BIOGRAPHICAL MEMOIRS

E. Peter Geiduschek

April 11, 1928–April 8, 2022
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A Biographical Memoir by James T. Kadonaga, George A. Kassavetis, Jonathan M. Geiduschek, Jeremy M. Geiduschek, Joyce B. Geiduschek, and Amy S. Harris

E. Peter Geiduschek was a true pioneer of DNA structure and gene expression. He was among the first scientists to develop systems for the study of transcription in vitro, and he carried out innovative and elegant biochemical studies that elucidated the roles of proteins required for gene expression in bacterial viruses and in eukaryotic cells. His studies provided key insights into the molecular mechanisms by which viruses take over the host's synthetic machinery and by which they control the timing of the expression of their genes to ensure efficient multiplication. These studies are of fundamental importance to our understanding of gene expression and of the multiplication of human viruses. Additionally, he was a major force behind the discovery and analysis of the factors and mechanisms involved in the synthesis of 5S rRNA and tRNAs by RNA polymerase III. Thus, Peter is one of the most prominent figures in the field of molecular biology.[1,2,3] In recognition of his scientific advances and contributions, he was elected to the National Academy of Sciences in 1974 and the American Academy of Arts and Sciences in 1975. Peter mentored scientists from all over the world, playing a major role in advancing molecular biology as a scientific discipline in several countries. For this, he was awarded the title of Grande Ufficiale Ordine al Merito della Repubblica Italiana in 1996—the highest honor able to be bestowed on a non-Italian citizen—and the Gregor Johann Mendel Honorary Medal by the Czech Academy of Sciences in 2004.

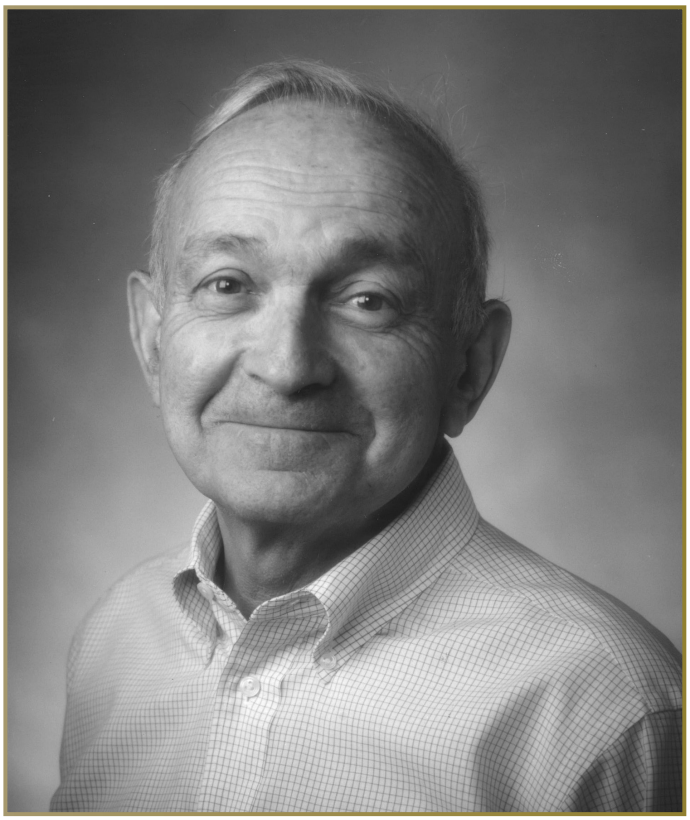

Figure 1 Peter Geiduschek.

