100 years of modern biology

Unesco

This ceremony commemorated the centenary of the deaths, two years apart, of Mendel and Darwin whose independent work so profoundly affected modern scientific thought. The talks which were given on this occasion are included in this present brochure.
Men have always been fascinated by the mysteries of life and have tried to fathom them by the light of their own philosophical conceptions and with the scientific means at their disposal. Several theories were thus put forward over the centuries, revealing one after another their merits and their shortcomings. Then the theory of evolution gave biology a fresh impetus which was reflected in several other disciplines of the natural and social sciences, revolutionizing one by one many areas of thought.

Biology enjoys a special status among the various branches of knowledge, for it deals with the question which for many constitutes the ultimate ambition of all knowledge, namely the question of man’s place in the universe; and for that reason the appearance of the theory of evolution was to raise fundamental questions in epistemology, ethics and politics, as well as in science.

That revolution was it is true, part of a long process of successive discoveries and hypotheses, crowning all that had gone before and at the same time transcending it; but it was also the handiwork of a man of genius who not only carried out long years of experimentation but brought to the task a brilliant capacity for synthesis.

Charles Robert Darwin was born in 1809; his grandfather, Erasmus Darwin, was also the grandfather of Francis Galton, the founder of the science of eugenics, which is closely related to genetics and the evolution of living organisms. Charles Darwin began by studying medicine and then theology, but at the age of 22 a chance occurrence was to determine his career: he was invited to set sail as a naturalist aboard a ship which left England in 1831 to carry out chronometrical surveys around Latin America and the Pacific Ocean.

His eager interest in the wonders of nature which he encountered in the Cape Verde Islands, Brazil, Patagonia, Tierra del Fuego, Chile, Peru and the Galapagos, and then in Australia and South Africa, gave Darwin his aim in life. He recorded thousands of observations on coral formations, rock
stratification, volcanoes, glacier systems and the prevalence and behaviour of countless animal and vegetable species. Everything Darwin was to publish later was directly derived from the information gathered on that expedition.

After his return to Great Britain at the end of 1836, Darwin came to the conclusion that the many questions raised by the diversity of animal and vegetable species could only be answered by proposing that species were capable of transformation, of gradual mutations. The evolutionary concept of the descent of a given species from preceding species thus appeared to him to be the most rational hypothesis.

The idea of evolution did, of course, exist long before Darwin’s time: Anaximander had thought that living organisms could undergo transformation, and Empedocles had arrived by intuition at a sort of natural selection; but these were still only philosophical speculations, having no direct connection with observation and experience. Modern transformism began in the eighteenth century, when several naturalists worked on the hypothesis of the variability of species.

Darwin provided scientifically verifiable evidence for the concept of evolution drawn from palaeontology, embryology, comparative anatomy and bio-geography which he used as a basis for building up a connected coherent theory providing a detailed explanation of how species originate and thus rendering intelligible a mass of previously inexplicable facts.

Although Darwin’s theory subsequently dominated the whole of biology, it was to remain basically incomplete until the mysteries of heredity had been fathomed. It was Mendel’s work which was to give evolution the underpinning it lacked, that of genetics.

Gregor Johann Mendel was born thirteen years after Darwin, in Silesia, then part of the Austro-Hungarian Empire. At the age of 21, he entered the Augustinian Monastery at Brno, Czechoslovakia. After being ordained a priest, Mendel left the monastery in 1847, with a certain amount of scientific knowledge to his credit. He then taught Greek and mathematics before taking an examination for certification as a teacher, which incidentally he failed because his marks in biology and geology were not high enough. After studying botany, zoology, chemistry, physics and mathematics for two years at the University of Vienna, the young priest returned to Brno where he taught natural sciences for fourteen years. Gregor Mendel carried out his first scientific experiments in a small monastery garden in 1856, the same year that Darwin, overcoming his last misgivings, started to put on paper his ideas on the origin of species. Two years later, Darwin and Alfred Russel Wallace were to read a joint paper on evolution and natural selection before the Linnean Society of London.
In the meantime, Mendel was continuing his experiments on the hybridization of the pea, noting constant differences in various physical characters such as height, colour, seed shape, pod shape and the position of the leaves and flowers on the stem. In 1865, Mendel presented the results of his research before the Brno Natural Science Society, and published them in 1866.

