On Saturdays, the paper would publish three letters. Anyone with a telephone number that ended in four digits included in the five published numbers and with a last name that included all three of the published letters would share in that week's prize, which like a lottery grew during weeks when no prize was claimed. All we had to do was to read the phone books and find winners. So we did. We telephoned people and told them they had won a substantial cash prize and that we would tell them what it was if they agreed to give us one-third. People, not surprisingly, were exceedingly dubious. However, almost everyone agreed to meet with us and when they saw the newspaper description of the contest were convinced of

our legitimacy. Only one person refused to pay us. Another invited me to tour the Chicago Mercantile Exchange and offered me a job there with him. One of my college roommates came to visit for a weekend and made a fair amount of money by joining us.

I was very unsure about what I wanted to do after graduation. Having worked each summer for IBM, I probably was expected either to join the company or to continue my education in the area of computer science. Graduate school in mathematics or economics as well as law school or business school also seemed to fit my undergraduate experiences. But the time was the late 1960's, and I wanted to do something "relevant," particularly if it did not involve wearing a three-piece suit. I began to think about medicine. However, I knew nothing about biology. A roommate, Al Singer, now a physician-scientist at the National Cancer Institute, convinced me that modern biology was more than formaldehyde-fixed specimens, and during the first term of my senior year I took the introductory course in biology. I loved it. As a text, we used Jim Watson's "Molecular Biology of the Gene." My interest in medicine became secondary to a growing intrigue with biology. Six weeks into the course I went to the professor in charge, Cy Levinthal. "Professor Levinthal," I said, "I am a senior, all I know about biology is what I have learned during the past six weeks from you, and I'm thinking about going to graduate school in biology. Am I crazy?" "I went to graduate school in physics," Professor Levinthal replied, "And I'm teaching your course. You're starting early." Biology it was. The next semester I took a course in Genetics from Maury Fox, and was captivated by Sturtevant and Beadle's "An Introduction to Genetics." I also took a laboratory course, which introduced me to neurobiology and to the electrophysiological methods used in the classic studies by Haldan Hartline of the eye of the horseshoe crab *Limulus*. I applied to Harvard, MIT and Stanford, was accepted at all three, and decided to simply move the mile up Massachusetts Ave. to the Harvard Department of Biology.

The summer after my graduation from MIT was an adventure. With three friends, I set out in June with a car, a tent and four sleeping bags. Our first stop was Chicago, where we earned some spending money doing office jobs for my father's trucking company. Our only subsequent obligation was a wedding in Omaha, Nebraska, in early August. We traveled across the Midwest, into the west, up to western Canada, down the west coast and back across the country. We met many people, and had a wonderful time. Even the night we spent in the Butte, Montana, jail was interesting. (We had befriended a boxer from Monterey, California, or so we thought. He was staying next to our campsite. When we returned from town, he and our sleeping bags had all disappeared. We went to the police station to report the theft, and the police kindly offered us a place to stay for the night.) Three of us had been math majors, and as we drove we studied the recently published book "Beat the Dealer," by Edward Thorp. From this book we learned how to play a winning game of blackjack and also how to spot a stacked deck of cards. We discovered such a stacked deck in a well-known Las Vegas casino and proudly told the dealer. He called the pit boss, who was very friendly and asked us accompany him to another room. There he became less friendly, and informed us, "If I ever see any of you in here again, no one else will ever see you after that." We left. I was not winning much money anyway. The other book I remember reading while traveling during the summer of 1968 was Jim Watson's autobiography, "The Double Helix."

At the end of that summer, I returned to Chicago in time to experience the Democratic National Convention, where the peace platform calling for an end to the Vietnam War was defeated and the pro-peace protestors were considered enemies of the country and in particular of Mayor Richard J. Daley's Chicago. Meeting Alan Ginsberg, standing face to face with the National Guardsmen, trying to help slow down the crowds running from the tear gas, watching the Chicago police beating innocent people, escaping by hiding in the back seat of a car driven by a resident of a nearby black ghetto through a neighborhood that on other occasions I might have feared entering - there are many images and memories engraved in my mind. These days still make me ashamed of my city and my country.

Graduate school at the Harvard Bio Labs

In September, 1968, I entered graduate school in the Harvard Department of Biology, located at The Biological Laboratories, or Bio Labs, in Cambridge. I felt like a fish out of water. Everyone else seemed vastly more prepared, more knowledgeable about biochemistry and biology and more engaged. Because of my limited background, I was assigned mostly to undergraduate classes. In a cell biology course taught by Keith Porter and Dick McIntosh, the first exam had a question involving ribosomes. I had no idea what a ribosome was. In Konrad Bloch's biochemistry course, one of the few graduate courses I was taking, we focused every day on how electrons moved in the series of biochemical reactions of the Krebs cycle. I had never heard of the Krebs cycle. In a genetics seminar course, I was simply lost. The experimental approach to problem solving was completely unlike the way I had been trained to think as a student of mathematics. I was a teaching assistant in an introductory biology course taught by Lynn Riddiford and Carroll Williams. For the dissection laboratory, the students had to choose between rats and lobsters. I encouraged them all to study lobsters, although I had no idea what was inside either a rat or a lobster, because after class the TAs were allowed to cook and eat the dissected lobsters. I decided that if at the end of the first year my understanding of biology had not improved substantially, I would leave and do something else. However, my comprehension increased, and I stayed. My advisor was Matt Meselson, and I was supposed to begin working in his laboratory my first summer, in 1969. However, I had long planned and was very excited about spending that summer in Europe. The only foreign country I had ever visited was Canada - once during my trip the summer before and once during my freshman year at MIT when I had rather cold experience hitch-hiking to Montreal from Boston in January - and foreign travel appealed to me enormously. No one told me that in graduate school you were supposed to work in the laboratory over the summer. Matt was incredulous that I planned to be away during the period my professional training was supposed to begin. Still, I went, and had a wonderful time exploring new places, foods and peoples. The only downside was my continuing problem with asthma, which left me in bed for days at a time in Paris, Milan, Malaga and on the island of Skiathos in Greece, from which I had to be carried on a stretcher through the village to get to a boat back to the mainland and to a hospital in Volos, where I stayed for some time.

