A Brief History of Science
Part 14: Genetics Becomes a Science

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AS WE HAVE seen earlier, two *different* theories of evolution were proposed by Lamarck and Darwin. Lamarck's theory saw evolution as the consequence of direct influence of environment on each individual organism's anatomy and physiology, and the theory rested on the hypothesis that the characteristics acquired within an organism's lifetime are inheritable. Darwin's position, in contrast, was that the main driving force of evolution was natural selection. There is variation within every population, and individual organisms with certain anatomical and physiological features are better adapted to a specific natural environment. These organisms are preferentially selected by nature: they have a larger probability of surviving to maturity and of producing the next generation. Thus certain characteristic traits are selected by nature and certain other traits are eliminated. This is the way the environment actsat the species levelto lead to the evolution of species.

For a long time following the proposition of these two theories it was not clear which theory was correct. There were questions faced by both theories that could not be answered at that time. For example, Lamarck's use-disuse theory could not explain how entirely new organs could evolve, and Darwin's theory could not explain why variation always exists in every population in spite of elimination of variations by natural selection. Initially the main struggle was to defend the theory of evolution in face of the severe opposition by the religious authorities, and only at the beginning of the 20th century did scientists start the serious attempt to subject each theory to strict experimental tests.

Mendel unravels the laws of heredity

For a long time it went unnoticed that Gregor Mendel (1822-1884) had done a series of experiments in the 1860s that provided the clue to understanding the laws of heredity. He did systematic experiments with plants like garden peas. In one experiment, he took the tall and dwarf varieties of garden peas, and first made sure that in successive generations pure-bred plants of the tall variety never produced any dwarf plant and vice versa, and that each variety was easily distinguishable from the other one even when raised in unfavourable environmental conditions. He then obtained hybrid seeds by fertilizing the flowers of one variety with the pollen of the other, and found that the resulting plants were all tall. The dwarf character had disappeared in the first (F_1) generation. Then he obtained the second generation by allowing the flowers to be fertilized by their own pollen, and found to his surprise that the dwarf character has again appeared in a few plants. Careful

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counting revealed that on an average tall and dwarf plants appeared in 3:1 ratio in the second (F_2) generation.

Mendel assumed that there is a 'factor' responsible for tall and dwarf varieties which is inherited through breeding and after hybridization, one of them remains suppressed by the other in the F_1 generation but reappears in the F_2 generation. In explaining the observation, Mendel hypothesized that living organisms transmit the characteristic traits through the reproductive mechanism in form of 'units of heredity' — things that are either there or not there, but do not mix. Some of these are dominant (like the tall character) and some are recessive (like the dwarf character), so that an F_1 hybrid plant carrying both units of heredity would invariably be tall. But in the next generation some of the plants would inherit dwarf-dwarf units of heredity and would exhibit dwarf character, while the plants inheriting tall-dwarf, dwarf-tall, and tall-tall units would all exhibit tall character. If the segregation occurs with equal probability, the F_2 generation will produce dwarf and tall plants in 1:3 ratios. This is Mendel's First Law, i.e., the Law of Segregation. Mendel confirmed the law by experimenting with plants with similarly distinguishable characteristic features (for example, those producing green and yellow seeds).

When he crossed organisms that differ with regard to two traits (say, seed colour: green/yellow and seed surface: smooth/wrinkled), he found that all the plants in the F_1 generation produce smooth yellow seeds, but in the F_2 progeny the characters were appearing in the proportion 9 (yellow-smooth) : 3 (yellow-wrinkled) : 3 (green-smooth) : 1 (green-wrinkled). On careful examination he found that these can be explained if he assumed that these physical features are determined by two

Gregor Johann Mendel (1822-1884)

such units of heredity that were independent with respect to each other. This led to his second law, i.e., the Law of Independent Assortment.

He read out his article 'Experiments in plant hybridization' at the Brunn Natural History Society in 1865, which was published in the Proceeding of the Society next year. But unfortunately scientists of that period failed to realize the importance of Mendel's experiments. Darwin did not come to know about it in his lifetime.