By providing a first description of the mechanism of heredity, Mendelian genetics gave Darwin’s theory a new depth that was thereafter to be investigated more and more systematically, in particular by such scientists as Fleming, Finlay and Claude Bernard. Although Darwin accepted the inheritance of acquired characters, it is now known that it is not the variations which subsist, but the genotypes. It is the chromosomes—strings of genes, each of which determines a particular character—discovered by Fleming in the nucleus of cells, which are transmitted from parents to offspring and at last explain how characters can be inherited. As Claude Bernard said, all hypotheses are thus permitted.

As we can see a century later, Darwin’s work was so rich in its implications that it is difficult to appreciate them all. From neo-Darwinism to gradualism and post-gradualism, the most significant contemporary theories are to be seen against the vast backcloth woven for them by *The Origin of Species*. Darwinism is still a fixed point of reference, even when it is criticized.

Others will speak in more detail than I about the vast fields of knowledge opened up by Darwin’s discoveries. I am about to give the floor to two eminent scientists, the first of whom, Professor Albert Jacquard, Head of the Genetics Department at the Paris Institute of Demographic Studies will speak to you about the links between genetics and evolution; Professor Josef Riman, of the Czechoslovak Academy of Sciences, will then talk about the aftermath of Mendel’s work.

I should like to conclude these remarks by drawing your attention to some of the qualities which Darwin and Mendel shared and which today are more than ever necessary in any scientific inquiry. Both of them combined an attachment to research and comparison, patience in the face of the complexity of facts and cautiousness as to the conclusions they were to draw from them, with an ever-alert curiosity and intellectual boldness which led them both to discover previously unknown horizons, one in his travels beyond the oceans and the other in the confines of a monastery garden.

That is why the quality more characteristic of them than any other is perhaps the gift, the truly aesthetic gift, of wrenching from the mysterious multiplicity of things the secret of their fundamental structures, that gift whereby scientists are akin to poets in perceiving, each in his own way, the hidden music of the world.
All living beings are related—
Selection and chance in nature

by
Albert Jacquard
Director of the Department of Genetics
Institut national d'études démographiques
Paris

What we are concerned with is living things—that is, everything on our planet that is capable of struggling to survive, both individually (a struggle which is, of course, destined to fail) and collectively, through reproduction. It is important that we should view living things lucidly. It is our responsibility towards Life which is at issue. It is significant that this meeting was organized jointly by two bodies which stress man’s responsibility—Unesco and the Universal Movement for Scientific Responsibility.

The starting-point for this discussion will be the observation that all living things are related. Everything on earth that is capable of reproduction or procreation—and we shall see later how the two terms differ—all these organisms, whose fabulous diversity we marvel at, share a common family tree, for it seems that the origin of life is indeed one. This is a very old idea, long based on anatomical resemblances, similarities in embryogenesis or the identical nature of mechanisms for regulation. We now have quite decisive additional evidence of this oneness. Take, for example, protein structures: a protein such as cytochrome C, having the same function in man, in certain animals and plants, even in the most primitive living things, has practically identical chemical structure in all. Further evidence of the common origin of forms of life has been found in the genetic code (which translates the information in the chromosomes into protein structures) which is the same for all living things. The oneness is proof positive in my opinion that all living things are related. But since we are all different from one another—and how different!—we must have branched off from our common origins; evolution, as it is called, must therefore have occurred.

Evolution, as the Chairman has just remarked, is an old idea. And although it is now associated with Darwinism, you should know that the term Darwinism existed—as recently pointed out by Jacques Ruffié—before Charles Darwin. Darwinism was the subject of controversy even before Charles Darwin was born, it being based on the ideas spread abroad by his grandfather, Erasmus Darwin. Charles Darwin, it is true, was indeed the
first to develop and propagate the idea. After Darwin, everyone understood that evolution was a fact that had to be taken into account.

However, the purpose of science is not only to describe and present facts, but also to seek explanations for them. Beyond the chronology of evolution, which palaeontologists are progressively putting together, someone must imagine a process or mechanism that tells us why it occurred in that way and not another. Darwin was the man who suggested such a process: natural selection. This resulted from the synthesis of two concepts. The first was the one Malthus invented in the early nineteenth century: in a given environment the resources are insufficient for all the living things born into it to survive; some of them are therefore eliminated. The second concept, which Darwin developed by observing animals, particularly in the Galapagos Islands during the long voyage that has just been described, was that there was a struggle among living things for access to resources. In nature, everything took place as if there were selection. The term selection suggested to Darwin the work of breeders to increase milk production in cows, wool production in sheep or speed in horses. Breeders selected the best animals and made them procreate more than the others. For wild species, there were no breeders, but nature did the same job. The battle between individuals, the struggle for survival, played the same part. There was thus selection, but instead of being artificial selection, it was natural selection. The process suggested by Darwin is therefore clear: the fittest survive and hence they can transmit the characters that helped them survive to their descendants. The reasoning seems flawless. However, upon analysis the first part proves self-evident—the fittest survive actually because the fittest are defined as those who survive—and is therefore arguing in a circle, but the second part is erroneous, assuming that the survivors transmit their characters, whereas sexually reproducing organisms like ourselves are incapable of transmitting their characters.

