# The Queen and the Scholars

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## Introduction

Fig. 1 illustrates at once the title and the content of this paper. The photo taken on August 31st, 1983, shows Queen Beatrix of the Netherlands, at the occasion of her 50th anniversary, hosting five Nobel laureates, including our compatriot Christian de Duve (second from left). For the Queen's jubilee a symposium was organized by the magazine "Natuur en Techniek" (today the NewScientist.nl) and held in the Congresgebouw of The Hague where the five distinguished scholars lectured on topics of their expertise.

There is no known evidence suggesting a particularly close or friendly relationship between the two physicists (Weinberg and Bloembergen). The three molecular biologists (Berg, de Duve and Eigen) surely were close friends. But it is doubtful that the biologists were acquainted with the physicists. Although there are quite a few physicists of that generation who ventured into molecular biology, the two physicists on Fig. 1 did not.

Sciences in the 20th century were dominated by the rapid progress in physics in the first half, followed by the rise of molecular biology in the second. With a delay of a few decades, the two disciplines converged in successfully applying the reductionist method which consists in cracking the object of study to explore the nature and function of its elementary constituents. Paul Dirac, one of the leading creators of quantum mechanics and quantum field theory, acknowledged the staggered developments, in his inimitable style: "*biology is catching up*". In the 70's, with the birth of genetic engineering, John Maddox who was well placed as former editor of the journal Nature, observed that "*to compare the speed with which understanding is being deepened in the life sciences with what happened in physics is probably flattering to physics".*

The mix of Nobel laureates in Fig. 1 is representative of the great advances just mentioned in both particle physics and molecular biology. I want to seize this opportunity by giving a coherent, albeit very sketchy, account of their works. With all its digressions, my narrative will be more an anecdotal story than a technical account.

Fig. 1 – Dutch Queen Beatrix meets five Nobel Prize winners at the occasion of her fifty's anniversary. From left to right, Paul Berg (1980, chemistry), Christian de Duve (1974, physiology or medicine), Steven Weinberg (1979, physics), Manfred Eigen (1967, chemistry), Nicolaas Bloembergen (1981, physics). Photo taken on 31 August 1983. Source: Dutch National Archives. CC BY-SA 3.0 nl via Wikimedia Commons Photo: Rob C. Croes/Anefo.

## Paul Berg

Paul Berg (1926-2023), in Fig.1, was an American biochemist whose development of *recombinant DNA* techniques won him a share in the 1980 Nobel Prize for Chemistry. His co-laureates were Walter Gilbert and Frederick Sanger for sequencing nucleic acid polymers. At the symposium in The Hague, Berg gave a talk entitled "*The promise of molecular biology and genetics for human health and industrial processes".*

Here are a few remarks about this group of laureates. First, the readers from the life sciences hardly need any explanation of how recombinant DNA works. For a general reader, suffice it to say that the technique consists of transplanting a piece of DNA from one organism to the DNA of another, something that Nature does all the time, but which Berg and others made into a laboratory technique. The details can be studied in any of the standard introductory texts in molecular biology, among which that of Paul Berg and Maxine Singer[1] is one of the best.

Second, while chemists often chose to do research in the sister sciences of biochemistry and hence in molecular biology, as mentioned in the introduction, quite a few physicists have made their mark in biology, despite the greater distance between the two disciplines. One of them is Walter Gilbert who indeed started his career with a PhD in theoretical particle physics in 1957 under Abdus Salam (co-laureate of Steven Weinberg in Fig. 1). Under the influence of James Watson of double-helix fame, Gilbert left physics and started anew in molecular biology. Twenty years later, he ended up being the first nucleic acid sequencer[2], an enormous achievement for someone who started with Quantum Field Theory, an abstract branch of

[1] BERG P. and SINGER M., *Dealing with Genes*, University Science Books, Mill Valley, California (1992). This introductory text is a condensate of the textbook by Maxine Singer and Paul Berg, *Genes and Genomes,* University Science Books, Mill Valley, California (1991).

[2] GILBERT W. *DNA sequencing and gene structure*, Nature, 265(5596), 687-695 (1977). https://doi.org/10.1038/265687a0.

theoretical physics. Remarkably, in addition to his sequencing performance, Gilbert was the first (in 1986) to develop the concept of *an RNA world* which is believed to be one of the early stages of life evolution on Earth (see the section on Manfred Eigen). The concept was supported by a discovery (1982) of Thomas Cech (Nobel laureate in 1989), that RNA possesses catalytic properties (ribozymes), including that of catalyzing its own replication. What may have happened before the RNA word is discussed in de Duve's books, such as "Life Evolving"[3].

