Walter Gilbert

RESEARCH INTERESTS //
Walter Gilbert is famous for his work on DNA sequencing technologies. Gilbert received the Nobel Prize in chemistry for his “contributions concerning the determination of base sequences in nucleic acids.” He has also made profound contributions to modern biochemistry and biophysics through his research on the lactose repressor—the first example of how enzymes are controlled genetically—and his work on the mechanisms of protein synthesis. Gilbert is also known for his work on the RNA world hypothesis in which the origin of life starts with self-replicating RNA molecules, first published in Nature in 1986.

A FOND MEMORY FROM MY EXPERIENCE AS A FELLOW //
I enjoyed being an NSF predoctoral fellow from 1954 to 1957 and a postdoctoral fellow for one year at Harvard in 1958. I went on to be Professor Schwinger’s assistant the next year, and then went on the Physics faculty at Harvard in ’59. In the Summer of 1960 I became interested in Molecular Biology and worked with Jim Watson and Francois Gros on the discovery of messenger RNA. I continued working in Biology and teaching Physics (and graduate students in Physics) until I came up for tenure (at 5 years) and was promoted as a Biologist into a position in Biophysics. My career highlights as a Biologist include messenger RNA, poly-ribosomes, the detailed mechanism of protein synthesis, the isolation of the first control protein, the Lactose Repressor, and the discovery of a rapid method for sequencing
DNA (the Maxam-Gilbert chemical method). The simultaneous discovery of rapid methods by myself in America and Fred Sanger in England changed the problem from insolvable to easy. Both methods depended on measuring the distance to each base by sizing fragments of DNA on polyacrylamide gels, and moved the problem from one base a month to hundreds of bases in an afternoon. These rapid methods were widely distributed and the world began to sequence DNA (and hence to decipher genes) at an evermore rapid rate (the rate of sequence accumulation has been going up by a factor of 10 every five years, 100 each decade, for the last 37 years. The ability to read the DNA sequence underlies all of modern biology, from cell function, development, medicine, evolution, and ecology. One outcome of this was the Human Genome Program: the first human sequence and after that the current sequencing of 1000's of human genomes. The sequencing of individuals (and often their cancers) will move in the next decade to the forefront of a medicine personalized to the individual's disease and biochemistry.

I remember with gratitude living on an NSF graduate fellowship in the late '50s. By being in England I and my wife could live on the fellowship. I went to Cambridge, in England, to study Theoretical Physics (there called Mathematics), and found my thesis supervisor, Dr. Abdus Salam. I remember arriving in Cambridge, fresh off the boat, and dashing in to find my first supervisor (not Abdus) who looked at me as this over-eager American and said "Go away, term has not started yet". Later I found a whole group of people around Abdus Salam eager to do Physics.

The second year I was in Cambridge, I remember going to the door to pick up the post and there was no letter from the NSF. I went to my wife and said "Sorry, too bad, I guess we did not get a fellowship this year, we will have to go home." She said "It is not due until tomorrow!" And that was true; the next day the letter arrived.

I spent two years in Cambridge, wrote several papers, and then went back to Harvard, thinking I would take a degree from Harvard. However, finding myself in classes again, I soon discovered that I could not bear listening to lectures, so I quit all my classes and wrote my doctoral dissertation and sent it in by mail to Cambridge (a bound final volume). Cambridge assigned Vicky Weisskopf and Hans Bethe to exam me for my doctorate, and one evening I went over to Vicky’s office at MIT and we had a thesis oral. I passed.

My entire graduate career was supported by the NSF fellowships, and would have been different without the independence they gave me. I was glad to get an NSF postdoctoral fellowship for my first postdoctoral year. The second year I gave up a fellowship to take a position at Harvard.