This is the fundamental problem, and Darwin was well aware of it, moreover. In attempting to explain the evolution of living things, that magnificent transformation which extended perhaps over three thousand million years, he realized that he could not understand what happened when two sexually reproducing organisms united to create a third. He could not explain sexual reproduction. He realized this and temporarily adopted a working hypothesis, 'pangenesis', according to which each character of the child tends, saving the chance exception, to be the arithmetic mean of its parents' characters. This seems like a perfectly natural idea; the child is the arithmetic mean of its parents: a tall man and a short woman produce a child of average height. However, in developing this hypothesis, Darwin realized that it would not concur with reality.
For, by definition, a character varies from one individual to another: there is an element of variability. If the child were really the arithmetic mean of its parents, the process of procreation would inevitably entail homogenization, since if a man whose head circumference was small had a child by a woman whose head circumference was big, the child's head would have an average circumference. In general terms—and this can be demonstrated mathematically—a process that makes of the child the average of its parents is a process that tends to lessen variability. In that event, all characters would become homogeneous, which is contrary to observed experience. So there is a mistake somewhere.

Throughout the latter part of the nineteenth century, biometry, that is the mathematical study of the characters of living things, was marked by the paradox of variability. The fact is there; variability has not diminished; whereas the hypotheses we put forward to explain the transmission of characteristics indicate that such variability should disappear. What is to be done? The reasoning is not false, nor are the calculations; the weakness lies in the concepts. As it happened, realistic concepts were known at the time, but no one had understood them. They were discovered by Mendel. Several years after the famous Darwinian revolution, another took place but remained imperceptible: the Mendelian revolution. To my mind, it was infinitely more profound and, in the end, more effective in clarifying our outlook on living things.

What was Mendel's contribution? He provided, at last, the answer to the mind-boggling paradox that two individuals could manage to make a third. How could a unitary being have two origins? The answer the Greeks gave was that only one of these origins counted: for them, the man who made a child was like a baker who put a loaf in the oven; the woman merely played the passive role of the oven. In the same way, even today, it is possible to read in works explaining procreation to children: 'You were born because one day your Daddy put a seed in your Mummy's tummy'. This explanation confers an important role on the seed, hence on the father, and a very minor role on the ground, the mother. All these views, which are false, give pride of place to one sex. Defenders were also found for the theory of ovism, as opposed to the theory of animalculism: the woman contributed everything and the man very little. The equality of the roles of man and woman was firmly denied.

This process was invented ages ago. For a long time, at the beginning of life, a being reproduced itself, that is to say, that it divided itself in two and made two beings resembling itself. This 'one makes two' provides the numbers, but does not provide diversity. One and a half thousand million or two thousand million years ago, two individuals, the real Adam and Eve, by virtue of quite extraordinary imagination, reversed the process: instead of
one becomes two', they achieved 'two becomes one'. But this changed everything, and, until Mendel, no one understood how it came about.

What did Mendel have to say? In order to explain the fact that two may produce one, it had to be supposed that the one, despite appearances, was not unitary, but profoundly dual. This is the essential Mendelian concept. The contribution of Mendel, rather than the famous laws of Mendel, is this extraordinary idea that, behind the unity of appearance, there is the duality of causes. So each individual was dual. Let us take a current example, unknown to Mendel. After a blood test, a laboratory may tell you that you belong to group A. On the surface, there is oneness, but in reality we possess two factors that define the type. This idea was so revolutionary—replacing unity by duality, admitting that there was permanent dual control of all our characters—that no one understood it. Admittedly, Mendel lived in a small town, little known at that time, Brno, and the Bulletin of the Natural History Society of Brno was not very widely circulated. But that does not explain the scant attention given to his ideas. He attempted to discuss them with several distinguished colleagues, but it was not until 1900 that his ideas were accepted. There was no choice, since the development of cytology showed that there were indeed, in the nuclei of our cells, these famous chromosomes that come in twos. If they came in twos, that was probably because they were the support of the dual factors mentioned by Mendel.