Gilbert's performance is not unlike that of this other most famous physicist, Francis Crick, arguably the "pope" of molecular biology. Crick also started in physics and mathematics at University College, London, where he engaged in research involving X-ray crystallography. His PhD was about finished in 1940 when the Nazi bombing of London destroyed his lab and all his research documentation. After the war, strongly influenced by Schrödinger's famous 1944 book *"What is Life"*[4], Crick decided to start anew in biology at Lawrence Bragg's laboratory in Cambridge, U.K., where, with James Watson, he discovered the double helix in 1953. This is a rare case where a PhD student does work worth of a Nobel prize. Indeed, only after that did Crick get his PhD, not on DNA structure as one would expect, but on *"X-ray diffraction of polypeptides and proteins"* submitted in 1954 to the University of Cambridge. It should be noted here that his former education in mathematical physics was important when, with other researchers[5], he worked out the Fourier-Bessel transform of an atomic helix, an essential ingredient for understanding the diffraction of X-rays by both proteins and DNA, their helical spatial structures and hence their functions.

The reader may ask what are the reasons for the migration of some physicists from the hard sciences towards biology. In the first half of the 20th century, with quantum mechanics and nuclear physics in full swing, only a few giants such as Niels Bohr, Erwin Schrödinger and Lawrence Bragg got involved early in biology. In the late 1930's, the young German Max Delbruck, under the influence of Bohr, was one of the first to quit physics and devote himself to biological research (on viruses). The period after the war saw an increased effort towards understanding biological processes at the *molecular level*, utilizing tools and concepts from physics and chemistry. However, it is mainly the Watson-Crick discovery of the double helix in 1953 that attracted several theoretical physicists to molecular biology. Examples are Georges Gamow, Maurice Wilkins, John Kendrew, and several others. There is no doubt that, beyond the convergence of reductionist methods in physics and biology alluded to before, the discovery of the intrinsic beauty of the spatial structure of biomolecules, the binary form of the genetic information, the rationality of the genetic code and many other fascinating aspects, exerted a powerful influence on physicists for exciting their imagination and way of thinking.

The second of Berg's co-laureates, Frederick Sanger, was the other genome reader who had already won a Nobel Prize for chemistry (1958) for determining the amino acid sequence of proteins such as insulin[6][7]. Since the inception of the great reward in 1901, only a handful of scientists earned the Nobel Prize twice: Marie Curie, Linus Pauling, John Bardeen, Fred Sanger, true pillars of 20th century sciences, and more recently the chemist K. Barry Sharpless.

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3 DE DUVE Chr., *Life Evolving,* Molecules, Mind, and Meaning, Oxford UP (2002).

4 SCHRÖDINGER E., *What is Life,* Cambridge U.P. (1944).

5 COCHRAN W., CRICK F. and VAND V., The Structure of Synthetic Polypeptides, I. *The Transform of a Helix,* Acta Chryst. 5, 581 (1952).

6 SANGER Fr., *Sequences, Sequences and Sequences,* Ann. Rev. Biochem. 57:1-28 (1988).

7 See recent biographies of F. Sanger: BROWNLEE G. G., *Fred Sanger, Double Nobel Laureate,* Cambridge UP (2014) or JEFFERS J. S., *Frederick Sanger, Two-Time Nobel Laureate in Chemistry,* SpringerBriefs in History of Chemistry (2017).

## Christian de Duve

The second guest from the left in Fig. 1 is our compatriot, Christian de Duve. The scientific work of de Duve had two major episodes. During the first, his laboratory research earned him the Nobel Prize, with Albert Claude and Georges E. Palade *"for their discoveries concerning the structural and functional organization of the cell"* (1974). Shortly after his Nobel award de Duve created the de Duve's Institute of Cellular Pathology (ICP) near Brussels, one of the leading centers for fundamental and applied biomedical research in Belgium. At the symposium for the Queen jubilee, de Duve spoke about "*Towards a second medical revolution based on the biological revolution*".

The second part of de Duve's large scientific-literary oeuvre consists of half a dozen books concerning the origin and evolution of life on Earth. His first book, the remarkable tutorial[8] *"A guided Tour of the Living Cell"*, is intermediate between these two career episodes. The reader is referred to my review[9] of de Duve's books in which his controversy[10] with this other giant of biology, the Nobel Laureate Jacques Monod, looms large.