In the fall, I continued with my courses and began research in Matt's laboratory. I had no idea what I was doing, and had to ask a fellow graduate student, Patricia Foster, to show

me how to use a pipette. Pat and I had gotten to know each other as teaching assistants in the introductory biology course, for which she and I had been exiled together to the cold room to grind spinach for chloroplast preparations. Pat very much educated me about and encouraged me to persevere in biology. We became a couple in 1970, and lived together for the next 13 years.

Me, at the Harvard Biological Laboratories (1973).

Matt Meselson is a great scientist, but he was more focused on the crucially important issues of chemical and biological warfare than on his laboratory. Matt was spending much of his time in Washington, D.C. as an advisor to the U.S. government. I had to be in an alternative environment to acquire the training I needed. I considered changing schools. I was intrigued about the idea of living in Europe and thought about a number of European laboratories. However, my cousin Ed Brody (eight years older than me and an older brother of Harvey, of Chicago little league baseball fame) convinced me that staying at Harvard was a better idea. It was one of a number of times Ed had a major influence on my life. Ed is a physician-scientist who trained at the University of Chicago, did postdoctoral work in Geneva, Switzerland, and then ran a research laboratory in Paris, France for many years. It was Ed who obtained for me the fruit flies I used in my high school science fair project.

I talked with Wally Gilbert and Jim Watson about transferring from Matt's laboratory into theirs. Jim had recently become Director of the Cold Spring Harbor Laboratory on Long Island, New York, and he suggested I go to the annual Cold Spring Harbor Symposium to be held in June, 1970, to become exposed to the field of molecular biology in a professional way. The meeting was focused on transcription, and was very exciting, with cutting edge research being presented in a way that made me want to know what was coming next. At the end of the meeting, still unsure if I was going to be accepted to join Jim's laboratory, I asked him what I should do. Jim told me to return to Cambridge and talk with Klaus Weber, another Harvard professor who with Jim and Wally ran a joint laboratory, about a project. I gathered his answer was yes.

The Watson-Gilbert-Weber laboratory at Harvard offered an unparalleled training experience. The three of them were all exceptional scientists, and they were highly

synergistic in their approaches and talents. Jim has a superb biological intuition, and it was he who defined the problems most of the students embarked upon. Wally has profound critical abilities, and could see the flaws in any experimental design or interpretation. Klaus has magic fingers, and could devise ways - old or new - to make any experiment work. It could not have been more stimulating, or more challenging.

My thesis project derived from Jim's interests in transcriptional regulation. He had written in his 1970 edition of "Molecular Biology of the Gene" about how development was likely to involve differential gene expression. With this in mind, Jim had focused a part of his laboratory on RNA polymerase, the enzyme responsible for synthesizing RNA from DNA. Jim's laboratory had shown that the enzyme consisted of two major components, a multi-protein complex that did the work of transcribing RNA and a more loosely associated protein that conferred specificity, i.e. that caused the enzyme to begin at specific sites along the DNA. This specificity factor they named sigma, and Jim's model for development was that a sequence of sigma factors defined a temporal series of distinct transcriptional products. The experimental basis for this model was some recent observations made in the laboratory concerning *E. coli* phage T4. These studies suggested that the bacterial RNA polymerase with a bacterial sigma factor transcribes a first set of T4-specifc RNAs, called "pre-early"; one of the pre-early genes encodes a viral-specific sigma factor, which then reads the "early" genes; and finally, a second T4 sigma factor encoded by one of the early genes reads the "late" genes. In this way, a series of three sigma factors defines three distinct developmental phases of T4 gene expression. However, no such factors had actually been isolated, and the evidence for this model was rather circumstantial. My project was to identify T4- specific sigma factors.

To begin, I purified *E. coli* RNA polymerase from bacterial cells infected with T4 and examined the subunit composition of the enzyme. I worked with the expert, constant and generous guidance of Klaus Weber and graduate student Chris Goff. (Chris was studying another change in the T4-modified *E. coli* RNA polymerase.) Indeed, the host RNA polymerase had a number of new subunits, as had been recently reported by Audrey Stevens at the Oak Ridge National Laboratory. In a cleverly designed experiment (the clever design was that of a postdoctoral scientist working next door, Jeff Roberts), I was able to show that one of these subunits was the direct product of T4 gene 33. Other studies had indicated that gene 33 regulated the transition from the early to the late stage of T4 development, so this result was quite exciting and led to my first publication, in *Nature New Biology*. I was very proud of this achievement. However, my enthusiasm was dampened a bit by a conversation with Larry Gold, a T4 researcher at the University of Colorado in Boulder. Larry knew how hard I had worked to prove that this small RNA polymerasebinding protein was the product of gene 33 and also knew the data that had suggested this was likely to be the case. Was it worth, he asked, working so hard to prove something that was clearly very likely to be true? Could I not have been better spending my time to find something that was unexpected, rather than something that was expected? Larry's questions were provocative - I'm still not sure I know the best answer - and I have thought about them often in designing further research projects.