In the year 1900, about 30 years after the publication of Mendel's work, three scientists (Carl Correns, Erich Tschermak von Seysenegg, and Hugo de Vries) each independently chanced upon this work, conducted the experiments themselves, and confirmed that the results were indeed correct.

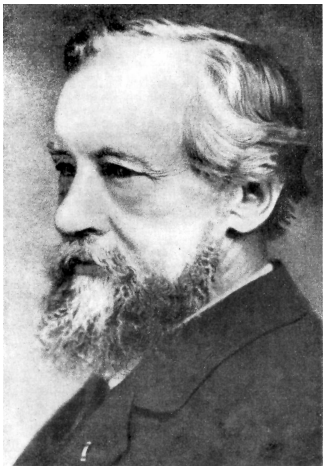
The Dutch botanist Hugo de Vries (1848-1935) did a detailed field study of a species called evening primrose that grew wild in the areas near Amsterdam, and noticed that once in a while plants with new physical traits (for example, a giant variety and a dwarf variety) appeared. He collected their seeds, cultivated them, and found that they bred true, i.e., produced plants with the same characteristics. Yet, in the place where he first noticed these plants, there were no other plant with the same charac-

ter. How did these new characters suddenly appear? De Vries hypothesized that the "units of heredity" can sometimes undergo sudden change on their own, which he called mutation.

The Swiss scientist Albrecht Koelliker (1817-1905) had earlier proposed that evolution proceeds not by slow incremental changes mediated by natural selection as theorized by Darwin, but by sudden changes. De Vries' mutation theory apparently supported this claim. This attracted sharp criticism from scientists of the time because mutation theory appeared to contradict Darwin. However, it was soon demonstrated that mutations do not necessarily lead to large changes in the physical structure of an organism; small variations can also result from mutations. Thus, this theory was not really at odds with Darwin's theory of natural selection. Not only that, it was realized that the occurrence of mutations can plug the big hole in Darwin's theory: It explains how new variations may appear in a species.

The discovery of Mendel's work created quite a stir among the biologists of that time, because it answered some of the questions that had been bugging them for quite some time. But were the Mendelian laws universally applicable? William Bateson (1861-1926), an experimental biologist of Cambridge University, conducted similar experiments on poultry, rabbits, and other animals that breed quickly, and confirmed that these laws apply to the animal world as well. He became instrumental in popularizing Mendel's work through his books "Mendel's principles of heredity — A defense" (1902), "Mendel's principles of heredity" (1909), etc. In 1906, Bateson gave the name "genetics" to the new discipline emerging out of the study of heredity.

Lucian Cuenot (1866-1951) did a very detailed study of inheritance in mice, and



Hugo de Vries (1848-1935)

established that coat patterns and colours can be treated as traits through which the Mendelian laws of inheritance can be tested. W E Castle (1867-1962) in the United States studied the heredity of other mammals in detail (including albinism in rats) and established that the Mendelian laws were valid. The Danish biologist Wilhelm L Johannsen (1857-1927) showed that ordinarily cross-fertilizing plants were more amenable to improvement by natural selection than the plants that normally self-fertilize. He also coined the terms 'gene', 'genotype' and 'phenotype' that are in common use today. Thus, within a few years of the rediscovery of Mendel's paper, the area of genetics was born and was making rapid strides.

But, were the Mendelian laws of inheritance always applicable? We have seen earlier that Mendel carefully selected the traits for study that were clearly segregated — like the tall and dwarf varieties — where there can be nothing in between. But there are many other traits that allow continuous variation. Plants bearing flowers of different colours may sometimes yield flowers of intermediate or 'mixed' colours when crossed.

Human parents of different heights may produce progeny of an intermediate height. How are these cases to be accounted?