I wish to relate an incident involving another famous evolutionary biologist, Richard Dawkins of *"selfish gene"* fame. Like de Duve, Dawkins wrote many books on various aspects of life evolution. His writing style is particularly engaging, and the content of his books is often presented from a highly original perspective. I think particularly of his Bible-size book[11] in which he describes evolution on Earth in reverse, that is, starting from existing species today, and traveling back to LUCA, the last universal common ancestor. Having admired that book and most of his other literary productions, I invited Dawkins to lecture at the Belgian Royal Academy, when I was serving as director of the Classe des Sciences. The occasion was a 1999 joint meeting between the science classes of the French and the Flemish academies. I was hoping that Dawkins would take the opportunity to expound his ideas on evolution, particularly his views on the de Duve-Monod controversy. Both Dawkins and de Duve gracefully accepted my invitation, and we all were eager to listen to great and informative lectures. Unfortunately, just one week or so before the event, Dawkins instructed his secretary to inform me over the phone that he cancelled his appointment. Thank you very much, but that left me with a big hole in the program and the embarrassment of finding an urgent replacement. When I informed de Duve, he confided to me that "Dawkins is accustomed to the fact" and "I will see what I can do". The next day or so, de Duve kindly told me not to worry: one of his close friends, a certain Manfred Eigen (Fig. 1), had accepted his invitation to come to Brussels, on a week's notice, mind you! That was a big relief, thank you Professor de Duve, and the meeting was extraordinary. In the evening, I had the great honor of sharing an elegant dinner with the two gentlemen at the good Faculty Club restaurant of the university of Leuven, in the magnificent Groot Begijnhof of old Leuven.

Returning to his laboratory research career, de Duve perfected and used the *cell fractionation* technique throughout his work. The method, introduced in cell biology by Claude and complemented by Palade with transmission electron microscopy (TEM), consisted in fragmenting the cells in order to identify, name, and determine the respective functions of the its constituents. Fractionation is a version, at the micron scale of cell biology, of the general

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8 DE DUVE Chr., *A guided Tour of the Living Cell,* W.H. Freeman and Cy, N.Y. (1984); *Une visite guidée de la cellule,* De-Boeck-Westmael, Bruxelles (1987).

9 LUCAS A. A., *A la Grand-Messe Darwinienne, les Evangiles selon de Duve et selon Monod,* Revue des Questions Scientifiques, tome 181 (2), 153-175 (2010). Professor de Duve himself approved this review by mentioning, in part, "…une analyse lucide et fouillée de la pensée de Monod et de quelques autres évolutionnistes contemporains… » (private communication).

10 Briefly, for understanding the origin of life, Monod claims that "le Hasard" did it while de Duve advocates "la Nécessité". See MONOD J., *Le Hasard et la Nécessité",* Seuil (1970).

11 DAWKINS R., *The Ancestor's Tale:* A Pilgrimage to the Dawn of Life, Houghton Mifflin, (2004).

reductionist method of atomic and nuclear physics (and, generally, of most experimental methods of knowledge acquisition) consisting of crushing or fragmenting the poor object of study by brute force and examining what the fragments and their functions are.

One component of the cell fractionation method is the physical technique of *centrifugation*, a further brute force treatment of the fragments themselves. The circumstances and the concrete application of the technique in the hands of de Duve can be followed in de Duve's Nobel lecture[12] or in the report of one of his collaborators[13]. The centrifugation was applied to large eukaryotic cells.

The next step into the deep was to apply the fractionation-centrifugation to much smaller cells (bacteria). One spectacular work along these lines was that of two American researchers, Mat Meselson and Frank Stahl[14] who used E. coli bacteria and applied *centrifugation of its DNA in a density gradient*. In a book by Holmes[15], the experiment has been dubbed *"the most beautiful experiment in biology"*, if not in the whole of sciences up to that time (1957-58). The experiment aimed at demonstrating the mechanism conjectured by Watson and Crick in the last sentence of their fabulous 1953 double helix paper: the replication of the DNA of all organisms is likely to proceed via a *semi-conservative mechanism.* Namely that each of the two complementary strands of a parent molecule could serve as a template for the synthesis of two daughter molecules identical to the parent. This was a major speculation which, if true, would constitutes a true jackpot for genetics, namely, to reveal at last the basis of heredity at the molecular level. I have explained elsewhere[16] in some detail what the experiment consists of. It is so beautiful that here I will try to describe its essentials, although the complete story has necessitated Holmes' full book.

The centrifugation procedure made a most elegant recourse to a modern isotope methodology as well as to a basic physical principle known since antiquity. The gist of the method was to fully mark the DNA molecules of a parental E. coli bacterial population with the heavy nitrogen isotope $N^{15}$ (by raising the bacteria in a broth containing exclusively $N^{15}H_4Cl$). Then at time t = 0, the bacteria were abruptly switched to a medium with a nitrogen source $N^{14}H_4Cl$, containing exclusively the light isotope $N^{14}$. After that switch, the newly grown bacteria would incorporate progressively more of the $N^{14}$ isotope in their DNA. By *"lysing"* the bacteria to recover the DNA, samples of the original heavy parental DNA and of the lighter DNA taken after the switch were then *"weighted"*. The weighting procedure was carried out by a powerful technique specifically designed for the purpose, that of DNA *centrifugation in the density gradient* of a CsCl aqueous solution. The method is based on the antique Archimedes principle of buoyancy (Fig. 2).

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12 DE DUVE Chr., *Exploring Cells with a Centrifuge*, Nobel Lecture, December 12, 1974.