Most of my days as a graduate student were spent in a cold room at 4°C, purifying RNA polymerase. After some time, I devised a rapid method for isolating small quantities of enzyme based upon precipitating RNA polymerase with antibody that had kindly been raised by Chris Goff. (Although I had tried, I proved to be too allergic to inoculate and bleed the rabbits myself.) Then I could work in my laboratory room at a normal temperature. To visualize changes in the enzyme, I used radioactivity, and routinely did bench-top experiments in the open laboratory involving 25 millicuries of radioactive phosphate or sulfate. I also worked with comparably high levels of radioactive iodine. Such experiments today would have to be done under special conditions, but during the early 1970s, scientists were much less cautious. After some years, I officially became Wally's student, as Jim left Harvard to spend full-time at the Cold Spring Harbor Laboratory.

I published four papers as a graduate student, all involving T4-induced modifications of the *E. coli* RNA polymerase. I was the sole author on all four publications. Both Jim and Wally put their names only on papers to which they felt they had made major and direct contributions. These papers were assembled into my Ph.D. thesis, which included an introductory chapter focused not on the biochemistry of RNA polymerase but rather on the biology of phage T4. I liked thinking about T4 as an organism, just as more recently I have enjoyed thinking about all aspects of the biology of the nematode *C. elegans*.

Life at Harvard was intense, which suited me well. Work started early in the morning and ended late at night. Students in the group were highly independent, relying more on other students and postdoctoral researchers than on faculty for input. "Sink-or-swim" seemed to be the prevailing attitude. If you managed to swim, you really learned to do science. However, there were a number of students who sank who I believed had outstanding potential. We had three group meetings a week, over lunch on Mondays, Wednesdays and Fridays. For each session, one student or postdoc presented his/her most recent findings. These were serious times, as an audience of Jim Watson, Wally Gilbert, Klaus Weber and often Mark Ptashne and David Dressler (two other Harvard faculty members) left little uncritiqued. Giving my first public talk, at a phage meeting at Cold Spring Harbor, was a very gentle experience by comparison. If you could survive a Harvard group meeting, you could survive anywhere. In preparing for these group meetings, I acquired a habit that I have continued to this day - writing a complete text of my presentation. I find this practice helps me organize my thoughts and time my talk, gives me an aide for those moments when I go blank on-stage and allows me to prepare a related talk at a later date very easily.

Some years into my graduate studies, our Harvard group meetings acquired a name. One of the underground Boston newspapers, either the Phoenix or the Real Paper, did a story about Wally Gilbert and entitled it "Stalking the Secret of Life." Thereafter, our group meetings were always labeled "Stalking the Secret of Life: Part 247," "Stalking the Secret of Life: Part 248," etc. I learned an enormous amount as a Ph.D. student, both about how to do and how not to do experimental biology. I came away with two beliefs that have driven my research ever since. First, do the do-able; working on an important but intractable problem would not suit me. Second, engraved in me from Jim Watson: since it

is no harder to work on a problem that is important than on one that is not important, always choose the former.

Studying the bacterial virus T4 introduced me to a community of interactive and cooperative scientists. During one visit to Chicago to see my family, I went to the University of Chicago to talk with a fellow T4 researcher, who kindly gave me a set of mutant strains I needed. My mother supplied a small mayonnaise tub for me to use to transport the glass vials. I carried the tub in my hand as I boarded the plane at O'Hare Field for my return to Boston. The woman sitting to my right was curious, and asked what I was carrying. "Oh, nothing important," I said, "Just some viruses." This was an error. "VIRUSES!!" she yelled. After considerable subsequent conversation, the viruses flew to Boston in the cockpit, and the woman to my right said not another word to me the entire flight. On another occasion, I visited biochemist Ray Gesteland at the Cold Spring Harbor Laboratory to ask for his advice about an experiment I had planned. As I spoke with Ray, he was emptying rack after rack of test tubes from a large refrigerator and pouring the contents down the sink. "Ray," I finally said. "What are you doing?" "Oh," he replied, almost gleefully. "These are my last six months of experiments. They didn't work, so I'm going to start something new." To me, six months literally down the drain seemed like a disaster. To Ray, they offered an opportunity to explore some exciting new idea. Ray was a scientist, and I still had a lot to learn.

As a graduate student, I lived in north Cambridge, sharing the top two floors of a house with my friend Joe Schwarz and a cast of others. After a year, Pat Foster also moved in. Our roommates were interesting and varied and included graduate students in biology and astrophysics, people who worked at a great diversity of occupations and people who did not work at all. At one point, both the front and back porches were rented, someone was sleeping on the living room couch and a total of 14 people (including my sister Carol) called our five-bedroom house their home. For a while, we also had a German Shepherd and, briefly, her 11 pups. We took turns cooking. Because I had the only car, I did the shopping. We joined a food co-operative and when handed a form that asked for "Name," I wrote "Bob." After that, our house became known as a commune called "Bob."

