A SHORT HISTORY OF MOLECULAR BIOLOGY

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Contents

UNESCO – EOLSS SAMPLE CHAPTERS

Summary

This chapter aims at giving a broadly conceived, but concise overview over the history of molecular biology from its beginnings in the early 1930s to the first steps into the age of genomics during the late 1980s and early 1990s. After a few introductory remarks on the

methodology and historiography of the history of the life sciences in general and the molecular biological revolution in particular, the first section deals with the most important lines of development in the two decades from 1930 to 1950. It contains paragraphs on seminal techniques and model organisms that were instrumental in setting the stage for the new biology. They include ultracentrifugation, X-ray structure analysis, UV spectroscopy, biochemical genetics based on fungi, the biophysics and biochemistry of tobacco mosaic virus (TMV), phage genetics, electron microscopy, work the transformation of pneumococci, the genetics of bacteria, nucleic-acid paper chromatography, the construction of protein models, and finally the introduction of radioactive tracing and its impact on physiology, especially protein synthesis research. All these technical innovations contributed to what has been addressed as a "new technological landscape" for the life sciences. The second section deals with the elucidation of the structure of DNA and the concomitant establishment of a new informational paradigm. Its paragraphs deal with the DNA double helix, the "central dogma" of molecular biology, the characterization of transfer RNA and messenger RNA, gene regulation, and the deciphering of the genetic code. The third section is devoted to the origins of gene technology in the 1970s. It briefly reviews the era of recombinant DNA technology and the beginnings of genome analysis. The paper concludes with a short remark on the impact of molecular biology on our views of evolution.

1. Methodological Introduction

"How, above all, does one recapture the sense of a maze with no way out, the incessant quest for a solution, without referring to what later proved to be *the* solution in all its dazzling obviousness. Of that life of worry and agitation there lingers most often only a cold, sad story, a sequence of results carefully organized to make logical what was scarcely so at the time" (Jacob 1988, p. 274).

Giving an overview of the history of molecular biology is not an easy task for two reasons: firstly, because the developments do not lie so far back in time; secondly, because there is a continuing discussion as to what really constitutes molecular biology. Historians of biology such as Robert Olby (1990) distinguish a "broad" from a "narrow" definition. The latter comprises the storage, expression and replication of genetic information and its molecular details. Today, the term "molecular genetics" is often used to cover this domain. It is evident that the narrow definition is itself the result of the development of this area of biological research. Therefore, in writing the history of molecular biology one must be aware that the use of the term is anachronistic to some extent. On the other hand, the broad definition encompasses under the concept "molecular biology" very generally any kind of research on the structure and function of biological macromolecules. It can, therefore, be said that – similar to the theory of evolution in the 19th century (cf. Lefèvre 1984) – molecular biology in the second half of the 20th century has come to assume a double status: on the one hand, it represents a specialized field (molecular genetics) within the framework of the other biological disciplines; on the other, it is a general experimental and theoretical paradigm which is spreading throughout all of biology.

The "revolution in biology" (Judson 1979) is marked by new techniques of

UNESCO – EOLSS SAMPLE CHAPTERS

representation in the analysis of organisms, which include X-ray structure analysis, ultracentrifugation, various types of chromatography, radioactive tracing, electron microscopy and the techniques of phage and bacterial genetics; further, we can observe a passage to new model organisms or quasi-organisms such as lower fungi (*Neurospora*), protozoa, bacteria, viruses and phages; in addition, a new type of support for research and interdisciplinary cooperation emerges. It started in the 1930s in the United States and Europe (France, England, Sweden, and Germany), and it was promoted to some extent by the Rockefeller Foundation. The goal of the latter was to bring together physical, chemical and mathematical approaches to the phenomena of life. Finally, in the course of this development, the processes of life thus far conceptualized in terms of mechanical and energetic principles came to be reconceptualized in terms of the (molecular) processing of information.