13 WATTIAUX R., *Christian de Duve et la découverte des lysosomes et des peroxysomes*, Revue des Questions Scientifiques, 181 (2), 203-214 (2010).

14 MESELSON M. and STAHL F. W., *The Replication of DNA in Escherichia coli*. Proceedings of the National Academy of Sciences of the United States of America, 44(7), 671–682 (1958). These authors certainly deserved a Nobel prize for their extraordinary feat but a prize for Physiology or Medicine was awarded, in 1969, to Max Delbrück, Alfred D. Hershey, and Salvador Luria for elucidating another replication mechanism, that of viruses.

15 HOLMES F. L., *Meselson, Stahl, and the Replication of DNA*: A History of "The Most Beautiful Experiment in Biology", Yale UP (2001).

16 LUCAS A. A., *Scribbles that changed the course of human affairs*, Mémoire de la Classe des Sciences de l'Académie royale de Belgique (2004).

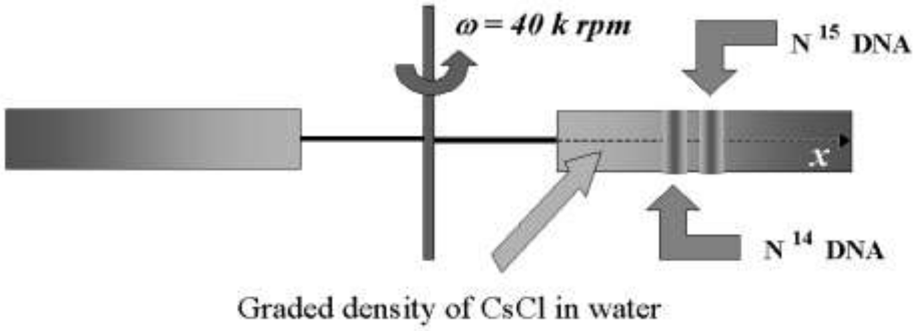


Fig. 2 – Principle of the separation of two isotopically different DNA molecules in a gradient density. The increasingly dark shading of the solution indicates an exponentially increasing density of CsCl towards large x. The two isotopically different DNA's sediment in two different bands. For this test two equal amount of isotopically pure bacterial populations were used (see last pattern in Fig. 3).

The lighter CsCl component sediments quickly with a density increasing exponentially towards increasing distance x from the rotor axis (Fig. 2). The DNA component itself sediments more slowly and comes to a resting distance where its so-called buoyant density coincides with the local CsCl solution density. The two isotopically and buoyancy different DNA become separated into bands at two different positions in the tube. Fig. 2 shows the banding pattern of a test sample containing equal amounts of the two isotopes.

The time evolution of the banding pattern for the real experiment is shown in Fig. 3. It is readily understood if it is assumed that DNA is a dimer, not necessarily a double helix, and that the replication is semi-conservative. The initial parental DNA dimer is designated by H-H (H for heavy) in Fig. 3 and gives one single band. Then after the switch to $N^{14}$ a new H-L band appears progressively while the original H-H band fades away. When the first bacterial generation is completed, a homogeneous H-L population is reached which sediments to a single band. In the second generation, the H-L dimers in turn are split and each monomer is again complemented with a freshly synthesized L monomer, leading this time to two distinct H-L and L-L bands of equal intensity, *etc*. The experiment fully demonstrated the semi-conservative replication proposed in the Watson Crick model. It had the additional virtue, rarely so clear cut in scientific research, of contradicting unambiguously other competing models, the conservative and dispersive replication models[17].