I began to think about what I wanted to do after completing my Ph.D. I had a strong desire to spend some time in Europe, and visited a number of laboratories there. Jim Watson thought I should go to Stanford - there was a regular exchange of graduate students and postdocs between Harvard and Stanford at that time. Klaus Weber had an alternative thought and suggested that I talk with Sam Ward, who had just moved to the Harvard Medical School from Sydney Brenner's group in Cambridge, England. Sydney and Sam had been using the nematode *Caenorhabditis elegans*, an organism that had been little studied previously, to pursue problems in neurobiology. I had long been intrigued by the nervous system, in particular by complex issues, like the mechanistic basis of learning, memory and consciousness. As an undergraduate I had taken a course given by Jerry Lettvin entitled "The Biological Basis of Perception and Knowledge," which had whetted my appetite but supplied few answers. As a graduate student, for a course about protein synthesis taught by John Hershey, I had written a term paper entitled "A Research Proposal on Protein Synthesis and Learning." Sam told me about Sydney's

efforts to reconstruct the worm's nervous system from serial section electron micrographs, promising to reveal the complete wiring diagram of a nervous system for the first time. *C. elegans* was eminently suited for genetic analysis, and I had become enamored with the power of genetics from my studies of T4. After a number of conversations with Sam, I wrote Sydney, and asked if I could join his laboratory. My expressed interests were developing methods for studying *C. elegans* at the molecular level and using genetics to analyze memory and learning. His response was "As far as I know, all attempts to show learning in nematodes have failed," but that I was free to choose my research project when I arrived. After some further correspondence, he wrote, "Go ahead and apply for fellowships." This meant "yes."

There were a number of other factors that influenced my decision to join Sydney's laboratory. First, Chris Goff, with whom I had worked closely, had gone there and raved about the place. Second, I wrote Ed Brody, in Paris, and asked him for his views of "Brenner and his nematodes," noting that the phrase "sounds like a new rock band." Ed was encouraging. Third, Pat was delighted at the prospect of living in England. Cambridge indeed was a great place to live, and the Laboratory of Molecular Biology a fantastic place to do science.

When I told Jim Watson that I planned to go to Cambridge, England, to study the neurobiology of *C. elegans* he asked me if I knew anything about neurobiology. I had to admit that I did not. Jim then suggested an immersion education - three consecutive Cold Spring Harbor summer courses in neurobiology. I enrolled in and took three such courses during the summer of 1974: An Introduction to Neurobiology, taught by John Nicholls; Experimental Methods in Electrophysiology, taught by Enrico Stefani and Dante Chiarandini; and The Neurobiology of *Drosophila*, taught by Bill Pak. Each course was intense and stimulating. I learned an enormous amount, and made many friends. Cold Spring Harbor courses have a reputation for being both exhilarating and exhausting, and I have been told that I am the only person who has ever taken three in a single summer.

England and worms

Sydney Brenner was my fourth official research supervisor, after Bob Solow, Jim Watson and Wally Gilbert. Amazingly, they, and I, now all have Nobel Prizes.

Pat and I arrived in England just before Guy Fawkes Day (November 5) in 1974. Chris and Eleanor Goff, friends from our Harvard days, kindly provided our initial lodging. My first assignment for laboratory space was a two-foot wide area of benchtop in a room in which biochemists on each side of me were labeling tRNAs using vast quantities of 32P-labelled phosphate. As I began my studies of *C. elegans*, I wondered whether the worms, or I, might acquire mutations as a consequence of the nearby radioactivity. Soon I moved down the hall, into a room that I shared for the rest of my stay with a number of scientists, including John Sulston, a young staff member in Sydney's group.

I had received a fellowship from the Muscular Dystrophy Association of America. The fellowship was for a much greater amount of money than Pat and I needed to live in England, and I deposited half of the funds I received into a Swiss bank account, believing

this would guard us against an unstable British economy and also against currency fluctuations between Europe and the U.S. This account remains untouched. My fellowship application had focused on an analysis of the chemosensory nervous system of *C. elegans*. However, studies of nematode chemosensation had been begun by Sam Ward, and I decided I should do something different. My interests and my MDA support both drove me to want to study aspects of worm biology that might relate to human neuromuscular disorders. In particular, just before I left the U.S. I had a moving conversation with a close friend of my parents who was dying of ALS. I did not know anything about the disorder, but could see that it was terrible. Her last words to me were, "I know it is too late for me, but please try to do something for others who suffer from this horrible disease." Beyond studying the worm's musculature and/or nervous system, I had no idea how to try to do so, and in any event it was the basic biology that intrigued me.

Sydney suggested I study muscle cell growth, in particular that I try to determine how individual muscle cells add new myofilaments as they increase in size. The problem sounded interesting, and remains unsolved. However, I had begun conversations with John Sulston and found a topic that excited me more. John had recently found that he could directly observe cell divisions in living *C. elegans* larvae and in this way determine aspects of the worm's cell lineage, the pattern of cell divisions and cell fates that occurs as a multicellular organism develops from a single-celled egg. So far, he had examined only the development of part of the nervous system. John and I decided that together we would explore more of the worm's cell lineage, with the goal of determining the complete pattern of cell divisions that generates the adult animal. I began by examining the musculature, in part because of my MDA fellowship. John had already noted that the number of muscle cells in the main body musculature increases as the animal develops from a newly hatched larva. My first goal was to determine the precise number of body muscle cells in the young animal and the cell lineage responsible for adding additional muscle cells during larval development.

Counting muscle cells proved more challenging than I had anticipated, in part because using Nomarski optics one visualizes nuclei, and the difference between the nucleus of a muscle cell and that of certain non-muscle cells was not always obvious. More importantly, the worm was not designed the way I thought it should have been. The animal is shaped like a tube, with four quadrants of muscle: dorsal-right, dorsal-left, ventral-right and ventral-left. It never occurred to me that these four quadrants might contain differing numbers of muscle cells. So I counted, recounted, re-recounted and finally asked John to count, too. The upshot was that the superficially radially symmetric young animal contains 21 muscle cells in each dorsal quadrant, 20 in the ventral- right quadrant and 19 in the ventral-left quadrant. By tracing the postembryonic cell lineages involved in muscle development, I discovered that to this number is added an additional 14 muscle cells, three in each dorsal quadrant and four in each ventral quadrant. I learned that preconceived notions in biology can be very misleading. Only observation and experimentation can reveal biological truths.