We are faced with a multi-layered and complex process which cannot be adequately described, for example, by the merger of already existing biological disciplines such as genetics, biochemistry and biophysics. It can also not be adequately represented as the simple addition of yet another biological discipline to the historical canon of disciplines. Neither is the discursive formation of molecular biology the result of the solitary efforts of a few brilliant researchers with their well-outfitted teams in a few research centers – for example, the phage group at the California Institute of Technology in Pasadena (Caltech), the X-ray structure analysts at the Cavendish in Cambridge and at Caltech, or the team from the Institut Pasteur in Paris. That is a myth which has been perpetuated by the protagonists as well as various commemorative publications (cf., among others, Rich and Davidson 1968, Monod and Borek 1971, Cairns et al. 1992). And it is just as clearly not the result of a comprehensive theory that guided research from the outset. Indeed, Richard Burian finds that there is no unifying theory at work at all in molecular biology, and that it is simply a "battery of techniques" (Burian 1994).

What Warren Weaver, the Director of the Natural Sciences Section of the Rockefeller Foundation, called "molecular biology" for the first time in 1938 a designation that was quickly taken up by William Astbury (1940) – arose out of a considerable number of experimental systems which at first developed rather apart from each other and were embedded in different institutional settings devoted to the physical, chemical and functional characterization of living organisms on the level of biologically relevant macromolecules. These different systems were at best loosely connected with each other at the beginning. Via the implementation of new instruments and techniques of analysis, these systems helped to form a new epistemic-technical space of representation within which the concepts of molecular biology were gradually articulated.

The historical development of this process is still poorly understood. First, one has to find an adequate level of analysis from which the key features of its dynamics can be elucidated, a development that has come to affect all of biology. There is no doubt that in Weaver's vision of a "new biology" and its massive financial support the agenda of eugenics and social control was virulent (Kay 1993). Unquestionably, there are also reasons why from the perspective of the philosophy of science one can speak of a "reductionist" program (Olby 1990). However, the historical movement

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that molecular biology owes its emergence to, is sufficiently determined neither by the global social, political and financial context, nor by equally global methodological premises. Processes of the unpredictable production of knowledge and the diffusion of practices which originally were local played a crucial role. Experimental systems, at first confined to very specific questions, as well as selected, comparatively simple model organisms created thanks to their subsequent dissemination and conjunction the momentum that led to the molecular biological revolution. The author would like to distinguish this perspective from technological determinism, on the one hand; on the other, the author would also like to contrast it with accounts based on the sociology of institutions or a history of ideas of great men. Due to lack of space the outlines of such an alternative narrative con only be sketched by drawing upon a number of general overviews and relying on a number of specific case studies.

2. Some Important Lines of Development between 1930 and 1950

This section will describe in an exemplary manner several lines of development of biochemical, biophysical and genetic research in the 1930s and 1940s. These researches at first developed in relative independence of each other. Looking back, however, they appear as the preconditions for that first synthesis which is associated with the names of James Watson and Francis Crick, and with their model of the DNA double helix.

2.1. From Colloid Chemistry to the Macromolecule: Ultracentrifugation

According to Robert Olby (1974), the "path to the double helix" cannot be seen as a continuous development based on a long-term research program that had its origin in, say, Friedrich Miescher's characterization of "nuclein" in the late 1860s. Around the turn of the century, organic chemistry was a chemistry of small molecules. Cellular protoplasm – envisaged since the 1860s as the seat of life – was seen as a colloidal aggregate of small molecules.