[17] LUCAS A. A., *ibid.*

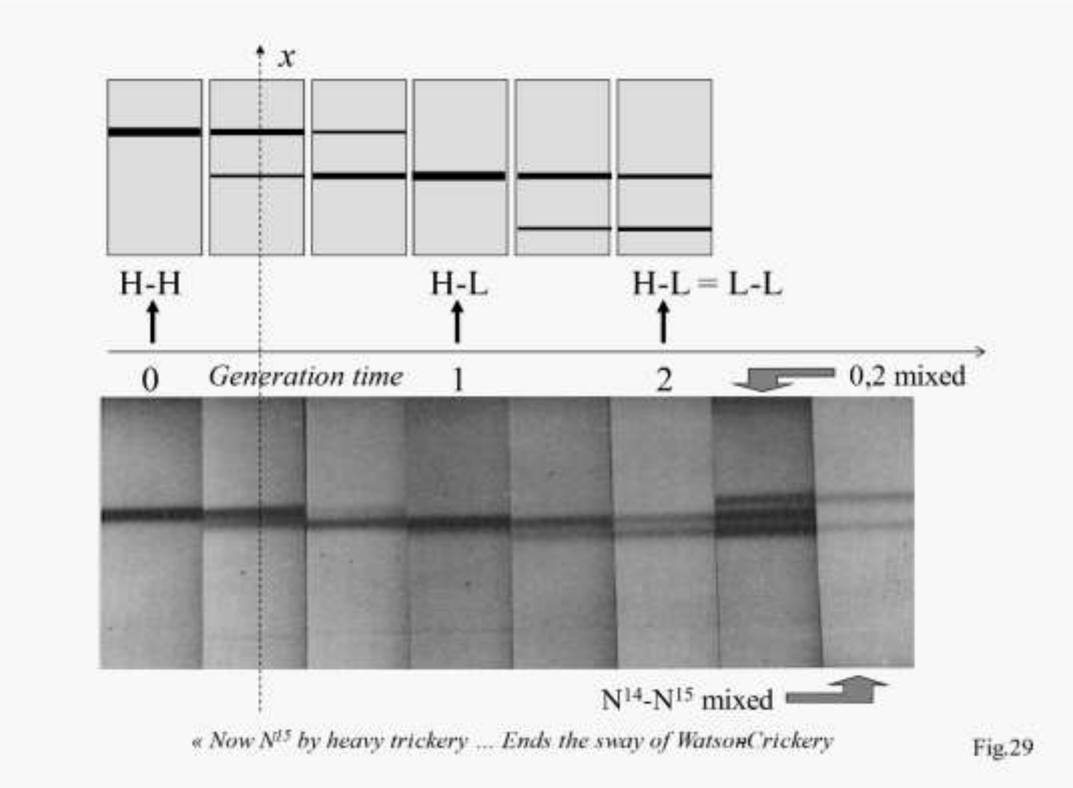


Fig. 3 – Observed DNA banding (bottom, composite photo) compared with the expectation (top) from semi-conservative replication. The two additional photo panels on the bottom right are control experiments: the first with mixed H-H and H-L samples and the second with mixed H-H and L-L.

After this exquisite experiment and the earlier crystallographic and biochemical data, there could remain little doubt that the Watson-Crick double helix was structurally as well as functionally correct. As a poet (Meselson)[18] said, *"Now $N^{15}$ by heavy trickery … ends the sway of Watson-Crickery"*.

The mathematical analysis of the experiment is a marvelous application of Einstein's treatment of particle diffusion (for the Brownian motion) in one of his epoch-making publications of 1905. I will not go into the reasoning here as it requires a strong mathematical background.

## Steven Weinberg

The third guest in Fig. 1, at Queen Beatrix's immediate right, is Steven Weinberg, co-laureate, with Abdus Salam and Sheldon Glashow[19], of the Nobel Prize in physics (1979) *for their contributions to the unified theory of weak and electromagnetic interactions*. This electro-weak theory laid the foundation for the *Standard Model of particle physics*. It included

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[18] HOLMES F. L., *loc cit.* p.126. This verse appears in a Letter from Mat Meselson to James Watson, Caltech, 8 November 1957. In this letter, Meselson states: *"Who would have imagined that, with all the other great good luck we've had, the DNA molecules would replicate at the same rate"*. Not only was the DNA replication rate the same but also a good synchrony of the division cycle in the entire cell population must have been achieved. Otherwise, the heavy band may have remained somewhat visible while the lighter bands developed.

[19] GLASHOW S. L., SALAM A. and WEINBERG S. (1961). Weak and electromagnetic interactions. Physical Review Letters, 8(4), 79-80. https://doi.org/10.1103/PhysRevLett.8.79

predictions about the existence of new particles, the W and Z bosons, which were discovered at CERN in 1983, the year when Queen Beatrix received Weinberg and company in The Hague (Fig. 1), one more reason to celebrate. At the symposium, Weinberg talked about *"A modern view of the Origin of the Universe*".

Weinberg's literary production, like that of de Duve, is quite impressive. One of his technical books is about the modern quantum field theory (QFT). This is an advanced, three-volume text for teachers and PhD students in elementary particles physics. In an attempt not to die without understanding the basics of QFT, I tried to read Volume I on "Foundations"[20] but I confess I was unable to make progress at this advanced level of abstraction. Which means, I suppose, that physics is also highly compartmentalized, like chemistry or biology. Fortunately, there are several, less demanding texts on introductory QFT[21]. However, some of Weinberg's popular titles such as *The First Three Minutes, Dream of a Final Theory* and *Facing Up* are very accessible and inspiring.

I talked to Weinberg once over the phone. In April 1999 I was privileged to organize a fantastic conference at the Académie Royale de Belgique (ARB) while I served as director of the Classe des Sciences. Since this was the last year of the century, I proposed to look back and set up a symposium on the grand theme *Reflections on 20th Century Sciences*. Of the 20 prestigious speakers initially invited by the organization committee which I chaired, 15 responded positively and attended, including de Duve and six other Nobel laureates. Two laureates declined: one was Steven Weinberg who honestly told me over the phone: "*Professor Lucas, thank you very much for your kind invitation, but you can't afford to invite me*", implying that my budget wouldn't be adequate to cover his astronomical travel expenses and honorarium; the other was Ilya Prigogine who dismissed the symposium by saying: "*I have already done this twenty years ago"*. Apart from these small annoyances, the conference was a great success and a landmark in the recent history of the outreach activity of the Belgian Academy.