Early Life

Peter was born on April 11, 1928, in Vienna, Austria, the third son of Sigmund and Frieda Geiduschek. Hans, born in 1921, died before Peter's birth; Martin was born in 1923. They lived a typical upper middle class Jewish life, which for Peter included lessons in French and music, the latter becoming a lifelong passion. Their lives changed drastically with the annexation of Austria by Germany in March 1938 (the Anschluss). In the pogroms of Kristallnacht in November 1938, Sigmund was arrested at his place of business and sent to the Dachau concentration camp for four months. At home, Peter watched as Martin, who looked older than his fifteen years,

was roughed up and arrested. Frieda frantically went from station to station until she found him and, with documented proof of his age, secured his release. Martin was soon sent to England on the Kindertransport and was eventually welcomed by a family in Manchester. Peter was sent to England four months later, also on the Kindertransport, and found refuge in St. Albans with the Bryer/Polack family.

What was meant to be a short stay in a safe haven turned into six years during which Peter and Martin lived as beloved members of foster families. In Peter's own words, "I am quite sure that my life has been formed by some extraordinary good fortune, and particularly the good fortune of the people who took me in as their ward in England." Peter remained devoted to his wartime family, ever grateful for their sacrifice. He visited them often and remained in contact with their children and grandchildren until his final days. The kindness shown to Peter during the war was reflected in his own family life and humanistic values. In 1945, Peter and his brother were joyfully reunited with their parents in New York City. Frieda and Sigmund had managed to flee Austria, and ultimately reached the United States. Many members of Peter's extended family did not escape and perished in the Holocaust.

In the summer of 1945, Peter was accepted to Columbia University and graduated in 1948 with a degree in chemistry. Graduate school followed at Harvard University, where Peter joined the research group of Paul Doty. In 1952, Peter received his Ph.D. in physical chemistry and accepted a position as an instructor in the Department of Chemistry at Yale University. In 1953, he was drafted into the U.S. Army and carried out research in the Department of Biochemistry at the Walter Reed Army Institute of Research (WRAIR) in Washington, D.C. Of Peter's time in the Army, Moselio "Elio" Schaechter recollected:

> We had both been drafted at the same time and sent to the Walter Reed Army Institute of Research. Same barracks. But Peter didn't relish having to get up at 5 or so every morning at reveille. He was running the model E [note: Beckman Model E ultracentrifuge], probably the only one around who knew how to. So, he told his boss that the machine was very sensitive to street noise and could only be run at night. To make that possible, he was placed in a room of his own, I seem to remember, along with a sergeant. No reveille for him![4]

This was an exciting period in biology with the recent elucidation of the double-helical structure of DNA.[5] Peter studied the biophysical properties of DNA and discovered that DNA structure changed upon progressive substitution of the solvent water with ethanol.[6] More generally, Peter's research at the WRAIR inspired him to study the properties of DNA. After his discharge from the Army in 1955, he returned to his position at Yale.

Physical Properties of DNA

Over the next several years, Peter continued studies on the physical properties of DNA, with a particular focus on DNA denaturation and renaturation. An early highlight from this work is the first direct thermochemical measurement of DNA denaturation, which was performed with Julian Sturtevant at Yale.[7] Peter continued this work after he joined the faculty as an assistant professor in the Department of Chemistry at the University of Michigan in 1957. In 1959, Peter took a position as an assistant professor of biophysics and research associate in biochemistry at the University of Chicago.

At Chicago, Peter examined the effects of nitrous acid, a mutagen, on DNA structure. Unexpectedly, nitrous acid treatment of DNA was found to result in the reversible reannealing of the separated strands, and Peter eventually determined that this phenomenon is the result of crosslinking of the DNA strands.[8] He also examined the effects of different ions upon DNA denaturation, and he observed that a series of ions exhibit a disorder-causing trend that is similar to the Hofmeister series seen with proteins.[9] He coined the term *chaotropic* for this phenomenon, and it has since been widely used in the scientific literature. His continued research on the reversibility of DNA renaturation with different solvents and ions led to a comprehensive study that he considered to be his best work on this subject.[10,11] In all, these studies provided a solid foundation for understanding the effects of ions and hydrophobic forces upon the stability of the DNA double helix.