It was Hermann Staudinger in Zurich (subsequently Freiburg) who, on the basis of his investigations of rubber in the 1920s, first introduced the expression "macromolecule" into colloid chemistry. This roused the opposition of the leading specialists of the day, which found memorable expression in the Convention of German Natural Scientists and Physicians [Versammlung Deutscher Naturforscher und Ärzte] in Düsseldorf in 1926. This debate reached a decisive turning-point with the first attempts by Theodor Svedberg and Robin Fahraeus to determine the molecular weight of proteins – major constituents of protoplasm – by means of ultracentrifugation. After a short stay in Wisconsin (1924), Svedberg, who was a recognized colloid chemist, constructed a high-speed analytical centrifuge in Uppsala, in the hopes of being able to sediment materials of higher molecular weight. In these experiments hemoglobin, one of the first test proteins, proved not to be a heterogeneous colloid, but a homogeneous particle with an estimated molecular weight of 68,000. The ultracentrifuge was a piece of technical equipment that owed its design to the program of measuring the physical properties of colloids. The irony was that the apparatus helped to replace the paradigm of colloid chemistry by that of

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a macromolecular composition of the living substance. Until the late 1930s the extremely labor-intensive and difficult technique of analytical ultracentrifugation remained a monopoly of Svedberg's group in Sweden. Together with Staudinger's viscosimetric techniques it made possible the first estimates of the molecular weight, the chain length and the form of proteins.

Torbjörn Caspersson in Stockholm, working together with Staudinger's colleague Rudolf Signer in Bern at the end of the 1930s, had indications of the macromolecular nature of nucleic acids. At this point in time, research on nucleic acids was still dominated by the tetra-nucleotide hypothesis of Phoebus Levene from the Rockefeller Institute in New York. Parallel to the work of Albrecht Kossel (Berlin, Marburg, Heidelberg) and then in continuation of it, Levene had worked since 1900 on determining the chemical structure of the nucleic acids. His book *Nucleic Acids* (1931) was the standard work on this class of molecules during the 1930s. The tetra-nucleotide hypothesis states that nucleic acid molecules consist of one set each of the four building blocks (A, C, G, T or A, C, G, U) of either DNA or RNA – at most out of shorter or longer monotonous sequences of such tetra-nucleotides. This meant that it did not seem that nucleic acids would be able to play a role as carriers of biological specificity.

2.2. X-Ray Structure Analysis

X-ray structure analysis was developed by Max von Laue and William and Lawrence Bragg. It was originally intended for the analysis of the crystals of small molecules, but it was soon discovered that powdery and fibrous substances also showed X-ray diffraction patterns. In the 1920s it was, above all, the work of Reginald Oliver Herzog's team at the Kaiser Wilhelm Institute of Fiber Chemistry in Berlin Dahlem that led to the concept of a regularly structured long molecular chain – in particular of cellulose. Among others Michael Polanyi, who went to Fritz Haber in 1923 at the Kaiser Wilhelm Institute for Physical Chemistry and Herrmann Mark, who changed to BASF in 1927, were members of Herzog's team. Richard Olby writes:

"The right ingredients for the development of molecular biology were, it seems, in Dahlem – chiefly a powerful school of theoretical and practical X-ray crystallography. But by 1933 Hitler had come to power." (Olby 1974, p. 40).

Haber and Polanyi gave up their positions, Herzog went to Istanbul, Mark had already returned to Vienna in 1932. The focus of European fiber research shifted to the center of the English textile industry when William Astbury, who had studied under Bragg in London, came to Leeds in 1928.

Here Astbury began his researches into the structure of keratin together with investigations on the elasticity of wool. Starting in 1934, the work was supported financially by the Rockefeller Foundation. Around 1935 Astbury obtained the first images of nucleic acid fibers, at first as a by-product of his protein-based wool fiber program. At the end of the 1930s Torbjörn Caspersson from Stockholm supplied him with DNA material of a high molecular weight. Together with Florence Bell, Astbury

