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EDITORIAL

Gunther S. Stent's centennial—a pioneer in structural biology and philosopher of science

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Abstract
The German-born American Gunther S. Stent (1924–2008) was a refugee from Nazi Germany. He studied in the United States, was a follower of Max Delbrück, and became a member of the phage group. He researched DNA replication and RNA transcription and translation, and made contributions to neurobiology. He loved paradoxes and was a great communicator and a philosopher of science.

Keywords Gunther Stent · Max Delbrück · Erwin Schrödinger · James Watson · Phage group · Molecular biology · Molecular genetics · Neurobiology · Philosophy of science · Paradoxes

Gunther S. Stent (1924–2008, Figs. 1, 3, and 4) [1, 2] was born as Günter Siegmund Stensch in a hardly observant, assimilated Jewish family in Treptow, a suburb of Berlin. His father, Georg, was a native Berliner and his mother, Elli, came from a family in the Silesian city of Breslau (today, Wrocław, Poland). She suffered from an inherited manic-depressive disorder and took her own life when Stent was eleven. From then on, his elder sister was acting for Stent as a surrogate mother. The family owned one of the largest bronze statuary and lighting fitting factories in Germany. Even before Hitler and the Nazis came to power, Judaism became a major factor for Stent. The Nazi storm troopers were marching through the Berlin streets trumpeting the words:

Wenn's Judenblut vom Messer spritzt,
Dann geht's noch mal so gut.
(When Jew-blood spurts from our knives,
We'll all have twice-better lives.)

Stent attended public schools until the fall of 1935, when the Jewish children were expelled from them, and he was enrolled in a private Jewish school. From that point on, their main educational goal was preparation for departure from Nazi Germany. They received intensive training in English, French, and Modern Hebrew. Following the infamous *Kristalnacht* pogroms, known also as the Night of Broken Glass, in November 1938, life became unbearable, and Stent escaped across the "Green Frontier" to Belgium on New Year's Day of 1939. He wanted to join his sister who had in the meantime married and emigrated to the United States. It took a while before Stent collected the necessary immigration documents and, in March 1940, he sailed for New York from Liverpool.

He started his American life living with his sister and her family in Chicago and enrolled in Hyde Park High School. Lacking some basic knowledge in mathematics and science, he had to start as a freshman. He caught up quickly and graduated in 1942. He continued in Champaign, at the University of Illinois, as a freshman in chemical engineering. Only when he took his first course in physical chemistry, did he start liking chemistry thanks to Frederick T. Wall's captivating lectures, and Stent switched his major to physical chemistry. Following graduation in 1945, he wanted to continue with PhD studies and dreamed of joining Linus Pauling at the California Institute of Technology (CalTech). When he was not accepted, he opted for doing his doctoral project with Professor Wall while working as a Research Assistant on the Synthetic Rubber Research Program of the War Production Board.

There was a significant interlude interrupting his doctoral studies. He became an American citizen in 1945, and after 8 years following his dramatic escape from Germany, he

Contribution to the Column "Foundation of structural science."

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Fig. 1 Participants of a scientific meeting in 1951 at the Institute for Theoretical Physics, Copenhagen; courtesy of Gunther S. Stent. Front: Ole Maaløe, Raymond Latarjet, Élie Wollman. Second row: Niels Bohr, N. Visconti, G. Ehrensvaard, Wolf Weidel, H. Hyden (much hidden), V. Bonifas, Gunther Stent, Herman Kalckar, Barbara Wright (partly hidden), James Watson, M. Westergaard

returned to Berlin in a U.S. Army uniform. In 1946 – 1947, he served in Germany assessing scientific and technological innovations in German industry.

Upon his return to Champagne, he continued his studies and his work for the rubber board acquiring useful experience for his future research career. He produced some innovations but did not get the expected recognition for it, which he ascribed to the lack of personal qualities needed to have them make an impact. These were lessons to learn as he eventually realized: originality and inventiveness are necessary, but to make a mark in science, intuition, stamina, and self-confidence are also necessary.