Weinberg co-laureate, Abdus Salam (after supervising Walther Gilbert's PhD, as mentioned before) dedicated part of his career to promoting scientific research and education. His commitment to advancing the scientific enterprise on a global scale led him to create the ICTP, now called the Abdus Salam International Centre for Theoretical Physics in Trieste, Italy. This institution has played a great role in providing training and support to students and researchers from developing countries in the fields of theoretical physics. Senior scientists from the developed nations were invited at ICTP to provide supervision and foster exchange of ideas and collaboration on research projects, including in condensed matter physics. I was lucky to take an active part in this program when I stayed at ICTP for several months in the early 1970's and where I met new colleagues and collaborators[22].

## Manfred Eigen

The laureate at Queen Beatrix's immediate left in Fig. 1 is Manfred Eigen. He is a major figure in the modern discussion of biological evolution. As stated earlier, he was a close friend of de Duve who himself, as I described, worked for a long time on researching the subject. De Duve would probably have approved my spending a little more time here commenting on Eigen's contributions.

Eigen was a German chemist awarded the Nobel Prize in Chemistry in 1967 with Ronald G.W. Norrish and George Porter *"for their studies of very fast chemical reactions, where the*

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[20] WEINBERG St., *The Quantum Theory of Fields* Volume I: Foundations, Cambridge University Press (1995).

[21] One of them is by MANDL Fr. and SHAW G., *Quantum Field Theory*, 2nd Edition, Wiley (1999).

[22] See details in LUCAS A. A., *I had a Dream,* Adventures of an Insomniac Physicist, Mémoire de la Classe des Sciences de l'Académie royale de Belgique (2023).

*equilibrium between reactants and products is disturbed by a light pulse or a shock wave."* At the symposium in The Hague, Eigen described "*Experiments on Biogenesis"*.

When members of the general scientific community discuss Eigen, the most important ideas which come up are not so much those mentioned in the Nobel citation but rather his later work on *quasi-species and hypercycle* in the evolution of *molecular populations*, the work which was also the topic of his lecture in The Hague. These were new concepts which should have earned Eigen a second Nobel Prize. However, his initial expertise in fast chemical kinetics was essential for his jump to molecular biology. By bridging this gap, Eigen's new ideas contributed significantly to the advancement in understanding the early steps in the origin of life. Indeed, before Eigen's new work, many people (not professional evolutionists of course) felt "in their bones" that the Darwinian intuitive argument *Survival of the Fittest* could be little more than a tautology. By giving precise mathematical meaning to the words *survival, fitness, fidelity, etc.*, Eigen *et al.*[23] were able to formulate quantitatively Darwin's powerful natural selection mechanism, at least for the simple test tube models of evolving populations of self-replicating molecules such as RNA.

The models of pre-cellular evolution of polymeric molecules constructed by Eigen *et al.* are based on three fundamental assumptions: i) the molecules must be self-reproducing; ii) reproduction occurs with errors, that is with variants or mutations; iii) the molecular population evolves far from equilibrium (by a steady supply of energy-rich monomers). To test his theories, Eigen and his collaborators conducted *experiments in vitro* (in test tubes) with RNA molecules and observed how the population evolved under a selection-mediated, *"error correction"* mechanism following replication.

Beyond these basic ideas, the theory is far too technical and goes beyond my competence to attempt a simplified presentation here. What I want to discuss a bit further, however, is one of the key concepts introduced in Eigen's models, namely this *error correction* mechanism just mentioned. In the general context of evolutionary theory, error correction leading to *fidelity in reproduction* is a fundamental aspect of natural selection. The importance of fidelity was acknowledged in evolutionary synthesis theories of the early 20th century which integrated genetics with Darwinian evolution. Eigen's mathematical models incorporate an error correction process adjusted to avoid the excessive loss of genetic information called error catastrophe. The correction involves a selection mechanism at the level of the kinetic equations for the evolution dynamics leading to *quasi-species*.