That made all the difference, especially for our understanding of procreation. The child was dual, and each of its parents was dual. The most natural hypothesis, that put forward by Mendel, was that each parent provided half of himself. But what half? A mixture. And who made this mixture? Certainly not the parents. The question 'who?' could not be answered. Half the genes of the father and half those of the mother were selected. The verb 'to select' is, however, a verb of action and logic requires that it should possess a subject. This subject is unknown to me, said Mendel, and I therefore call it 'chance', thus providing the following definition of this highly awkward and controversial word: I call chance the subject of the verb 'to select' when I use the verb 'to select' without knowing its subject. Perhaps this subject does not exist, in which case we are faced with a different problem, a metaphysical one this time. However, logic demands that chance be introduced as a third agent. When procreation occurs the two parents think that there are only two of them involved. In fact, there are three, and it is the third agent, chance, that plays the most important role.

This conceptual revolution was so radical that even now it has not been brought home to people, and the role of those bodies that wish to make scientists assume their responsibilities, and to perform the function of promoting the cause of clear thinking consists of spreading this idea more
widely. What has changed is our entire outlook on living things. And also the explanation of evolution.

In 1900, when Mendel’s views were vindicated, a keen struggle took place, for there were some who felt that these represented a reversion to pre-Darwinian ideas. Mendel was portrayed as an opponent of Darwinism. At first Mendel was rejected, and then, when there was clearly no means of getting away from him. Darwinism was, so to speak, given a Mendelian flavour. By dint of mathematics this neo-Darwinism was developed, which was a revised version of Darwinism in which Darwin’s hypothesis regarding pangenesis was discarded and Mendel’s theory of genetic transmission was retained. By means of a great deal of mathematical calculations a theory of evolution was thus able to be developed which, some twenty years ago, had fairly well carried the day. It provided a sound explanation of observed facts.

For some years now, however, this note of triumph has come to be sounded far less often, for this neo-Darwinism is a long way from being able to explain things as they are. Curiously enough, as the twentieth century draws to a close, we find ourselves faced with a paradox quite similar to that which exercised men’s minds in the late nineteenth, taking the form of the maintenance of polymorphism. For while neo-Darwinism clearly makes it possible to explain how it is that some measure of diversity is maintained between the species and, above all, within the same species, the diversity that is thus explained is necessarily limited. And we discover that polymorphism, i.e. the variation between one individual and another within the same population, is far more pronounced than had ever been imagined. First the techniques of electrophoresis and then those processes that now enable us to describe proteins, and even the structure of DNA by means of which we produce proteins, reveal to us the prodigious spectrum of diversity. The very crux of the neo-Darwinian theory of evolution is, however, that, in a given population, the survival of the fittest leads to homogeneity.

However, the fact of the matter is that there is no homogeneity. Once it was realized that reality could not be explained by a theory, however well founded and sound, basic assumptions had to be called into question. At the present time geneticists, and more specifically population geneticists, whose field of study is concerned with the working out of models of evolution, have the impression that, for them, everything remains to be done, or has to be done all over again. They adopt one of two approaches. Some reason as though they had understood Mendel before understanding Darwin. Admittedly, it is a somewhat derisory intellectual game to rewrite history by inverting dates, but imagine that Darwin had not been able to make his ideas known and that those of Mendel had rapidly gained acceptance, what theory of evolution would have been developed? A theory of evolution whose main
feature would have been the taking into account of the role of chance, of random factors, in the shaping of an individual. It would not have taken into account the varying abilities of individuals to survive and procreate but, rather, the influence of chance upon the transmission of the genetic heritage from one generation to another. This is the approach adopted by some mathematicians—the most renowned is a Japanese mathematician, Kimura—who are developing what is referred to as a ‘neutralist’ theory. Of course they do not claim that Darwin was wrong, but they seek to propose a theory of evolution in which, at least in its initial phases, Darwin is conspicuous by his absence: we have not heard about Darwin, we do not know what natural selection is, but we are faced with the fact of evolution; we note that, on the basis of a line of reasoning that simply introduces the random drift of gene frequencies, we are able to explain a large number of observed facts. In particular, the structural evolution of such proteins as cytochrome C, haemoglobin, fibrinopeptides, and so on, can be explained fairly satisfactorily by means of a theory of evolution that is keyed not to natural selection but simply to the role of chance in transmission from one generation to another. What can be demanded of a theory other than that it should concur with the facts? And it so happens that a number of facts, not all of course, can be satisfactorily explained by this neutralist theory.