Life as a postdoctoral researcher at the Laboratory of Molecular Biology was exceedingly stimulating, great fun and involved far more conversation than did life at the Harvard Bio Labs. Morning coffee and afternoon tea on the second floor, where the Division of Cell Biology was housed, were key, whether or not one drank coffee or tea. These breaks were opportunities to talk, to think, to listen and to learn. Sitting in the tea room with Sydney Brenner after lunch never failed to be both amusing and interesting. Sydney has an incredible wit, an amazing breadth of knowledge and always enjoys a good conversation. Latenight science - and sleep - were often endangered by Sydney. A number of times when I was working at 2 or 3 a.m. and desperate for a cup of tea, I would go to the tea room only to find myself soon joined by Sydney, attracted by the rattle of the spoon in the tea cup. In Sydney's (but not my) view, 2 a.m. was an excellent time to talk! I learned to stir silently.

Lunch was an especially good time for scientific interaction. Everyone in the building went upstairs to the top floor to a cafeteria run by Gisela Perutz, the wife of the famed structural biologist Max Perutz. Here one would pick up lunch - bangers, spuds, faggots, toads-in-the-hole or whatever (I quickly saw that despite the U.S. and England ostensibly sharing a common language, much of the English spoken in England was completely foreign to me) - and sit at whatever table had an open seat and talk about whatever science came to mind. I had the opportunity to meet many outstanding scientists. One of these lunches, with fellow worm researchers Jonathan Hodgkin and John White, led to an experiment by Jonathan that revealed a fundamentally new aspect of *C. elegans* sex determination. Monday nights were special. Dinner at the University of Cambridge's Clare Hall, hosted by Tim Hunt and often led in conversation by Francis Crick, was followed by a research seminar, in which Peter Lawrence and/or Michael Ashburner, two *Drosophila* developmental geneticists, would invariably ask the speaker why he or she had bothered to do whatever it was that he or she had done. Friday evenings involved a short walk to the Frank Lee Center, for a pint (or more) of England's best brew.

The worm group was very much the center of my scientific and much of my personal life. I worked most closely with John Sulston, who became a mentor, a friend and in some ways a hero. I had the impression that John could do anything. He was warm, personable, unassuming and completely dedicated. Often after his bicycle ride to the laboratory (John bicycled to reduce the pollution that results from driving cars), insects and other debris would fall from his long beard onto his samples. John argued passionately that research biologists should receive salaries much lower than those of trash collectors, because the former have so much more fun. I made many other friends, including Jonathan Hodgkin and John White. Toward the end of my stay, I had the opportunity to renew my high-school friendship with Marty Chalfie for the months that we overlapped. I developed scientific collaborations with Jonathan, John and Marty. The collaboration with Jonathan was particularly instructive to me. He had discovered a class of *C. elegans* mutants abnormal in the segregation of the sex chromosome during meiosis, and I had isolated a number of additional mutants of this sort. We decided to characterize our mutants together. We sat down, agreed upon a set of experiments, and assigned one of us to do each experiment. However, neither of us had ever collaborated in such a way before, and we each felt that we would trust our own data more than data from someone else. When

we met again to examine our collected data, Jonathan had done all of his experiments as well as all of mine, and I had done all of mine as well as all of his. Luckily, our results agreed. The upshot was a paper in which we had counted precisely 183,001 worms for the published data alone. This experience made it easier for me later to trust the data of my students without having to repeat everything they did. (Even so, in the early days of my laboratory, there were some experiments I did repeat, privately, just to be sure.)

Pat and I lived first in Cambridge, not far from the train station, and later in the village of Great Shelford. Going to and from the lab meant driving past open farmland, which was highly refreshing after having lived my previous 27 years in Chicago and Boston. I found the whole area, with its charming villages, thatched cottages, beautiful flower gardens and comparatively slow pace, extremely appealing. The nearby village of Grantchester, with The Green Man pub and a lovely tea garden, was a particular favorite. One could punt to Grantchester from the center of Cambridge and stop for a pub lunch or just a pint of beer. For food, Indian cuisine seemed vastly better than in the U.S., and the Curry Queen in Cambridge was a common target. Pat, who had left Harvard to work in what was a very early version of a biotechnology company (she was the Biology Department), resumed her studies as a Ph.D. student at the University of Cambridge, which gave us both the opportunity to partake of life at Wolfson College. Pat and I used Cambridge as a base for travel, and visited most of Britain and much of Europe during my three years in Sydney's laboratory. I considered staying in England, but decided that a return to the U.S. would allow me greater flexibility in developing an independent research program. My job at MIT came about through a misunderstanding. Sydney had visited Brandeis University, and he suggested that I apply for a faculty position there. I did not want to leave England yet, but I could not pass up such an opportunity. I sent my curriculum vitae and a statement of research interests, but no publications, as I had not yet published any of my postdoctoral studies. I decided that if there was a possibility that I might be offered a job, I should also apply to other places and see what the options might be. I came to the U.S. for a six-week visit and gave seminars at 11 institutions. My first visit was to Cornell University in Ithaca, N.Y. I was lucky to be offered a job while I was still there, just before I flew to Boston to visit Brandeis and MIT. This offer made my subsequent visits very relaxed. To my surprise, when I arrived at Brandeis I was told that although they wanted to meet me, no faculty position was currently available. Thus, I need not have started sending out job applications at all. Not long after my return to England I was contacted by Boris Magasanik, Chair of the MIT Department of Biology, and offered a faculty position. I accepted.