Here, I wish to make a connection between Eigen's error correction and an explicit molecular correction process, proposed about the same period, by John Hopfield[24] who called it *kinetic proofreading* or *editing* in replication. Today these textbook terms are associated with DNA or RNA replication (as well as with translation in ribosomes). They refer to the ability of the gene replication enzyme to identify a mismatched nucleotide and replace it by a correct one following the prescription of the biological code. Already in the 1960s researchers suggested that in view of the observed high fidelity of replication in the prevalent Brownian noise of the biochemical fluid environment, a correction mechanism of one type or another must operate during the copying process. The proposed models, however, lacked the functional detail of Hopfield's mechanism. The proofreading efficiency described by Hopfield is easy to understand, along the following lines. It is generally accepted that the initial step of nucleotide insertion occurs with an error rate of order $10^{-4}$, consistent with the free-energy specificity of the nucleotide interactions. Now, suppose that the polymerizing enzyme, while working, is also able to edit the transcript with a similar error rate of $10^{-4}$. Then the overall replication will have

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[23] EIGEN M., MCCASKILL J. and SCHUSTER P., *Molecular Quasi-Species,* J. Phys. Chem. 92, 6881-6891 (1988). This is a shorter version of the paper by the same authors in Advances in Chemical Physics, 75, 149-263 (1988).

[24] HOPFIELD J. J., *A New Mechanism for Reducing Errors in Biosynthetic Processes Requiring High Specificity*, Proc. Nat. Acad. Sci. USA, Vol. 71, No. 10, pp. 4135-4139 (1974).

a fidelity of $10^{-4} \times 10^{-4} = 10^{-8}$, which is about the accuracy required (and observed) for genomic stability. Hopfield calls the process *"kinetic"* because the correction is applied to the *kinetics of the replication steps* rather than relying solely on the Boltzmann factor of the free-energy difference between the correct and faulty nucleotide insertions.

It is important to note that while Eigen's error correction is operating at the level of the entire molecular *population*, Hopfield's editing takes place at the level of each *individual molecule*. Although Hopfield's paper is not mentioned in Eigen's publications, both concepts complement each other, and aim to explain the reduced errors in the transmission of the biological information.

Like many of his predecessors and contemporary researchers in molecular biology, Hopfield started (and pursued) his research career as a physicist. His PhD (1958) was on the *polariton*, a hybrid quasiparticle emerging from the interaction of light with polarizable matter at long wavelengths. In my own PhD thesis (1966) of which I sent a copy to Hopfield, I improved on his polariton theory by extending it to all wavelengths. I have exchanged with him some of my results on the dielectric constant of molecular solids. In turn, he publicized the dispersion relations of polarization waves in rare-gas crystals, a concept which I introduced in my thesis to discuss the relative stability of two crystal structures of this material.

## Nicolaas Bloembergen

The guest at Queen Beatrix's far left in Fig. 1 is Nicolaas Bloembergen. He shared the 1981 Nobel Prize in Physics with Arthur Schawlow and Kai Siegbahn "*for their contribution to the development of laser spectroscopy*". At the symposium in The Hague, Bloembergen spoke in Dutch about "*De toepassing van lasers in de natuurwetenschappen en de techniek"*.

Bloembergen, a Dutch American physicist, was born in the Netherlands, studied in Leiden and Utrecht, and emigrated to the USA in 1948, spending all his professional career at Harvard University. His major contributions to physics and lasers were in nonlinear optics which describes phenomena occurring when light of very high intensity interacts with matter.

It can be surmised that the presence of Bloembergen among the five distinguished scholars in Fig. 1 stems from his Dutch origin. Note that monarchs in the Netherlands who want to invite Nobel laureates have a wide choice, given the abundance of Nobel Prize winners from their country. Indeed, there are two dozen of such highly distinguished personalities of Dutch nationality or of Dutch origin in all fields, as many as 10 in Physics alone. This is a rather puzzling statistic given that Belgium can boast of only about 5 such ultimate distinctions, among them Christian de Duve and Albert Claude. One possible origin of such a large difference between the two countries of similar populations is that the first Dutch physics laureate (1902) was the formidable physicist Hendrik Antoon Lorentz who was awarded the Prize one year after the creation of the Nobel awards (the first one in physics in 1901 being Wilhelm Roentgen[25] for his discovery of X-Rays in 1895). However, centuries before Nobel, the open intellectual environment and public support of academic scholarship in the Netherlands were very conducive to scientific achievements. Witness such Renaissance giants as the telescope inventor Hans Lippershey, the French philosopher-mathematician René Descartes (religious refugee in Amsterdam), Anton van Leeuwenhoek (Microscopy) and Christiaan Huygens (master of light). More recently, Johannes van der Waals (thermodynamics of fluids), Pieter Zeeman (magnetism), Kamerlingh Onnes (superconductivity) and several others enhanced the impetus for achievements in the sciences.

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[25] Roentgen's family moved from Germany to the Netherlands in 1845 when he was three years old. He grew up and received his early education in the Netherlands before returning to Germany for his higher education.

Bloembergen spent his entire research career on understanding various aspects of the interaction of light with matter, from infrared to ultraviolet frequencies. He gave a fascinating *interview* on his work for the Vega Science Trust website[26] created by my late friend Harry Kroto, Nobel laureate for the discovery of the molecule C60 of platonic geometry. About the only thing that I share with Bloembergen is that I have also been privileged to be invited by Harry to record a video in his studio of the University of Sussex in Southampton on the subject *"How X-ray cracked the structure of DNA*"[27].