Stent kept watching out for interesting projects, talking with colleagues, and reading the literature. He came across Erwin Schrödinger's recently published book, *What Is Life?* [3]. This was the beginning of Stent's lifetime fascination with what would become molecular genetics and perhaps even more with Max Delbrück (Fig. 2) whom Schrödinger's book identified as a young German physicist. Schrödinger posed the profound question of how do genes manage to preserve their hereditary information over generations? Schrödinger introduced a "Delbrück model," and anticipated a Delbrück cult that would develop during the 1950s – 1960s and beyond. Schrödinger was impressed by Timoféeff-Ressovsky, Zimmer, and Delbrück's 1935 article about the nature of the gene [4]. It was a substantial paper with a conclusion that sounds trivial today but was revolutionary at the time. They investigated the extraordinary stability of the gene, at about 37 degree Celsius, whose nature was not yet known. According to the authors, the stability of the gene indicated *chemical* stability and that the gene was a *molecular* substance. Schrödinger' hypothesis was that the gene-molecule is an *aperiodic crystal*, which is comprised of a long sequence of a few different, over-and-over-repeated basic elements. The exact sequence pattern of

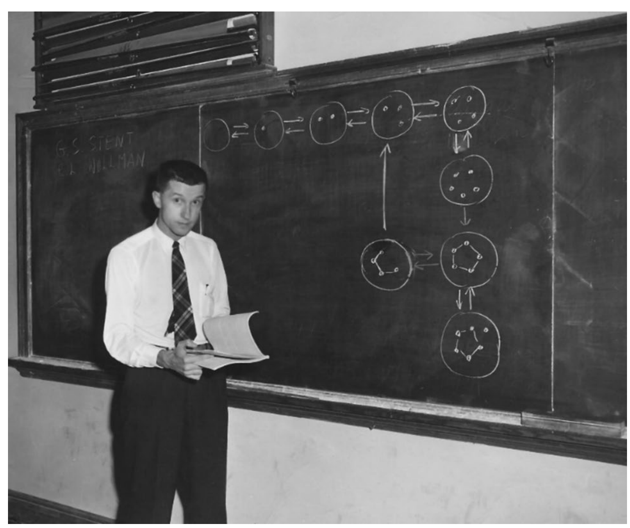

Fig. 2 Max Delbrück during his presentation of Stent and Élie Wollman's theory; courtesy of Gunther Stent

these elements would represent a "code" encrypting the hereditary information. This idea anticipated the variable sequence of DNA as well as what is known today as the genetic code. Schrödinger opined that "new" laws of physics will have to be discovered to understand the science of life. This sounded exciting and fascinating for Stent and budding scientists.

Stent learned in 1947 that Delbrück was alive, he was in the United States, and was just appointed Professor of Biophysics at CalTech. Stent thus made a second attempt to join CalTech. He applied for a postdoctoral fellowship to the National Research Council (NRC) sponsored by the Merck Chemical Company. He proposed to use his knowledge of physical chemistry to the study of biophysical problems with emphasis on life processes. He received the fellowship, and his work began with attending a conference in the Cold Spring Harbor Laboratory on Long Island. It was organized by Delbrück together with Salvador Luria and Alfred Hershey on phages (bacteriophages), the viruses that infect bacteria. That is when Stent met James D. Watson (Fig. 1), another exceptional scientist, who was also electrified by the prospects of the new science.

Upon the completion of the Cold Spring Harbor meeting, which was more a training course than a conference, Stent began his phage research at CalTech. He had a research partner, Élie Wollman (Fig. 1), a young French bacteriologist and a disciple of André Lwoff at the Institut Pasteur in Paris. By 1949, Delbrück brought together a spectacular group of researchers of future international fame. This was augmented by the similarly strong groups around Linus Pauling and George Beadle at CalTech. They represented a broad spectrum of research interests, such as the mathematician Benoit Mandelbrot, and had considerable intellectual impact on Stent (Fig. 3).

Stent and Wollman devised a model, based on their experiments, which was a forerunner of the cooperative models of the interactions of small molecules with enzymes and other protein molecules. The model helped understanding the regulation of protein function. Alas, their work may have been somewhat premature as the emerging vast literature of cooperative protein interactions hardly ever cited it.

When Stent's postdoctoral fellowship ended, he did not find possibilities in staying at CalTech, nor joining the Institut Pasteur to continue his joint research with Wollman. In 1950, Stent moved to Copenhagen to work with the Danish biochemist Herman Kalckar (Fig. 1), and so did Watson. They hoped to learn about DNA but for a variety of reasons, this did not work out. Stent and Watson continued in Ole Maaløe's (Fig. 1) laboratory, also in Copenhagen. They investigated the metabolism of phage DNA. They carried out radioactive tracer studies and their results helped generating interest in the intracellular transactions of phage DNA. During this time Stent observed first-hand the development of Watson's interest in the structure of DNA and his decision to move to Cambridge to work on it. Stent, as all others, thought this to be an impossible task.

After Copenhagen, Stent moved to Paris with his Icelandic pianist fiancée, Inga Loftsdottir, for her music studies. They were married in Paris, had one son, Stefan Stent, and lived together until her death in 1993. Mary "Molly" Burgwin Ulam (Fig. 4) was Stent's second wife; they married in 2003. Previously, she was married to the Harvard historian and political scientist Adam Ulam, the mathematician Stanislaw Ulam's younger brother.