My laboratory at MIT

I moved back to Boston in January, 1978, between the two huge snowstorms that blanketed the northeastern U.S. that month. My friends Fred Ausubel and Stephanie Bird kindly offered me a spare room in their home on Irving St. in Cambridge, near the Harvard Bio Labs. They also let me use their cross country skies to get to and from MIT, skiing over barely detectable mounds of snow that had cars beneath them. Pat joined me in April, and we rented an apartment in north Cambridge.

Setting up the new laboratory was a busy time. I had arrived with more than 500 strains of *C. elegans*, the transport of which had proved slightly problematic: to import nematodes, I needed permission from the U.S. Department of Agriculture. However, the Department of Agriculture gave import approval only for parasitic nematodes, and *C. elegans* was not a parasite. Therefore, they could not grant my request. It took a number of letters back and forth before they finally agreed that they could not be sure that *C. elegans* was not a parasite and thus could approve my importing a potential parasite. I also had arranged to avoid having to subject the living animals to X-rays at Heathrow Airport in London. The airline noted that this permission had been granted in my reservation information in their computer system. When I checked in, the woman behind the counter became wide-eyed as she looked at the computer screen, and said, "The computer says you have worms. Can I see them?" I explained that they were too small to be seen and that they were packaged in sealed boxes in any event. She let the opportunity pass.

Every day in my new laboratory I transferred worms, establishing and then freezing each of my many mutant strains. In April I was joined by Nancy Tsung, whom I hired as a technician. Nancy could not get over the fact that a professor could be so young, and for some years referred to me as her young boss. Nancy stayed in the laboratory for over 21 years, and she provided crucial technical and emotional support for projects and people, respectively. Soon thereafter, my first two graduate students joined the laboratory, Iva Greenwald and Chip Ferguson. Each proved to have a deep interest in biology and a natural flare for genetics, and the new lab was off to a very strong start in the areas of the genetic analysis of *C. elegans* development and behavior. Chip focused on the genetics of intercellular signaling, while Iva studied a muscle mutant with what then appeared to be unusual genetic and behavioral properties. Iva discovered that although this mutant had a severe muscular disorder, the inactivation of the gene responsible had no discernable effect whatsoever. This finding led to my first publication as a mentor, a paper with Iva in the journal Genetics in 1980.

Next, graduate students Paul Sternberg, Bill Fixsen and Carol Trent and postdoc Victor Ambros entered the lab. Paul started by studying the cell lineage of another nematodes species, *Panagrellus redivivus*, with an eye toward an analysis of the genetic basis of evolutionary change at the level of cell lineage. Bill studied the genetic control of cell migration. Carol analyzed the genetic basis of the behavior of egg laying. Victor pioneered studies of genes that control developmental timing.

The diversity of problems - intercellular signaling, muscle, the genetics of evolution, egg laying and developmental timing - seems unusual and perhaps dangerous for a beginning faculty member. "No focus," would be the criticism made by some today. However, these projects were highly coherent, in history, in philosophy and in experimentation. Each had derived directly from the studies of cell lineage and cell lineage genetics I had begun in collaboration with John Sulston in England. Most of my time examining the *C. elegans* cell lineage was spent observing the development of the musculature, including the muscles used for egg laying, and of the vulva, also used for egg laying. In large part for this reason, in seeking cell lineage mutants, I primarily sought those abnormal in egg

laying. Amongst those mutants were all of those to be analyzed in our initial explorations into intercellular signaling, muscle, developmental timing and the behavior of egg laying. The comparative evolutionary project had a similar rationale - unlike *C. elegans*, *Panagrellus* does not lay eggs but rather releases hatched larvae; furthermore, the vulva of *Pangrellus* is displaced posteriorly compared to that of *C. elegans*. The cell lineages of the egg-laying systems of the two species seemed very likely to be different.

In addition, intellectually and experimentally, there was a single driving theme behind almost every project: use analytic genetics to define the genes and genetic pathways responsible for each biological phenomenon. How you design a mutant hunt, isolate additional mutations in a known gene, define a null phenotype, and order genes into a pathway is the same, whatever the problem being addressed. Each member of the laboratory could help each other member in thinking about such issues. There were two other factors that drove me to initiate so many distinct projects. First, given my experiences at Harvard and the LMB, I believed that one of the most important aspects of training a young scientist is to give that person the freedom to pursue his or her discoveries. Discovery leads to excitement, commitment, and fun. Elbow room is crucial. Training has always been one of my major goals, with the belief that training outstanding scientists will of necessity generate outstanding science. (The converse statement - that generating outstanding science will necessarily train outstanding scientists - in my view, is not necessarily the case.) In addition, the training environment is enhanced by exposure to a breadth of biological problems. A second factor that drove me to initiate so many distinct projects was, as I noted above, the fact that I am fascinated by the biology of the organism. The diversity of problems helped satisfy my personal curiosity.

My philosophy for the lab, then as now, was that we should be a community of scientists, with each graduate student and postdoctoral researcher focused on a biological problem of interest. Lab members should be independent, but highly interactive. Postdocs should be free to continue their projects independently after leaving the laboratory.

The next two young scientists to join my laboratory were graduate students Eun-chung (Joan) Park and Hilary Ellis. Again, I advised each to begin projects descended from but also distinct from projects already underway. Joan took a genetic approach that derived from the studies of Iva Greenwald to estimate the number of genes in *C. elegans*. Joan found that animals have a large number of genes that when inactivated have no obvious consequence to the organism. This finding was not broadly known and when rediscovered some years later in the field of mammalian genetics, as a consequence of the study of the first mouse "knock-out" mutants, was generally regarded as a great surprise. Hilary Ellis embarked on the study of the genetics of programmed cell death.