In this theory, which owes a great deal to mathematics, Darwin has been well-nigh forgotten. Another approach is being explored, especially by biologists and zoologists. They take into account the manifest truth that in nature the struggle for life exists. The various beings do not all have the same power to survive, the same power to procreate. If neo-Darwinism as it has been developed in the second third of the twentieth century does not provide an explanation for everything, it is because it over-simplifies. As with every theory in its infancy, it has had to proceed by way of reductionism. No doubt it has overdone it. In particular, attempts have been made to link the ability to survive and procreate, in other words, the selective value or fitness, to a single pair of genes, that is, to a single elementary character. It is, however, quite clear that selection does not act upon any particular one of our characters but upon the individual as a whole, i.e. upon an entire complex of characters. Let us try, then, to build up a theory which instead of linking the selective value to a single pair of genes, links it in the first instance to two such pairs. It turns out that the transition from one to two, as is often the case, reveals a radical change in the theoretical findings. For if the combined effect of the two characters studied on the ability to survive and procreate is not simply the result of multiplication or addition, then it is clear that there are other forces of interaction at work. It is seen that a particular unfavourable gene may become widespread in a population for it is associated with
another, favourable, gene. The very concept of a good or bad gene becomes utterly meaningless since a gene's ability to be good or bad for an individual depends not only on what is contributed by the gene itself but also on what is contributed by the genes with which it is associated. A great deal of research is currently being carried out, in particular by biologists like Richard Lewontin at Harvard, with a view to defining these interactions more closely. Certain strange phenomena are thereby being brought to light, such as that known to the Americans as hitch-hiking, in which one gene appears to get a lift from another. A gene that has a slightly negative effect upon the selective value is carried along by a neighbouring gene that exercises a highly positive effect. The final upshot is that we no longer know whether the gene that has been propagated was good or bad. What becomes of a gene results not only from its specific contribution to the individual but also from the interaction between its specific contribution and the contributions of the genes with which it is associated. In other words, the outcome is the result of the interaction between independent series of causes, a phenomenon described a century ago by Augustin Cournot as chance. Thus the two approaches currently being explored in order to explain polymorphism lay emphasis on the role of chance. In one, chance is what I might term the raw material of evolution and is at the root of diversity. In the other, it is accepted that everything is determined, but chance has to be introduced in order to develop the necessary probabilistic reasoning.

In both these approaches the key term is 'chance'. Admittedly, this is no more than a blanket term and needs to be more closely defined. The fact remains that our attitude to living things and, in particular, our attitude to man and to human societies largely hinges on the importance we assign to chance. If everything is really deterministic, if everything is really the result of mechanisms in the face of which we are helpless, then there is no longer any scope for freedom. Conversely, if chance is present, if man is really able to help create not only his environment but also to some extent, himself, then there is scope for freedom. True, we are greatly indebted to Charles Darwin, but it seems to me, as a geneticist, that we are even more indebted to Mendel. He it was who was the first to understand the strange mechanism of procreation that came into being more than a thousand million years ago, which had from time immemorial defied our understanding.
A new high technology—modern biotechnology—has now been put at the disposal of mankind. It provides a real prospect for the recruitment of energetic sources by self-reproducing sources of phytomass and for the utilization of living systems of cells of micro-organisms, plants and animals for work. In the latter case the utilization of the work of living systems for production, processes and services is based on a rational use of, in theory, about 3,000 genes of microbial cells, 10,000 genes of plant cells and 30,000-50,000 genes of mammalian cells. This is a technology with a broad range of practical applications, and is the tool capable of challenging the three acute global problems of our planet, the food, energy and ecological crises.

The major innovative factors of biotechnology are essentially the modern techniques of genetics, a branch of science officially established in 1906 by the English scientist W. Bateson on the occasion of the International Conference on Hybridization and Plant Breeding in London. The foundation of genetics, however, is intimately associated with the name of Johann Gregor Mendel. We shall remember the 160th anniversary of his birth on 22 July this year and the centenary of his death in 1984.

Allow me now to recall briefly his contribution to the development of science in the light of the knowledge of his day and the environment in which he lived, as well as in the context of subsequent development in our knowledge of heredity up to the present time.