UNESCO – EOLSS SAMPLE CHAPTERS

created the first model of a nucleic acid. It had the shape of a single-stranded helix with the bases standing at right angles to its axis. Astbury noticed – and was fascinated by – molecular "fit", that is the comparable distance of the building blocks in proteins and nucleic acids. According to the then current ideas of biological specificity he concluded that the gene material was a nucleoprotein in which the protein molecule was kept in a stretched position by the DNA molecule, enabling it to replicate itself. Astbury's interest in genetics had been aroused by discussions at a couple of conferences on the structure of genes and chromosomes (above all, in Klampenborg in 1938) which had been funded by the Rockefeller Foundation. However, his work came to a halt when World War II broke out. This also happened with the X-ray crystallographic investigations of John Desmond Bernal, a Bragg pupil who had worked in Cambridge until 1937, where in 1934 he had succeeded in producing the first images of a single-crystal protein. After having moved to London, he began to concentrate on the diffraction pattern of crystallized tobacco mosaic virus.

By the end of the 1930s the development of X-ray structure analysis at Caltech in California and, above all, at the Royal Institution in London (father and son Bragg), as well as at the University of Leeds (Astbury) and at the Cavendish in Cambridge (Bernal, Max Perutz as of 1936, Lawrence Bragg as of 1937) had reached such a level of refinement that the determination of the structure of crystallized macromolecules became conceivable. Later, Gunther Stent called this structurally oriented "biology of molecules" the "structuralist school" of molecular biology (Stent 1968). Just as with the phage group, which will be described below, one of its starting points was an informal, transdisciplinary circle of scientists, the "biotheoretical gathering" in which Bernal played a leading role (Abir-Am 1987).

2.3. UV Spectroscopy

Torbjörn Caspersson developed a cytological approach to the quantitative, physical and chemical characterization of nucleic acids following on Einar Hammersten's work in Stockholm on the extraction of macromolecular DNA. Caspersson quantified Feulgen's color reaction and was able to demonstrate an increase of DNA in the course of the synthesis of nuclear material. Since the beginning of the 1930s he had been developing a technique for recording UV absorption spectra of nucleic acids, as well as a method of UV microscopy of cells. Around 1940, while working together with Jack Schultz at the California Institute of Technology in Pasadena, he observed a correlation between the synthesis of proteins and the amount of cytoplasmic ribonucleic acid in metabolically active cells. Around the same time, the embryologist Jean Brachet in Brussels made similar observations (Brachet 1942; Burian 1994). However, his observations did not lead Caspersson to revise the "nucleoprotein theory of the gene" (Olby 1974). He continued to see genes as "proteins, in a broad sense", and nucleic acids as "supporting substance":

"It seems hence that the unique structure conditioning activity and self-reproduction, possibly by successive polymerization and depolymerization, may depend on the nucleic acid portion of the molecule. It may be that the property of a protein which allows it to reproduce itself is its ability to synthesize nucleic acid." (Caspersson and

UNESCO – EOLSS SAMPLE CHAPTERS

Schultz 1938, p. 295).

This statement is characteristic for the "protein paradigm of life" which dominated the discourse of genetics at this time (Kay 1993, pp. 104-120). In this connection one also has to mention the work of Edgar Knapp and Alexander Hollaender, who determined that the effective spectrum for triggering mutations by UV radiation corresponded to the absorption spectrum of the DNA in the chromosomes. But neither Knapp and his colleagues in Germany nor Hollaender at the National Institutes of Health in Bethesda drew the conclusion from this finding that the DNA of the chromosomes might represent the hereditary substance.

2.4. Biochemical Genetics: Neurospora

George Beadle and Edward Tatum fit their own work leading to the formulation of the "one-gene, one-enzyme hypothesis" (Beadle 1945) into the same paradigm. In 1952 Beadle was still speaking of protein macromolecules as the key to genetic replication (Kay 1993, p. 210). As of 1937 Beadle had begun concentrating in his work with Tatum in Stanford on the model organism *Neurospora*. Because of its easy-to-control metabolic processes and its short reproductive cycle it became the focus of one of the most productive experimental systems of biochemically oriented genetics (Kay 1989; Kohler 1991).