Postdoctoral researcher Gary Ruvkun entered the laboratory slightly later. Gary and I shared a driving desire to find a way to clone the many genes our laboratory was defining by methods of classical genetics. We devised more than a dozen distinct possible approaches, involving a variety of molecular techniques. Gary was a Junior Fellow at Harvard University and his Harvard sponsor was Wally Gilbert. Gary was able to do many more molecular experiments using Wally's funds than could have been supported

by my rather limited budget. Gary, Wally and I published one paper together, my only publication with my official Ph.D. advisor. Gary introduced current methods of molecular biology to the laboratory. He succeeded in cloning one of the genes that Victor Ambros had shown to be key in the control of developmental timing.

The MIT lab grew in number, but not in physical size. Our only laboratory room, with seven lab benches, soon housed 11 scientists, three of whom worked at small desks where previously there had been a single -70°C freezer and one of whom sat at the end of a high bench with a cabinet door open so he would have some place to put his legs. I asked the Department Chair, Gene Brown, for more space, and he instantly provided it, moving his own laboratory, which was across the hall from mine, to do so. David Botstein, whose laboratory was located one floor upstairs, proved to be my major mentor on issues of science and non-science both. Lunches were a special treat, as varying groups of faculty would assemble in the faculty lounge at precisely noon (when Gene Brown began his lunch) and sit and talk. Collected wisdom concerning science and life was shared by all, and I had the good fortune to be able to learn from many of my senior colleagues, including Salvador Luria. Salva was a humanist, an independent thinker and a scholar, and I was struck by the fact that he offered the first-year graduate students the opportunity to get together with him once a week to discuss literature, primary fiction, because he believed that a single-minded focus on science was intellectually stifling.

Other professional activities

My scientific pursuits have led to many opportunities and responsibilities beyond those of simply doing research. For example, as a beginning graduate student it never occurred to me that the life of a scientist could involve so much travel, something that I have always loved. In the course of presenting lectures, attending meetings, serving on advisory committees and teaching courses, I have visited Alaska, most European countries, Russia, Israel, Egypt, India, Japan, Korea, China and Tibet. (Out of interest, and without scientific excuse, I have also traveled to Peru and Senegal.) I have been an advisor to many national and international organizations, including the U.S. National Cancer Institute; the National Human Genome Research Institute (the U.S. sponsor of the Human Genome Project); the Sanger Centre (the British arm of the Human Genome Project); and the Tropical Disease Program of the World Health Organization, which amongst other interests is concerned with diseases caused by parasitic nematodes, relatives of *C. elegans*.

I have also been very involved with scientific societies. I served as the President of the Genetics Society of America in 1995 and have been a member of the Public Policy Committee of the American Society for Cell Biology and of the Joint Steering Committee for Public Policy, an organization that advocates for biomedical research funding from the U.S. government. I feel strongly that the support of biomedical research is an important investment for society as a whole and that both the Congress and the public have the right to know what is being done with their funds. We, as scientists, have a responsibility both to advocate and to educate. Toward this end, in 1997 I presented a briefing of the Congressional Biomedical Research Caucus. I was hosted by Massachusetts Representative Joe Kennedy, and my lecture was entitled "All Creatures

Great and Small: The Universality of Genes." My theme, based in part upon findings of my research group, was that studies of simple non-human organisms - such as a yeast used for baking bread or making beer, a tiny fruit fly or a microscopic worm - can provide crucial breakthroughs important for the understanding, prevention and cure of human disease.

My laboratory and our studies of *C. elegans* have progressed in new directions and new dimensions. Our current interests include cell lineage and cell fate; programmed cell death; signal transduction; morphogenesis, micro RNAs; nervous system development; behavior; and the modulation of behavior by the environment and by experience. This last topic is essentially the one that drew me to *C. elegans* and was the interest that I wrote about when I first contacted Sydney Brenner - the genetic analysis of memory and learning. In addition, I have become increasingly interested in aspects of human disease. Much of the reason is that I have been repeatedly intrigued by the striking molecular genetic conservation between processes we have analyzed in *C. elegans* and those involved in human biology and human disease. The basic science has driven me toward human disease. My active involvement started in 1979, when Ed Kravitz, from the Department of Neurobiology at Harvard Medical School, invited me to a meeting about cell death. The meeting was sponsored by the Hereditary Disease Foundation, which is focused on Huntington's Disease, and was until very recently run by Nancy Wexler and Allan Tobin, both of whom became good friends. This meeting opened my eyes to the possibility that our studies of programmed cell death in *C. elegans* might prove relevant to a variety of human neurological disorders and also indicated that discussions of some of the basic principles of analytic genetics used to study simple organisms like *C. elegans* might be helpful to those working on human genetic diseases. My involvement with the Hereditary Disease Foundation continues to this day.

In 1986, when my father was diagnosed as having amyotrophic lateral sclerosis, or ALS, he came to Boston and was seen by MGH neurologist Bob Brown. Bob proved to be a highly supportive and sympathetic physician. Bob and I talked and soon agreed to establish a collaboration to try to better understand ALS though genetics. This collaboration has involved my having a small group of people working in Bob Brown's laboratory at MGH. This effort, in conjunction with the work of many others from around the world, led to the discovery in 1993 that one gene responsible for familial ALS encodes the enzyme copper-zinc superoxide dismutase.

During this period I began thinking that I might want to deepen my knowledge of medicine by attending medical school, but another friend, Mark Fishman, who later became Chief of Cardiology at MGH and is now the Global Head of Research for the pharmaceutical company Novartis, persuaded me not to do so. He told me that what I would learn in medical school I could more efficiently learn by reading text books, and that to understand medicine I should simply follow him while he did rounds in the clinic. So for brief periods during two summers, I did so.