An analysis of the origin of J.C. Mendel’s work shows the signs characteristic of every great creative feat of man. It shows its genius of place and time and the originality of the scientific personality with a new methodical and intellectual approach. The work of Mendel is based on the tradition of his native land, Moravia, where from the beginning of the nineteenth century great attention had been paid to sheep breeding for wool production and development of the textile industry, and to the utilization of the principle of hybridization to obtain more productive varieties of cereals,
fruit trees and flowers. *Spiritus movens* of this trend was the educated naturalist Ch.C. André who, shortly after the battle of Slavkov (Austerlitz), submitted in Brno a programme for the cultural and economical advancement of the country. In the same town in 1814 was established an association of sheep breeders encompassing members of middle Europe which, instead of the pioneer English ‘art of breeding’, stressed ‘scientific breeding’ directed at the elucidation of the bases of artificial selection and heredity. There was also created in Brno in 1848 the Agricultural Society with a special Horticultural Section, and after 1861 there existed a special Natural Science Society. Another centre of natural history activity in Moravia at that time was the University in Olomouc, with an outstanding scientist J. Nestler who attached great importance to the problems of heredity.

An integral and significant part of this scientific movement at that time was the place where Mendel worked, the Augustinian Monastery in Brno. Its abbot, F.C. Napp, who was himself an enthusiastic naturalist, directed all members of the monastery towards natural sciences, much against the will of the bishop. Mathematics, physics, meteorology, mineralogy and botany, these were the fields the monks, including Mendel himself, were not only skilled in, but which they also taught at the technical secondary school in Brno. Moreover, Mendel had the chance to complete his education with studies at the University in Vienna, where his main interests were directed towards not only botany, but also mathematics and physics. This erudition, quite unusual in a botanist at that time, markedly influenced his methodical and intellectual approach to the experimental solution of plant hybridization on his return from Vienna. For this purpose Mendel used numerical and probability analysis to transform the seemingly chaotic mixture of various characters in the progeny of hybrids into a simple mathematical regularity. His education in physics is particularly evident in his work on the interpretation of heredity as a set of independent discontinuous elements (now known to be genes). This is quite different from the concept of a uniform, indivisible basis for heredity, which was represented, for example, by the so-called idioplasm of Carl von Nägeli.

Mendel’s work on plant hybridization, to which he gave his attention for ten years, was of a rare, systematic character. It dealt with a single experimental model of the plant *Pisum sativum* prepared by the breeding of twenty-two constant variants with distinct pairs of characters. Results of experiments with some 30,000 *Pisum* plants lent themselves to mathematical processing and made it possible to express for the first time in mathematical terms the basic rules of heredity, later named Mendel’s laws of heredity: the principle of trait segregation and principle of independent trait assortment. They also led to the finding that plant traits are distinct units and
determinants of the material transferred by germ cells from one generation to another, in agreement with the theory of cells expressed by Mendel’s countryman, J.E. Purkyně.

Today we can appreciate the work of Mendel particularly as a basis for the new fundamental method used with all living organisms after the year 1900. In this respect his work differs distinctly from that of the French scientist Gustave Naudin, who also formally expressed the law on gamete purity in hybrids and was thus very near to Mendel’s results.

Mendel reported the results of his ten years’ work to the Natural Science Society in Brno early in 1865. In 1866 his paper on the same topic appeared in its journal.¹ This paper was referred to by Focke in his own paper on plant hybrids, but this was the only citation of Mendel’s work until the end of the nineteenth century. Fortunately, this one citation, led to the work of G. Mendel being independently rediscovered in 1900 by three outstanding biologists, Dutchman Hugo de Vries, German Carl Corrense and Austrian Erich von Tschermak. A similar fate befell the paper by G. Naudin on plant hybrids; this was officially recognized by the French Academy of Sciences as late as 1900, and probably only then thanks to the sudden appreciation of Mendel.

There are two reasons why the works of these two authors were neglected for such a long time. Firstly, there was the increasing authority of Darwin’s theory published in 1859 in his book On the origin of species by means of natural selection, in which hybridization was not directly related to the origin of the species and which therefore generally suppressed interest in hybridization work for a long time. Darwin himself was sceptical of Naudin’s hypotheses and Naudin, as well as Nägeli, did not even take into consideration the results of Mendel. The other reason why Mendel’s work was temporarily forgotten was probably the fact that the biological world between 1865 and 1900 was not yet sufficiently prepared for a full utilization of his pioneering methods. There was no real knowledge of the fertilization process and the mechanism of cell nuclear division so necessary for an explanation of Mendel’s laws. Such data only started to accumulate in 1875 (on the discovery of the fertilization process of the egg by Hartwig, of mitosis in plant cells by Strasburger, of chromosomes by Fleming and the discovery of a constant number of chromosomes by Van Beneden) and this led to the first ideas on the transfer of inheritance by means of a substance of a certain chemical constitution (A. Weissmann in 1885). These ideas were

then supported by the discovery of a special chemical rich in phosphorus, the so-called 'nuclein' (now known to be nucleic acids), in the nuclei of mammalian cells (Miescher, 1869-1871).