In Germany Richard Goldschmidt and Carl Correns had from relatively early on established a tradition of physiological genetics (Harwood 1993), which was then pursued by Fritz von Wettstein and Alfred Kühn, among others, but which became increasingly isolated in the 1930s and during World War II. The transplantation experiments carried out on *Drosophila* mutants by Boris Ephrussi and George Beadle at Caltech and in Paris between 1934 and 1936, were designed on the Göttingen *Ephestia* experiments of Alfred Kühn and Ernst Caspari (Rheinberger 2000a). Kühn left his position at Göttingen University in 1937 and became Goldschmidt's successor at the Kaiser Wilhelm Institute of Biology in Berlin, where he intensified his collaboration with the organic chemist Adolf Butenandt. Goldschmidt, like Caspari, had to emigrate and went to the United States. Burian has correctly drawn attention to the fact, however, that there is no linear story of biochemical genetics to be sketched here. Ephrussi's research perspective, for example, was embryological rather than biochemical from the beginning.

"The classical history says that Ephrussi and Beadle laid the first stones of the future edifice of biochemical genetics… But everything in this history is inexact, as is typical in the 'myth of the precursor'" (Burian et al. 1988, pp. 390-391).

It is, therefore, not surprising that in this early research the idea of gene-controlled cascades of metabolism was not sharply delineated. The "one-gene, one-enzyme hypothesis" emerged in a rather convoluted research process and was clearly stated neither by Beadle around 1940, nor by Kühn who, in 1941, spoke of a network of "gene action chains" in the formation of the eye pigments in insects (Kühn 1941). Doubtless, the decisive change in Beadle's physiological genetic studies came when he joined forces with the biochemist Tatum and turned his attention to the *Neurospora* system. Both moves led to a strategic inversion in genetic experiments:

UNESCO – EOLSS SAMPLE CHAPTERS

instead of trying to follow the path from the gene to the gene product, Beadle, Tatum and their co-workers took the path from the gene product to the gene.

2.5. Tobacco Mosaic Virus (TMV)

When, in 1935, Wendell M. Stanley at the Rockefeller Institute in Princeton announced the "isolation of a crystalline protein possessing the properties of tobacco-mosaic virus" (Stanley 1935; cf. also Kay 1986, Creager 2002), it was something of a sensation. Martinus Beijerinck's (1899) "*contagium vivum fluidum*" had become a crystalline particle. At that time viruses had come to be considered as prototypes of hereditary particles which were able to reproduce "autocatalytically", if only with the help of living cells. Stanley did not hesitate to call his virus an "autocatalytic protein". The fact that this material could be crystallized seemed to finally tear down the boundary between biology, on the one hand, and physics and chemistry, on the other. The TMV fit seamlessly into the "protein paradigm of the gene". When two years later Frederick Bawden and Norman Pirie in Cambridge showed that there was a nucleic acid in TMV, this brought Stanley to speak somewhat more carefully of "virus proteins" as "nucleoproteins", but it changed nothing in his conviction that the protein component was the actual autocatalytic agent of the virus. He found himself in good company: among the many others who adhered to the same view were, not least, George Beadle and Max Delbrück.