Early Work on RNA Polymerase

For eleven years (1959–70), Peter was a member of the Committee on Biophysics at the University of Chicago. During this time, he initiated two new major research directions. He learned about RNA polymerase from Samuel B. Weiss, and he became an expert in phage genetics and physiology during a sabbatical year (1964–65) in Geneva, Switzerland.

Peter's early work on RNA polymerase started when he arrived in Chicago. Weiss had also recently arrived as an assistant professor at the Argonne Cancer Research Hospital. Their respective labs were only about a block and a half apart, and they began a productive collaboration. Weiss first reported the activity[12] that he and others had later shown to be RNA polymerase, which catalyzes the synthesis of complementary RNA from a DNA template.[13] Peter's expertise with nucleic acid biochemistry was very useful for the study of this new and exciting enzyme.

A key problem was understanding the relationship between the in vitro-synthesized RNA and the DNA template.

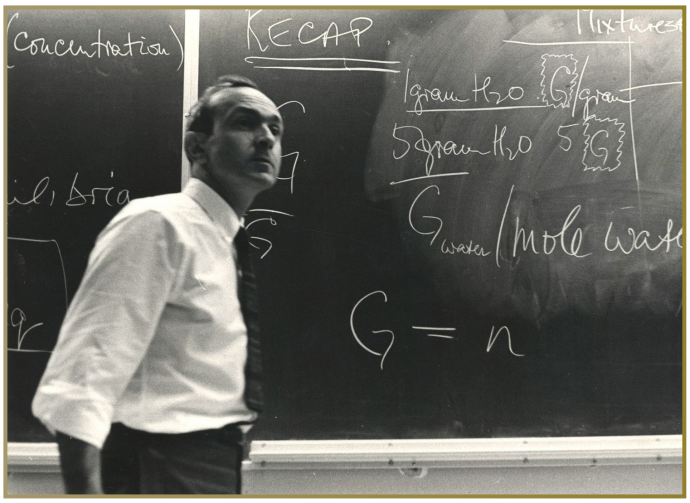

Figure 2 Peter, early 1960s. The photograph is from the collection of Dr. Joyce B. Geiduschek (Peter's wife), who is a co-author of this memoir.

In an impressive analysis, Peter and Weiss conclusively demonstrated that RNA synthesized in vitro is entirely and faithfully complementary to the DNA template sequence and that the DNA helix does not unwind completely during transcription as it does in DNA replication.[14] In that biochemical study, they observed transcription from both DNA strands. They further investigated this issue in vivo, and in a landmark paper, they demonstrated that transcription of bacteriophage DNA in bacteria is asymmetric (only one DNA strand is copied into RNA).[15] This finding implied that there is directional specificity in the transcription process. Peter made seminal early contributions to our basic understanding of the transcription process and continued to make major advances in transcription throughout the rest of his career.

Phage and Transcriptional Regulation

As noted above, Peter spent a sabbatical year in Geneva. He was a Guggenheim Fellow at the Institut de Biologie Moléculaire. He initially intended to work with Eduard Kellenberger (who had been and remained a good friend) but ended up spending most of his time with Richard H. "Dick" Epstein learning "serious phage genetics and physiology."

Peter used bacteriophage T4 as a model for understanding mechanisms of transcriptional regulation. In this regard, he examined transcription in the early versus late stages of T4 infection of *Escherichia coli*. He found that transcription in vitro yielded the early bacteriophage RNA[16] and that T4 late transcription in vivo required the products of phage genes *33*, *45*, and *55*.[17,18,19] On the matter of T4 late transcription, he wrote:

> The T4 late transcription problem fascinated me as soon as I learned about it. I even started doing some in vitro experiments on it during my stay in Geneva, when it looked likely that only early RNA was made in vitro by *E. coli* RNA polymerase. Finding out what is required for accurately initiating late transcription in vitro became a challenge of which I never let go.[11]