These and other discoveries led the German scientist T. Boveri (1887) to think about the relationship between the chromosomes and heredity. A great stimulus to the utilization of Mendel’s analytical method was brought about by the paper by H. de Vries (1900) dealing with the phenomenon of mutation of the genotype leading to permanent changes in the progeny and accompanied by a theory that development may proceed in jumps. All this was considered by the American school of T.H. Morgan (1910-1932), which studied in detail the mutations of genes in the fruit fly *Drosophila melanogaster*. confirmed the results of Mendel and formulated the chromosomal theory of heredity. This theory is based on the discovery of the relationship between the number of groups of genes linked one to another and the number of chromosome pairs, as well as the detection of a linear arrangement of genes.

Another path leading to the discovery of the principle of heredity had appeared shortly after 1910; this was a deeper analysis of the chemical and biological properties of the suspected chemical carrier of genetic information, Miescher’s nuclein. In the period up until 1943, it was found that nucleic acids are composed of four basic units, the nucleotides, and two chemical types of nucleic acid, DNA and RNA, were distinguished (Kossel, Jones, Gulland). Further studies resulted in the elucidation of the tetranucleotide composition of nucleic acids (Levene) and in the analytical approach to the determination of nucleic acids in cells by means of spectrophotometry (Casperson), histochemical (Brachet) and chemical (Davies and Belozerskii) methods. About the same time the first evidence of the biological activity of nucleic aids was being offered by Griffith (1928).

The period from 1944 to 1960 brought forth the first direct evidence that DNA was a carrier of genetic information (thanks to bacterial transformation work carried out by Avery, MacLeod and McCarthy, 1944). At the same time, the existence of transposable genetic elements in maize was being disclosed (Barbara McClintock, 1949, 1950). These two discoveries pointed to a paradox between the stability and variability of the basic genetic material. The mystery of the transmission of genetic information, including the principle of its stability, was explained as late as 1953, when the structure of nucleic acids was disclosed. The problem of variability (i.e. instability) of DNA and its role in genetic processes was resolved as late as the 1970s after the techniques of DNA recombination, so-called genetic engineering, had been introduced. The discovery of genetic recombination of phages (Hershey, 1946) and rapid development of phage genetics
(Benzer, 1959) represent another strong element in the development of molecular genetics over this period.

The fundamental discovery, however, was that of the complementary structure of double-stranded DNA (Watson and Crick, Wilkins, 1953); indeed, this has been considered the discovery of the century. It enabled scientists to elucidate the methods of storage, multiplication and transmission of genetic information from its chemical DNA-form to the RNA-form. This breakthrough, supplemented by the discovery of DNA-synthesizing enzymes (Kornberg, 1961), gave rise to molecular genetics proper, and speeded the development of genetics towards its great goal, the elucidation of the molecular principles of heredity.

The period from 1960 to 1969 was noted for complex chemical, biological and biochemical studies leading to the dramatic disclosure of the genetic code (Nirenberg, Ochoa and Khorana), the determination of the primary structure of RNA and the discovery of the molecular mechanisms of transcription and translation of genetic information (Holley, Sanger, Bayev, et al.), including the idea of the regulation of gene expression (the operon theory of Jacob and Monod, 1962). During the decade the mechanism of DNA synthesis *in vitro* and the existence of extrachromosomal DNA were also disclosed.

Since the early 1970s up to the present time our understanding of the principles of genetics has increased rapidly. This period has been characterized by consecutive discoveries and the increasing role that interdisciplinary work has played in the development of new methods in molecular biology, such as molecular hybridization, DNA sequencing, cell fusion and the large-scale culture of mammalian cells.