The tobacco mosaic virus became one of the model objects that the physico-chemical techniques existing at the end of the 1930s concentrated on: ultracentrifugation (Svedberg in Uppsala, Stanley in Princeton), X-ray structure analysis (Bernal and Isidor Fankuchen in Cambridge and London), electron microscopy (Helmut Ruska in Berlin, Stanley in Princeton). Less well-known is the biochemically oriented TMV research that had been carried out since 1937 at the Kaiser Wilhelm Institutes for Biology and Biochemistry by the group including Gerhard Schramm, Georg Melchers, and Hans Friedrich-Freksa, as well as by Gustav Kausche and Edgar Pfankuch at the Biologische Reichsanstalt, in cooperation with Hans Stubbe at the Kaiser Wilhelm Institute for Biology (Deichmann 1999, Macrakis 1993, Rheinberger 2000b). Among the early results obtained by these researchers was the finding that for different virus strains the electrophoretic mobility of the nucleic acid in contrast to that of the protein was different; that after chemical modification of the protein the particle remained infectious; and that a phosphatase inhibited the infectiousness of the particle. All of these findings pointed to a nucleic acid as the active component of the TMV. But with the exception of Kausche and Pfankuch, nobody seriously pursued the idea that the viral nucleic acid might be the hereditary material. The work in Germany was followed closely in England and the United States, but confirmed only in part. With Stanley's departure from Princeton the center of TMV research shifted to the newly created virus laboratory in Berkeley (Creager 2002) after the war.

2.6. Electron Microscopy

The pioneer in electron microscopy was Ernst Ruska who, in 1931, built the first transmission electron microscope and, together with his brother Helmut in Berlin, also obtained the first images of biological material toward the end of the 1930s. In

UNESCO – EOLSS SAMPLE CHAPTERS

1939 Siemens produced a commercial transmission microscope. However, the work in Berlin came to a standstill because of World War II. Although the development of electron microscopy shifted during the 1940s largely to the United States (Rasmussen 1997), Ruska and the group around Kausche were still able in 1939 to obtain the first images of tobacco mosaic viruses (Kausche, Pfankuch and Ruska 1939), and of phages in 1940-1941. In 1942 Thomas Anderson and Salvador Luria followed with electron-optical images of phages (Luria and Anderson 1942). After the war Geneva became one of the centers of molecular biological electron microscopy (Strasser 2002, 2005).

The actual difficulty faced by researchers with the new technology involved less the resolution capacity of the instrument than the preparation of the samples. Application of the technique to biological material confronted the electron microscopist with completely new preparation requirements. Among other things, these included the uniform spreading of the specimen on a substrate that had to be as unstructured as possible; strong fixation of the specimen; thin layers; and a complete dehydration or, alternatively, shading of the probe leading to metal replicas. In 1944 Ernest Fullam and Albert Claude of the Rockefeller Institute in New York successfully obtained images of isolated mitochondria. Working together with Keith Porter they made, in 1945, the first images of cells *in situ* (Porter et al. 1945), and in 1946 they followed with *in situ* images of the Rous sarcoma virus (RSV). The 1950s, then, was the great period of ultrastructural imaging of the cell membrane, the nucleus, the endoplasmatic reticulum and mitochondria. This work became possible with the development of the technique of embedding of the specimens in hard resinous substances, the introduction of glass knives for cutting ultra-thin sections and of microtomes with a greatly reduced feed and, finally, the use of osmium tetroxide for fixation. George Palade of the Rockefeller Institute and Fritjof Sjöstrand of the Karolinska Institute in Stockholm (Rasmussen 1997) played a significant role in these developments.

UNESCO – EOLSS SAMPLE CHAPTERS

2.7. Bacteriophages

The protein paradigm of the gene was not shaken by research in the area of plant viruses, nor – at least at first by research on bacteriophages. These virus-like entities which attacked bacteria causing them to lyse were first characterized by Frederick Twort in England and Felix d'Herelle in France towards the end of World War I. Emory Ellis at Caltech was doing research on them when, in 1937, Max Delbrück arrived in California with a Rockefeller scholarship. Delbrück, whose training was in physics, had first done work together with Karl Zimmer and Nikolaj Timofeeff-Ressovsky in Berlin on gene mutation and the physical properties of genes (Timofeeff-Ressovsky et al. 1935). He was fascinated by the relatively simple visualization techniques of phage research and the possibilities of quantification by means of counting plaques and creating dilution series, techniques that he developed over the next years together with Salvador Luria into a standard instrument for working with phages (Luria &and Delbrück 1943). Theoretically he saw the phages as simple gene models with autocatalytic properties. In 1942 he expressed his hopes concerning the problem of self-reproduction synthesis as follows:

"It is likely that its solution will turn out to be simple, and essentially the same for all viruses as well as genes.... The study of the bacterial viruses may thus prove the key to basic problems of biology." (Delbrück 1942, p. 30).