Sir Francis Galton, Carl Pearson, and W F R Weldon favoured a statistical approach in biometry to settle the issue. But that was in apparent contradiction with the genetics school led by Bateson. Was inheritance really 'particulate', or was it a continuous variable? Controversy, scientific debates, and heated exchanges ensued. Finally when the dust settled, it became clear that continuous variations can also be explained in Mendelian terms if one assumed that these traits are determined by a large number of genes acting in a cumulative manner. The Swedish plant breeder H Nilsson-Ehle demonstrated evidence of such inheritance through experiments on cereal crops. Though Yule (1873-1949) was the first to propose this hypothesis, R A fisher (1890-1962) was instrumental in uniting the two schools of thought to produce a coherent picture of genetic inheritance.

It became recognized that there is a physical unit of inheritance, called gene. These units are 'particulate', in the sense that a gene is either there or not there in an organism, and cannot be further divided or mixed with each other. The physical characteristics of an organism are determined by the existence or non-existence of specific genes in its body. There can be two or more alternative forms of a gene, called alleles, which can determine a characteristic trait of an organism. Each organism carries a pair of alleles coming from the mother and the father, and its physical characteristics will depend on which of these is dominant and which is recessive. This was the initial hypothesis which was supported by experiments. But later more complex forms of inheritance were found. For example, in some cases neither of the alleles is dominant, resulting in physical expression

William Bateson (1861-1926)

of both the characteristics and intermediate forms. Sometimes multiple genes working together determine the physical characteristics of an organism, resulting in complicated expressions of the Mendelian laws of heredity that can be understood only through statistical analysis of the measured physical features.

Where do genes reside?

Even though Mendel formulated the correct mathematical pattern governing transmission of genes from the observed expressions of their characteristics, he had no idea about the biological mechanisms of their transmission. After the concept of gene was established, scientists directed their attention to this issue. It was clear that the genes responsible for heredity must reside in the sex cells because they are transmitted through sexual reproduction. But by what mechanism does the daughter cell receive the genes from the parent cells and become a complete cell?

Way back in 1879, Walter Flemming (1843-1915) of Germany had shown that the nucleus of every cell contains a thread-like substance that readily absorbed dye and could be studied under the microscope.

These were called chromosomes. Flemming (and another scientist Edouard van Beneden) observed that, when a cell divided, the chromosomes were duplicated and were shared between the two daughter cells.

In the last decade of the 19th century August Weismann (1834-1914) proposed that inheritance only takes place by means of the germ cells, such as egg cells and sperm cells. Other cells of the body, the somatic cells, do not function as agents of heredity. His idea was that changes in the somatic cells do not affect the germ cells, and genetic information cannot pass from somatic cells to germ cells, and on to the next generation.

Wilhelm Roux (1850-1924) formulated several models of the mechanism of transmission of genetic information and concluded that the observed behaviour is possible only if the genes were lined up in a row like beads on a string, and were duplicated exactly. Where can one find such bead-like structure inside a cell? T Bovari and W Sutton made careful study of the components of a cell and realized that the chromosomes fit the bill, and so the bead-like arrangement of genetic information must be residing in the chromosomes in each cell.

Thomas Hunt Morgan (1866-1945), the American geneticist, adopted the fruit fly Drosophila melanogaster for his experimental studies because these organisms reproduce very fast and so successive generations can be studied in a short span of time. Moreover, the individuals carrying a gene and those not carrying a gene can be easily distinguished. His studies established that there is direct association of a particular chromosome and particular features of the organism. In 1920, Morgan conclusively demonstrated that the chromosomes in the nucleus of a cell carry the genes.

He and his students did detailed mapping

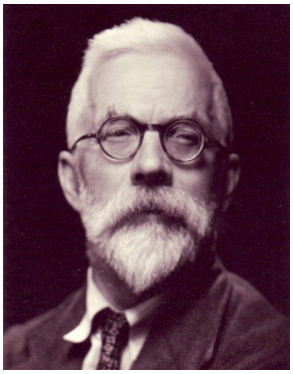
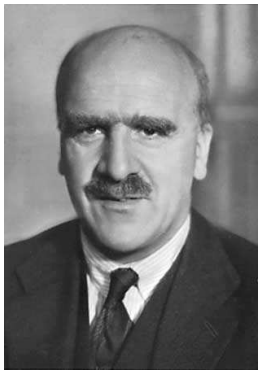
Thomas Hunt Morgan (1866-1945)

of the four chromosomes of the drosophila using techniques available in his time, and showed that genes are discrete units lined up in the chromosome.