This last period has brought forth a series of extremely important discoveries and results, leading to a speeding up of development in molecular biology and genetics, and their introduction into practice. There has been, for example, the reverse transcription performed by an oncovirus enzyme and the mechanism of reproduction of oncoviruses through a DNA-provirus form (Temin and Baltimore, 1970). Further there was the disclosure of sequence-specific deoxyribonucleases, the so-called restriction endonuclease (Smith, 1970), their rapid utilization in physical DNA mapping (Nathans), and the elucidation of the significance of restriction—modification systems (Arber). Of paramount importance not only for cell biology but also for the genetics itself has been the formation of cell hybridomas (Milstein and Köhler, 1975) capable of producing monoclonal antibodies. This work was based on the principles of cell fusion discovered earlier.
In general, this period can be characterized as an era of the most intense
development of molecular biology, and molecular genetics in particular,
opening the way to the elucidation of the structure and expression of genes,
including eukaryotic genes. There were disclosed the post-transcriptional
and post-translational arrangement of the primary products of gene ex-
pression (for example, the existence of Cap-structures and polyA-ends); the
mosaic structure of eukaryotic genes consisting of expressed regions (exons)
and silent regions (introns); the proteolytic splitting of the primary protein
products; and the existence of the so-called splicing process of mRNA,
allowing even the sequence of genetic information to be changed. Direct
evidence was provided for the existence and special properties of the
primary structure of transposons, insertion genetic elements present in
plasmids and in eukaryotic cells which are responsible for the possible
instability of genetic material. Moreover, it was shown that even the
oncoviruses have the properties of transposons. A great arsenal of DNA
vector molecules (plasmids, phages and viruses) was accumulated and
techniques for their modification in vitro were prepared. These techniques,
in conjunction with other techniques of genetic engineering, have enabled
scientists to mix the genetic material and even to cross the interspecific
barriers, thus leading to the creation of new groups of genes and even
genetically changed 'new organisms'.

At the top of the pyramid of accomplishments in this era of gene
manipulation, DNA recombination, or genetic engineering, must be the
development of the automated programmed chemical synthesis of the
eukaryotic gene in solid phase (Edge, et al., 1981). It even opens the door for
the construction of genes which do not occur in nature. Last, but not least,
this period has led to the practical application of all this knowledge to
produce monoclonal antibodies, vaccines, rare human hormones and biolo-
gically active proteins, as well as to develop the productive potential of
micro-organisms in technology.

All the results achieved since the age of Mendel have served to modify
gradually the theories of heredity and evolution. They have provided new
facts to fill the gaps in the existing theories, and have facilitated their more
precise explanation, as well as the creation of new theories. However, they
have not threatened the basic principles and analytical methods of
G. Mendel himself, since he never generalized his results. He regarded
himself as an empiric and never asserted that all his elements (now known as
genes) should behave according to his laws. Such views appeared only after
his death. However, Mendel was well aware of the fact that his findings were
new and original, even if he did not live to see their recognition. He avowed:
‘I knew that it was not easy to tune the results achieved with the present state of science and that under these circumstances the publication by an isolated experimentalist might become twice as much dangerous both for the experimentalist and for the idea he defends.’

Another aspect of current genetical knowledge directly concerns the perspectives of the whole of mankind: this is the potential to utilize living systems rationally for its own service and welfare. This is directly reflected in modern biotechnology, representing an extension of fermentation technology applying the principles of system and process engineering by techniques of gene manipulation, i.e. techniques of genetic engineering and cell fusion, techniques of immobilized living organisms, enzymes, cells and specific cell organelles, as well as large-scale cultivation of mammalian and plant cells, all directed towards bioproduction, bioprocesses and bioservices. This technology now offers the real possibility of increasing fodder and food resources, of extending the medical care at the level of diagnosis, prevention and therapy, of increasing the sources of energy by the production of biogas and bio-alcohols from waste phytomass, of increasing reserves of raw materials for heavy industrial chemistry, of utilizing bioprocesses in light chemistry at the level of hemisyntheses and for the production of waste-free bioplastic materials, and of re-establishing the ecological balance in nature. Here the biotechnological processes can replace those of the chemist, and they include the utilization of immense stores of air nitrogen (estimated at \(10^{15}\) tonnes) by means of soil nitrogen-fixing micro-organisms, thus further increasing plant production. Finally, modern biotechnology also opens real possibilities for the exploitation of poor ores to obtain copper, uranium and many other important metals. On the other hand, they may also be used for the purification of soil and water from toxic metals and chemicals.

Modern biotechnology thus offers great prospects for mankind. It is now up to mankind how these achievements will be used and what conditions and facilities will be established for the purpose. Answering such a question, it would be wise to remember the heritage of another great man, Louis Pasteur, the founder of scientific fermentation technology. He was the contemporary of Mendel, and was actually born in the same year (1882). He hoped that the heritage he left to mankind would result in a very careful consideration of two principles currently operating on our planet: the law of blood and death ever imagining new means of destruction and the law of peace and health, ever evolving new means for delivering man from scourges which beset him. It is up to us to endeavour in genetics, as Pasteur did in microbiology and immunology, such that all practical applications serve the progress and prosperity of mankind. Like Pasteur in his time we all now
believe that ‘science and peace will triumph over ignorance and war’. There is no doubt that such also were the aims of J.G. Mendel’s work, which was an integral part of the stream of scientific activities of his country directed towards the elevation of cultural and economic conditions.