Fig. 3 Gunther Stent (right) with Istvan Hargittai in the Hargittais' home in Budapest, 2003; photograph by and courtesy of Magdolna Hargittai

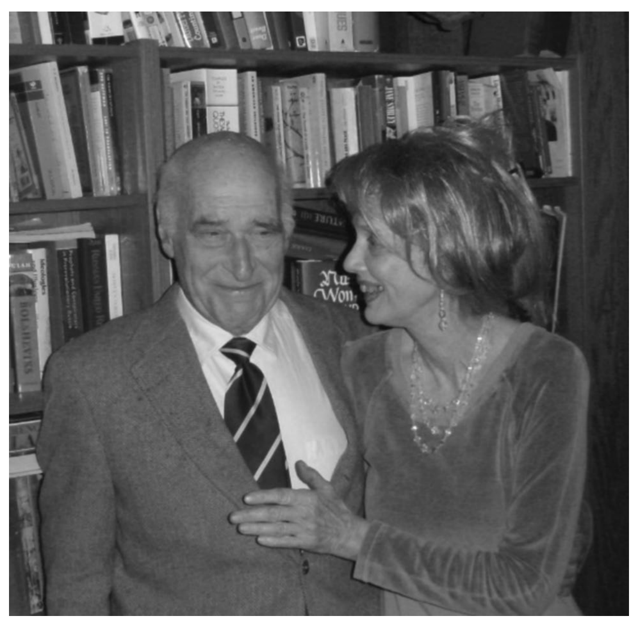

Fig. 4 Gunther Stent and Molly Stent in Berkeley, California, 2004, photograph by Istvan Hargittai

During the Paris sojourn, Stent received an appointment to the new Virus Laboratory at Berkeley built for the Nobel laureate Wendell Stanley. Soon, Roger Stanier, the Canadian microbiologist who had joined the Berkeley faculty as Professor of Bacteriology, arranged for Stent's tenured professorial appointment to teach Berkeley's first course in bacterial genetics. Stent stayed for his entire career at Berkeley as Professor of Molecular Biology, and even after retirement, he remained active there almost to the end.

Stent devoted his first twenty years of research at Berkeley to the molecular biology of phages and bacteria. However, he enjoyed most his working on the neurobiology and developmental biology of leeches. He made this switch by the late 1970s. To catch up with the field, he joined Steven Kuffler at the Neurobiology Department at Harvard Medical School for his next sabbatical. Kuffler was a superb experimentalist and pedagogue, and to Stent, he resembled Delbrück in being the leader of a newly established field of science. Stent learned the techniques of neurobiology from John Nicholls in Kuffler's laboratory. Stent's research during this sabbatical resulted in a paper providing a neurophysiological explanation of Donald O. Hebb's hypothesis of learning by modulation of synaptic strengths. He published it in the *Proceedings of the U.S. National Academy of Sciences* [5] and the paper became Stent's most cited publication.

On his return to Berkeley, Stent set up a neurobiological laboratory and worked on how the leech nervous system generates its swimming rhythm. He learned that this research could be considered a continuation of Leonardo da Vinci's interest in the locomotion of animals, including the swimming movement of leeches. In another project, Stent and his colleagues investigated the embryonic development of the leech nervous system and devised a novel method for tracing the origin of nerve cells from the fertilized egg to the mature animal.

Stent found his intellectual home at Berkeley and Berkeley appreciated his broad worldview. It provided him challenges, support, and when needed, freedom from his regular academic duties. In 1968, he had a temporary appointment as Professor of Arts and Sciences, which was dotted by his seven public lectures, developed into his book *The Coming of the Golden Age: a view of the end of progress* [6]. He takes a broad view of molecular genetics and does not paint an optimistic view of his expectations of the science of the future when all major discoveries will have been made and what remains would be merely filling in the details.

Stent was among the pioneers of molecular biology and his moving away from it might be considered symbolic. For molecular biology, it was a transition from being a field of research to becoming an arsenal of research tools. He liked prognosticating the future of the biological sciences and made some general observations in science history. For example, the easier scientific problems are solved before the more difficult ones. He opined that four of the fundamental problems central in biology have been solved in the twentieth century, viz., metabolism, heredity, embryonic development, and organic evolution. Others still await their solution in the twenty-first century, and they are likely to be more difficult than any that have been solved thus far. Stent mentioned the origin of living matter and consciousness in our conversation in 2003. He discussed the research problems of consciousness in detail ([1], pp 519–527). In this and other instances, I felt the power of skill in his communication. He was especially interested in two issues: the nature of premature discoveries and the relationship between arts and science that he thought was more intimate than many had supposed.