The solution turned out to be not quite so simple; and in the 1950s phages surprisingly proved to be the key to questions that were of no particular interest to Delbrück, a point we will come back to below.

A lot has been written about the phage group (cf., among others, Stent in Cairns et al. 1992; Stent 1968; Kay 1985a; Kay 1985b; Fischer 1988). As told by the actors themselves, the origin of molecular genetics lay in Niels Bohr's vision, which was then taken over by Delbrück (Bohr 1933), of tracking down a new complementarity in the search for the fundamental laws of life. In keeping with this "romantic" story was the fact that in the phage group Erwin Schrödinger's *What is Life* (1944) held a significant place in the conceptualization of the process of heredity. Schrödinger spoke in this book of genes as "aperiodic crystals" and of an "inheritable code script". Accordingly, Stent has apostrophized Delbrück's group as the "informationalist school" (Stent 1968).

There is no doubt that Delbrück was one of the leading theoreticians in the development of molecular biology. In retrospect, however, it was less his theoretic vision than his technical and organizational innovations which gave phages their place in the history of molecular biology: the introduction of quantitative techniques in the analysis of virus replication; the "standardization" of the phage systems (with a focus on work with T phages); and the establishment of a network of international cooperation and exchange of information. As of 1945 the focus for this international activity was the legendary annual phage course in Cold Spring Harbor. Delbrück was able to turn his phage system into a community-forming enterprise. Nonetheless, the expected breakthrough regarding the nature of the gene did not come from phage work to begin with.

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UNESCO – EOLSS SAMPLE CHAPTERS

Biographical Sketch

Hans-Jörg Rheinberger was born in Grabs (Switzerland) in 1946. From 1966 to 1973 he studied philosophy in Tübingen and Berlin, Germany. After receiving his M.A. in philosophy in 1973, he began studying biology in Berlin and received his Ph.D. in 1982, and completed his habilitation in molecular biology in 1987. His main topics of interest are protein-synthesis, the history of molecular biology and the history and epistemology of experimentation.

In 1982 Rheinberger became a researcher and head of a group of scholars at the Max Planck Institute for Molecular Genetics in Berlin. A sabbatical at Stanford University in the Program of the History of Science from 1989 to 1990 was followed by a lectureship at the Institute for the History of Medicine and Science at the University of Lübeck, Germany, and an Associate Professorship in Molecular Biology and History of Science at the Institute for Genetics and Biology, University of Salzburg, Austria until 1996. Since 1997, he has been a Scientific Member of the Max Planck Society and Director at the Max Planck Institute for the History of Science in Berlin.

He has published: *Toward a History of Epistemic Things* (1997); *Experimentalsysteme und epistemische Dinge* (2001); with Frederic Holmes and Jürgen Renn: *Reworking the Bench: Research Notebooks in the History of Science* (2003); with Jean-Paul Gaudillière: *Classical genetic research and its legacy: the mapping cultures of twentieth-century genetics*, and: *From molecular genetics to genomics: the mapping cultures of twentieth century genetics* (2004); *Iterationen* (2005); *Epistemologie des Konkreten* (2006); with Staffan Müller-Wille: *Heredity Produced: At the Crossroads of Biology, Politics, and Culture, 1500-1870* (2007).

Prof. Dr. Rheinberger is Member of the Berlin-Brandenburg Academy of Science, and of the German Academy of Sciences Leopoldina; he is also Honorary Professor at the Technical University Berlin, Honorary Doctor of the ETH Zürich, and Editor of *NTM, Journal of History of Science, Technology and Medicine*.