Bloembergen's recent biography[28] characterizes him as a *Master of Light*. As such he belongs to a very long, ongoing *"line of candles"* in the history of light. A final digression here on that history will show the reader how much the nature of light has fascinated humanity throughout the centuries since the advent of the scientific method.

## The Nature of Light

The dynasty began with the master of classical physics, Isaac Newton, who claimed that light is made of particles. Christiaan Huygens, whom I mentioned previously, already contested Newton with a model of wave propagation. Then the polymath Thomas Young proved Newton wrong and Huygens right by demonstrating, with his double slit experiment, that light is a wave phenomenon. During the 19th century, several researchers, including Joseph von Fraunhofer and Gustav Kirchhoff, established the principles of spectroscopy and used atomic line spectra to investigate the star elemental composition. Then the genial Scottish physicist James Clerk Maxwell confirmed theoretically that light was indeed a wave, propagating at a constant velocity independent of frequency. This demonstration was a consequence of Maxwell's unification of electricity and magnetism, two formerly unrelated fields. Next Heinrich Hertz confirmed experimentally Maxwell's prediction that electromagnetic waves (of low frequency, later called radio waves) could be generated and detected in the laboratory. Then came the most prominent of all *"Masters of Light"*, Albert Michelson[29][30], whose interferometer works on the principle that light can interfere with itself, that is behaves like a wave. In 1900, Max Planck discovered that light energy is granular, proportional to its frequency hν, where h is a new constant of nature. No dynasty in science can be recounted without mentioning the supreme *"troublemaker"*, Albert Einstein who asserted that light in the photoelectric effect indeed behaves as a stream of discrete energy packets, that is as particles later called photons. Shortly afterward, Niels Bohr was first to relate atomic line spectra to absorption and emission of light in transitions between discrete atomic energy levels. Skipping some fifty years, Edward Purcell, and Felix Bloch, in the late 1940s and early 1950s, used microwaves of the electromagnetic spectrum to produce nuclear magnetic resonance in bulk matter (NMR). At about the same time Willis Lamb also exploited microwaves to demonstrate the *"Lamb shift"*, a subtle effect in the sixth decimal place of the energy levels of hydrogen. Lamb's measurement launched quantum electrodynamics (QED) on its final formulation by the trio of theorists Sin-Itiro Tomonaga, Julian Schwinger, and Richard Feynman. QED finally reconciled the particle and wave aspects of light by showing that photons are the elementary excitations of the quantized electromagnetic wavefield. An experimental group of *masters*, the Nobel Laureates Charles Townes, Arthur

[26] *Reflections on Science Videos*, http://www.vega.org.uk/video/programme/27.
[27] *Reflections on Science Videos*, http://www.vega.org.uk/video/programme/80.
[28] HERBER R., *Nico Bloembergen, Master of Light*, Springer (2019).
[29] MICHELSON LIVINGSTON D., *The Master of Light*, A biography of Albert A. Michelson, The University of Chicago Press (1979).
[30] LUCAS A. A., *Albert Michelson and his Interferometer, Master of Light, Lord of the Spinning World,* Cambridge Scholar Publishing (2023).

Schawlow, and *Nicolaas Bloembergen* (see Fig. 1), invented masers and lasers for everyday use. Another theoretical trio of Nobel Laureates, *Steven Weinberg* (see Fig. 1), Abdus Salam and Sheldon Glashow, lengthened the series by showing that light was a manifestation of the unified electro-weak force.

Cosmology also has a profusion of masters of light, particularly the saga cosmologist Edmond Hubble who, in 1929, demonstrated a correlation between the distance of a distant galaxy and the redshift of its light. Our compatriot Georges Lemaitre found a solution of Einstein's equations which described an expanding cosmos, thereby explaining Hubble's observations. Later, Robert Wilson and Arno Penzias accidentally discovered the cosmic microwave background radiation, one of the major observational pieces of evidence for the Big Bang theory of cosmology.

This list of masters of light is very partial. It includes only what comes to the mind of a typical professional physicist. I have not searched for candidates in the interim period since the 1970's. And the list is not about to close : just last year a new trio of masters, Anne L'Huillier, Pierre Agostini and Ferenc Krausz, have been awarded the 2023 Nobel Prize in physics *"for experimental methods that generate attosecond pulses* ($10^{-18}$ s) *of light for the study of electron dynamics in matter".*

There will be no pause in the study of the interaction of light with matter.

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Résumé

L'auteur présente cinq savants, lauréats d'un prix Nobel, qui apparaissent sur une photo aux côtés de la reine Beatrix des Pays-Bas, à l'occasion de son 50$^{e}$ anniversaire.

Abstract

The author introduces five Nobel Prize-winning scholars who appear in a photo with Queen Beatrix of the Netherlands at the occasion of her fifty's anniversary.