In 1910, Morgan and his associates observed the first spontaneous gene mutation in the drosophila in his lab that resulted in the change in colour of the eye. He also discovered a mechanism of genetic inheritance, including linkages and crossovers in chromosomes. In 1915, he and his associates Sturtevant, Bridges, and Muller wrote a very influential book "The mechanism of Mendelian heredity" which summarized all the progress that had been made in genetics till that time.

These developments strongly supported the Darwinian theory of evolution by natural selection and removed its weaknesses. In the 1920s, R A Fisher and J B S Haldane combined Mendelian inheritance with Darwinian natural selection through application of mathematical analysis to population genetics. Through this rigorous approach, they put the genetic theory of heredity and evolution (called modern evolutionary synthesis or Neo-Darwinism) on a firm footing. On the other hand, the developments in genetics were used to refute the Lamarckian mechanism.

What light did genetics throw on the process of evolution? In a population of a

Ronald Aylmer Fisher (1890-1962) and John Burdon Sanderson Haldane (1892-1964)

certain species, the DNA molecule of every individual is not the same. Though grossly similar, there are some finer differences in the DNA molecules in the members of a species. This is what gives them the variation that Darwin talked about. New variations come about when, in the process of copying the DNA in reproductive cells, some errors or mutations occur.

All the animals of a given species are in contradiction with the environment, and the variation caused by minute differences in their genetic code give them unequal survival probability. The ones that survive to reach maturity can transmit their genetic code to their offspring. Thus natural selection favours certain genes while it weeds out the genes that are unfavourable for survival of the animals. This is what causes gradual and quantitative changes in the population. In modern terms, the relative frequency of competing genes changes with time.

Qualitative changes may occur when a new gene that has significant impact on an organism's physiological organization enters the species. In the beginning the mutation happens in one individual. If the result of the mutation is favourable for the survival of the individual, it survives to maturity and transmits the mutated new gene to its progeny. If those with the gene have better survival probability than those without it, the new gene spreads fast through the population, and within a few generations it is found that all the individuals of the population have the new gene. If one looks at the species as a whole, one sees that the characteristics of the population have changed, and it is now a qualitatively new species.

However, such single-line evolution is rarely observed. Branching is a characteristic feature of evolution. How does is come about? When some organisms of a species get isolated from the main population due to some reason and find themselves in a different environment, evolution progresses in different directions in the two populations. As a result, the two populations may become significantly different in their physical characteristics and habits, so that even if they come in contact with each other at a later time, they do not mate. They are then identified as different species. The different lines of evolution can continue after that, due to the reproductive isolation.

This is how quantitative change in the relative gene frequency can lead to a qualitative change in the species.

What are genes made of?

Now that the theory of genes based on their behaviour in determining heredity was firmly established, people turned their attention on the chemistry of genes. Earlier in 1909, A F Garrod had shown that a gene produces an enzyme. Following the lead, many scientists conducted directed experiments and demonstrated that each gene is responsible for the production of a specific protein molecule.

But what kind of chemical structure carries the genetic information? The first conceptual break was produced by the eminent

physicist Erwin Schrödinger. In 1944 he wrote a book titled 'What is life?' in which he argued, citing the stability of genetic information in spite of continuous jostling and collisions among the components of a cell, that the carrier of hereditary information must be a molecule. But what type of molecule? Schroedinger guessed that it would have to be some kind of 'an aperiodic crystal' in order to carry information.