I venture to predict that Stent's books will far outlive his research discoveries. From 1963, he published books on molecular biology [7] and molecular genetics [8], and treatises on the philosophy of science. He had already had three decades of a successful writing career when he produced a most fascinating book, *Nazis, Women and Molecular Biology. Memoirs of a Lucky Self-Hater* [9]. It is an expanded autobiography with considerable twentieth-century history. It is a puzzle that he could not find a publisher

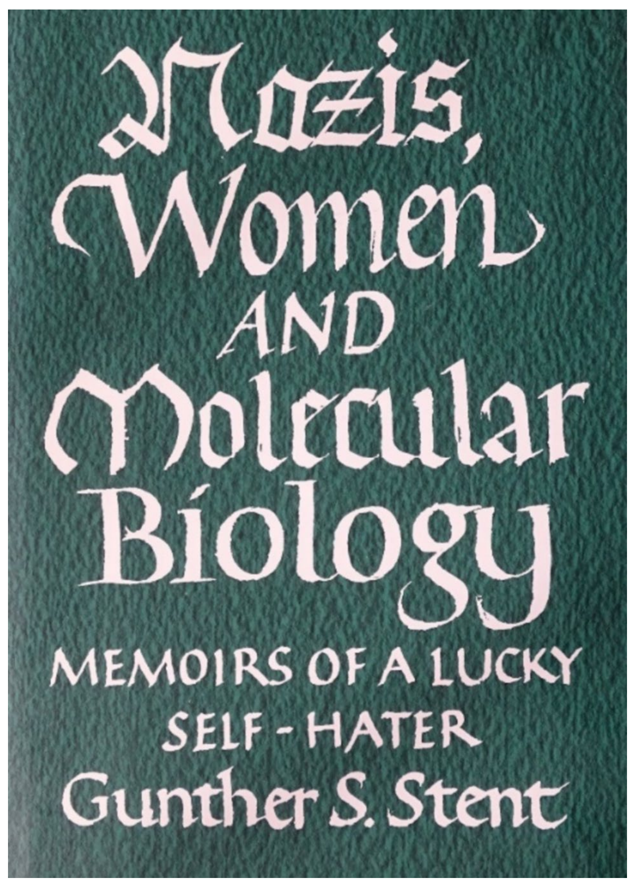

Fig. 5 Dust cover of Stent's autobiographical volume [9]

to bring it out and had to restore to have it published as a private edition (Fig. 5).

In his books about paradoxes, *Paradoxes of Progress* [10] and *Paradoxes of Free Will* [11], Stent discussed his views of the relationship of humans, nature, and science, taking a broad view of science history and the history of philosophy. Beside twentieth-century science, he pays tribute to such giants as Immanuel Kant, and reaches back even to ancient times. He does not shy away from making references to and conclusions about contemporary events either. I single out one example ([11], p 226) because it is related to various debates in which I had also participated. He mentions Leo Szilard's little book, *The Voice of the Dolphin* [12], about the time of high tension between the superpowers during the Cold War. Some young molecular biologists in an international Vienna institute manage to save the world from a U.S. – Soviet nuclear conflict that would result in annihilation of our civilization. Szilard's story was a prescient description of what happened decades later when a project by scientists contributed to preventing a nuclear skirmish and facilitated ending the Cold War. President Reagan adopted a "Star Wars" scenario called Strategic Defense Initiative, which was expensive and, probably, unworkable. However, the Soviet leadership could not ignore it though could not match it either. So, this was a major factor in the collapse of the Soviet Union. This is a succinctly realistic presentation of the events but to many others, this description ascribes an exaggerated role to the science component in them.

With John Cairns and James D. Watson, Stent co-edited a festschrift book honoring the 60th birthday of Max Delbrück. This 1966 volume [13] turned out to be a major document about the science of phage and the origin of molecular biology. Stent introduced it with a brief chapter entitled "Waiting for the Paradox" ([13], pp 3 – 8). This contribution refers to the profound influence Schrödinger's *What Is Life?* [3] had on a generation of physicists (though not so much on biologists). As it was alluded to above, Schrödinger's book represented a challenge (especially to the physicists) because it implied that the already known laws of physics might not suffice to understand life. This turned out though not to be the case.