Peter's tenacity was well rewarded. His studies on T4 late transcription led to many key discoveries that include the coupling of late phage transcription to DNA replication,[20,21] the function of gene *55* protein (gp55) as an alternate sigma factor,[22] and the activation of transcription by gene *45* protein (gp45) by a fascinating mechanism that involves the sliding of doughnut-shaped gp45 along DNA with the DNA in the center of the doughnut.[23] These findings are an important part of our current knowledge of gene regulation.[24]

Eukaryotic and Archaeal Transcription

In the mid-1980s, Peter initiated a new project on transcription by RNA polymerase III in the yeast *Saccharomyces cerevisiae*. His many contributions to eukaryotic transcription include the identification of TFIIIB as the core transcription initiation factor of RNA polymerase III,[25] the use of photochemical cross-linking for identifying the subunits in multiprotein complexes that interact with specific DNA sequences,[26] the identification of two of the subunits of TFIIIB by purification as well as by photochemical cross-linking,[27,28] and the cloning and analysis of the B" subunit (now known as BDP1, for B double prime 1) of TFIIIB.[29] This work has had an immense impact upon our understanding of this complicated and important process.[30]

In the early 2000s, Peter became interested in transcription in archaea, in which the basal transcription system resembles the eukaryotic RNA polymerase II system and the sequence-specific activators resemble those in bacteria. With his expertise in both prokaryotic and eukaryotic transcription, he was quickly able to make impressive progress in archaeal transcription. Some of these achievements include the demonstration that a sequence-specific activator recruits archaeal TBP (TATA box-binding protein) to the promoter[31] and the reconstitution of a completely purified and recombinant archaeal transcription system.[32] This work has illuminated some of the missing links between transcription in bacteria and eukaryotes.

Impact at the University of California, San Diego

In 1970, Peter moved from the University of Chicago to the University of California, San Diego (UCSD), which was founded only ten years earlier in 1960. He had an enormous positive impact upon the biological sciences at this young university. For forty-four years, Peter was the foundation of molecular biology as well as the intellectual leader of a faculty that grew both in numbers and distinction.

Peter was also uniquely notable for his participation in the departmental seminar program. In the question-and-answer period after each seminar, he would wait until all of the regular questions were discussed. He would then carefully ask an incisive question on the most critically important shortcoming of the presented research. In each seminar, this was a highly anticipated moment for all of the other local attendees. It was also a moment that was feared by visiting speakers, who knew of this ritual.

At UCSD, Peter was a leader and a role model for undergraduate students, graduate students, postdocs, and his fellow faculty. He was a major driving force behind the excellence of science in biology, and he mentored generations of scientists who have in turn made countless discoveries and advances. Moreover, with his wit, charm, and warm personality, Peter was a much-loved colleague. He is honored and fondly remembered as a remarkable and singular individual who has provided much of the basic knowledge of DNA and gene expression that we enjoy today and significantly and selflessly contributed to the establishment of UCSD as one of the premier research universities in the world.

In 2014, Peter moved to Palo Alto, California, to be near family, and he took an appointment as a consulting professor in the Department of Structural Biology at Stanford University School of Medicine. He worked closely with the laboratory of Roger Kornberg and continued to be an inspiration to the scientific community.

An Extraordinary Individual, Scientist, Teacher, Mentor, and Colleague

E. Peter Geiduschek was an extraordinary individual who had a remarkable and complex life and career. Through his research, teaching, and mentorship, he made lasting contributions that will enable new and important discoveries by future generations of biologists. To his family, colleagues, and students, Peter was the model of rigor and scientific precision as well as of generosity, kindness, and collegiality. He also carried out his research with a style and panache that transcended the typical completion of a scientific project. Indeed, Peter's research was carried out with such a level of artistry and elegance that he truly achieved a convergence of science and art in his work.

Peter is lovingly remembered by Joyce, his wife of sixty-six years; his children, Jeremy (Susan) and Jonathan "Joss" (Amy Harris); and his grandchildren, Anna, A. Max, Emma, and Mia.

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