Earlier in 1869 the Swiss biochemist Friedrich Meischer (1844-1895) had shown that chromosomes contain two kinds of molecules: proteins, and nucleic acids. Since proteins, comprising large amino acid chains, can be of immense complexity, people at that time assumed that the protein component of chromosomes is the carrier of genetic information. There was another factor contributing to this belief. The American scientist, Phoebus Levene (1869-1940), chemically analyzed a large amount of RNA obtained from yeast, and found that it contains almost equal amounts of the bases guanine, adenine, uracil and cytosine. He concluded, erroneously, that the RNA was a repetitive arrangement of these bases, and hence cannot contain much information.

But one experiment by the British microbiologist Fred Griffith (1881-1941) indicated otherwise. In this experiment, he took pneumococci bacteria (that causes pneumonia) which has two strains: a virulent one, and another that does not produce much ill effect. He killed the virulent bacteria by heat and injected it into mice. The mice did not develop any disease. But when he mixed the dead bacteria with living bacteria of the non-lethal variety, the progeny developed virulence.

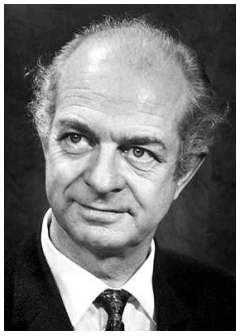
The American microbiologist Oswald Avery (1877-1955) carried this line of work further. He extracted nucleic acid from the chromosome of the virulent bacteria, purified it, and kept it in contact with the non-lethal strain of living bacteria. It was found that the progeny of the living bacteria developed some of the features of the dead bacteria from which the nucleic acid was taken. These transferred traits perpetuated generation after generation, indicating that some genetic change has occurred in the recipient bacteria. Thus, genetic information was transmitted from the killed bacteria into the living ones through the medium of nucleic acid. This showed that nucleic acid and not the proteins in a chromosome contain genetic information. This was further substantiated by A Hershey and M Chase using radioactive tracers. The experiments of Zinder and Lederberg (1952) showed that when a bacterium enters a host cell, it leaves the protein part behind. Only the nucleic acid part enters, multiplies, and takes up a new protein envelope.

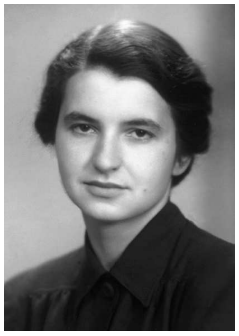
Out of the two types of nucleic acid molecules, it was found that deoxyribonucleic acid (DNA) was the genetic material in most organisms. Erwin Chargaff (1905-2002) then showed that the DNA molecule allows great variability — there are as many different DNA molecules as there are species. The bases found in DNA molecules come in two varieties: guanine (G) and adenine (A) belong to the family of purines, and cytosine (C) and thymine (T) are pyrimidines. Different DNA molecules can have different sequences of these bases. Chargaff additionally showed that the amount of adenine is always equal to thymine, and the amount of guanine is always the same as cytosine.

This was the primary clue when people tried to work out the structure of the DNA molecule. The second clue came from the group led by Linus Pauling who showed in 1951 that some of the complicated protein molecules have a helical structure — the so-called alpha-helix. The third clue came

from crystallographic studies of the DNA molecule (some of the clearest x-ray diffraction pictures were obtained by Rosalind Franklin at King's College, London). A Ph.D student named Francis Crick and a postdoctoral student named James Watson at Cambridge University took a shot at the problem outside of their official assignment. They pieced together the leads provided by the earlier researchers and in March 1953 came up with the double-helix structure of the DNA molecule.

This was the crowning glory of the half-a-century long quest to understand the material basis for heredity. After this discovery, pieces of the jigsaw puzzle came together to form a unified picture. Genetics became a mature science, and progressed in leaps and bounds.