I have also been introduced to aspects of clinical medicine through my involvement with biotechnology companies. Although for some time I was adamant about being "pure," a

conversation with friend and co-*C. elegans* researcher Jonathan Hodgkin changed my mind. When I told him I was about to turn down an invitation to become a company consultant, he said to me, "Don't you ever want to do anything useful?" I thought about his comment, and accepted the consultancy. I now feel that my three hats, under which I supervise basic research concerning *C. elegans* at MIT, help with medical research concerning ALS at MGH and advise companies how to apply basic knowledge of biology and medicine to drug development, together both foster my continuing education and synergistically enhance my efforts in all three arenas.

My personal life and family

My scientific life would be empty were it not complemented by my personal life. Since becoming a research scientist, I have enjoyed the companionship and support of a small number of women with whom I have had close, intense long-term relationships. All have been dedicated scientists, strongly independent and understanding of the demands of my professional obligations while working similar hours themselves to fulfill their own professional goals. They have provided me with enormous support and helped me to grow emotionally and intellectually.

Since 1991, I have shared my life with Martha Constantine Paton, now my wife. Martha studies the development of the nervous system. I first met Martha soon after we had both begun jobs as assistant professors - she was my host when I visited Princeton University to present a seminar in 1979. However, it was only years later, in 1991, that we became romantically involved. We have interests that are shared and interests that are complementary - all in all, a good match. In 1991, Martha was a professor at Yale University, and she had two sons, Joe and Chris, ages 13 and 17, respectively. Martha and I married, and I suddenly acquired a family, complete with a station wagon, two dogs, two teenage stepsons, and before long, a house in the suburbs. Joe and Chris are wonderful, and being close to them as they have grown into independent, intelligent and interesting adults has been a special pleasure for me. At present, Joe is immersed in neurobiology and is currently a graduate student at Columbia University, while Chris has had no interest in science whatsoever and spent some years working in the music industry before recently entering law school at St. John's University in New York City.

Our marriage is a partnership with love. While I do most of the cooking and laundry, Martha is responsible for preventing the house and garden from degenerating into chaos and for maintaining our extensive indoor foliage, including our growing collection of orchids. Shopping we do together, which may not be efficient but preserves time with each other. We very much wanted to have a child together. Given our ages, we were very lucky. On September 2, 1993, when Martha and I both were 46 years old, our daughter was born. We had discussed extensively what to call her. We agreed that the last name of Horvitz was appropriate. Martha wanted her father's name, Constantine, to be continued, so we had a Constantine Horvitz. But what should her first name be? We needed something substantial - a one syllable name would not suffice if followed by Constantine Horvitz. I desired a name in memory of my father Oscar, whose Hebrew name was Asher. So we focused on the A's and O's and decided upon Alexandra: Alexandra Constantine Horvitz.

Alex's birth had a direct but little known consequence on the MIT Department of Biology. The Department was planning a new building, and I was chair of the building committee. The day we were selecting color schemes for the reading rooms, I was called out of the meeting for a phone call from Martha, who had just learned that she was pregnant with a healthy baby girl. I was elated! The reading rooms ended up with rather exuberant purple couches. Later, I telephoned my mother to tell her the news. "Mother," I said, "How would you like to be a grandmother?" After an exceedingly long pause, in which my mother was no doubt thinking about Martha and me, both 46, she replied, "How would that happen?" I could think of no answer other than the obvious, "In the usual way."

Alex has given me an unprecedented excitement and joy. Nothing delights me more than to spend time with her and to see her happy. She is a wonderful, loving, intelligent, engaging and strong-willed nine year-old girl. Alex enjoys math, puzzles, games and piano, like me (we play piano about equally well), and, like Martha, arts and crafts, swimming and animals. Alex also has talents that are not obviously derived from either of us, such as in music. Alex's and Martha's combined love for animals seems boundless, and were it not for my allergies our home would no doubt resemble a zoo. As it is, we have two dogs, a bearded dragon and two aquaria with tropical fish. Our family lived a hectic two-city life for six years, commuting between Boston and New Haven. I listened to and became a fan of books-on-tape. Our marriage and Alex's birth have completely changed my life, which is now much more chaotic, much more interesting and much more fulfilling. In September, 1999, Martha moved from Yale to MIT, and we now all live in the lovely Victorian house in Auburndale, Massachusetts, we had purchased in 1994 and then renovated in 1999 in preparation for new lives together.

Thoughts and dreams It is easy to look back over the years that have brought me to writing this autobiography. I have been very lucky, both professionally and personally. I have had a fantastic family, wonderful friends and the opportunity to explore and experience much of the world. I have had the pleasure of running a successful research laboratory and the greater pleasure of having helped train a large number of young scientists, many of whom will contribute to the discoveries of the future. I hope that I have helped them develop not only the technical and intellectual abilities to do research and the confidence to persevere but also an approach to research that will make their efforts fun. Messages that emerge from my life's experiences so far are less obvious. One, which I believe strongly, is that one should not be afraid to try something new: becoming an undergraduate at MIT instead of staying in the Midwest; studying biology as a graduate student after having earned degrees in mathematics and economics; and embarking upon the study of *C. elegans* at a point when nothing was published about the organism and many of the techniques of modern biology could not be applied to its analysis - all of these decisions proved to be good. What comes next for me I cannot know. I have three dreams. The first and most important is to be as good a father as I possibly can for Alexandra. The second is that some of the discoveries for which I can claim some credit, or perhaps my discoveries yet to come, will lead to applications in medicine that will alleviate human suffering. My third dream is that I will be able to use

my new label of Nobel Laureate to contribute to the world in ways that will benefit society and mankind.

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