Stent managed to end his introduction to the festschrift book with a paradox, and he loved paradoxes: "There exist processes which, though they clearly obey the laws of physics, can *never* be understood" (Stent's emphasis, [13], p 8). Stent developed this relatively brief introduction into a major lecture to the Collége de France, Paris, on June 12, 1967. Then, in the 1992 expanded edition of the Cairns – Stent – Watson book [14], he added a longer treatise, reproduced from *Science* magazine in 1968, "That Was the Molecular Biology That Was" [15], which he ended with almost exactly reproducing the above sentence: "There exist processes which, though they clearly obey the laws of physics, can *never* be explained" (Stent's emphasis, [15], p 395). It is curious that Stent changed one word in this sentence, "understood" to "explained." He was famous for his care of words and his mastery of the English language. Using "explained" in this context rhymes with the way Eugene P. Wigner expressed the limitations of physics in his Nobel lecture: "… physics does not endeavor to explain nature. In fact, the great success of physics is due to a restriction of its objectives: it only endeavors to explain the *regularities* (Wigner's emphasis) in the behavior of objects. … The regularities in the phenomena which physical science endeavors to uncover are called the laws of nature" [16].

In 1980, Stent edited a Norton critical edition of Watson's book *The Double Helix* [17]. It consisted of a preface, a three-part introduction, the reproduction of the book itself, a selection of its reviews, and a set of original papers. I could not express my appreciation of this volume better than to suggest building around it a university course. It could be offered to non-science majors just as well as to science majors. Here, I single out the value of the dozen reviews reproduced from among the avalanche of reviews of Watson's book. Leading scientists and science writers produced substantial evaluations of the book and the diversity of opinions is impressive. Far from all reviewers thought the book would become what it has, and Stent was among those who erred profoundly. Somehow, this, and his self-critical approach to it, enhances the weight of his long and detailed review of the reviews.

Two reviews are conspicuously missing from this selection. One is Erwin Chargaff's review [18] because he did not give permission to reproduce it. However, Stent compensates the reader by copiously discussing it. The other missing review is by J. Desmond Bernal's [19]. This was an oversight by Stent and the reason may have been that it appeared in an obscure venue, *Labour Monthly*, a British magazine between 1921 and 1981, associated with the communist party. The inclusion of Bernal's review would have been justified by Bernal's stature, its rich content, and because of his intimate involvement with molecular biology in general and the double helix story in particular. The Watson–Crick paper announcing their suggestion for the double helix structure of DNA [20] quoted some details of the Norwegian Sven Furberg's model of the DNA chains. He worked it out in Bernal's X-ray crystallography laboratory at Birkbeck College, London. I provide references to Furberg's reports here [21–23] because, as Bernal noted, "Furberg's contribution [to the double helix story] has been grossly overlooked." It must be noted though that one among the scarce six references in the original Watson–Crick report [20] was to one of Furberg's papers [23].

Bernal's review is most instructive, and I reproduced it as an appendix in my own Watson book [24], for its relevance and its difficult accessibility. To me, the most interesting lesson of the review was Bernal's statement that "A strategic mistake may be as bad as a factual error." This was how he referred to his gentleman's agreement with William Astbury. The two crystallographers divided their field of research in which Bernal took the crystalline components of nucleic acids, the nucleosides, and Astbury the amorphous nucleic acids. The less ordered structures proved to be much more exciting than the fully ordered ones. Beside the truth in Bernal's revelation and the consequence of the agreement on his research activities, this is also of interest for another aspect of the bigger picture. At Bernal and Astbury's time, it was still possible for two individuals to dominate a significant portion of structural science.

For *Paradoxes of Free Will* [11], Stent received the John Frederick Lewis Award of the American Philosophical Society for the best book published by the society in 2002. His other recognitions were mainly elections to learned societies whose value was in that they come from his peers: American Academy of Arts and Sciences, National Academy of Sciences of the U.S.A., American Philosophical Society, European Academy of Sciences, and Akademie der Wissenschaften und der Literatur.

Above I merely selected examples to steer the reader toward Stent's oeuvre and the world view of this highly sophisticated and broadly informed individual who was at home equally in the "two cultures." His books are enriching, illuminating as well as entertaining. His biographer, Samuel H. Barondes, summarized it thus: "Gunther Stent's professional interests progressed in stages from the simple to the complex: from physical chemistry to molecular biology to neuroscience to philosophy. One feature remained constant: his gift for writing about his ideas in well-crafted prose" [2].

I met Stent twice and they were substantial encounters. One was in 2003 when he visited us in Budapest so that we could record our conversations. This was three days of talking and the level of intellectual excitement never waned [1]. Then, in 2004, my wife and I visited the Stents in Berkeley and continued our conversation for a few days, now, without recording. I have carried with me the great experience of our stimulating exchanges ever since.

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