Linus Carl Pauling (1901-1994) and Rosalind Elsie Franklin (1920-1958)

The Philosophical Confusions

All these developments were happening at a time when scientific materialism had developed significantly, and was slowly finding acceptance in the scientific community, but the older modes of thinking — including metaphysics and mechanical determinism — were still prevalent. During the early days of the development of genetics, a lot of things were unclear and confusion prevailed among scientists. In such situations the philosophical position of individual scientists becomes the predominant factor dictating their interpretation of theories. As a result, we see various sorts of confusions in different stages of the development of the theory of genetics.

For example, many scientists viewed the carrier of heredity—the gene—as static and unchangeable. Some viewed an individual organism's physical structure as being fatalistically given by its genetic makeup, with practically no role being played by the environment. Some scientists negated the causal link between the environment and the evolutionary process and opined that the changes are random. We see evidence of such confusion in books, even textbooks, written in that period.

But the most important confusions came from a different angle.

We have earlier seen that in the early phase, capitalism opposed religious bigotry, promoted rationality, and encouraged the development of science and technology. But in the late 19th century, capitalism was approaching old age and was developing signs of chronic diseases. In this system of production, the capitalists own the means of production and employ wage labourers to produce goods. The value created by the labour of a wage-worker is more than the wage paid by the owner to the worker. This is called surplus value and is appropriated by the capitalist owner. The process invariably leads to pauperization of the masses and accumulation of wealth in the hands of a few. Now, the success of the system crucially depends on the market. But since most of the population has very little purchasing power, the market cannot expand in step with production capacity. This results in periodic market crisis and surplus production. From their zeal to gain maximum profit, the European powers had colonized the rest of the world to exploit

James Dewey Watson (born 1928), Francis Harry Compton Crick (1916-2004)

their cheap labour and natural resources of the colonies. But that could not stem the crisis. The early half of the 20th century saw two world wars between imperialist powers over the control of the restricted markets and natural resources.

People do not like war, and in order to get them to support war and the subjugation of one people by another, some theoretical justification needs to be provided. Initially the concentration of wealth in the hands of a few was justified by citing "survival of the fittest"[1]. But the fact is, ever since humankind transcended the phase of purely biological evolution and entered the phase of bio-cultural evolution, natural selection is no longer effective. The survival of individual humans is no longer subject to the vagaries of nature: we wear clothes and build houses so that weather extremities do not affect us; predators no longer pose much threat to us; we are no longer dependent on specific niche diets — we cook and prepare food from a variety of materials available in nature. That is why nature can no longer 'select' specific genetic makeups. Yet it was argued that since man is also an animal, in human society also the fittest should survive. The same "law of nature" was cited to justify the subjugation of the Indian people by the British.

But with the development of genetics, things took a new turn. Now some people started claiming that the white race was genetically superior to the others. In Germany, Hitler took it a step further, to claim that the "Aryan race" was genetically superior to all other races on Earth (including non-Aryan whites like the East Europeans), and so it had the right to rule over the whole planet.

Not only that. An idea was floated that it is possible to improve the human race by selective breeding and by exterminating the people who are perceived to be genetically inferior. Even many common Germans started seeing the Nazi concentration camps as a necessary evil, aimed at creating a better world in future. Thus support of a majority of Germans was obtained by citing a wrong science.

The idea of improving the human race by selective breeding was not confined to the German fascists. The idea was caught by many people, even scientists, of different countries, and a movement, called the Eugenics movement was born out of it!

Yet, at base of such notions was the idea that human qualities like intelligence, compassion, mental abilities, etc., were genetically governed. It has been shown by many scientists that this is a false idea, not supported by evidence. Our physical features — the colour of the skin and eyes, curliness of hair, etc. are genetically governed. Height, weight, physical build, etc., are determined by a combination of genetic factors and our life-style. But intelligence and other mental faculties are completely the product of an individual's interaction with the environment, especially social interactions, through his or her life-time. We obtain the ingredients of our thought from

[1]Darwin did not use this phrase. It was in fact coined by the biologist Herbert Spencer and was promptly caught hold of by the media.

the surrounding society. Through social interactions we come in contact with the thoughts of others, with the cross-currents of various lines of thought. Our minds form through these interactions. And a person who grows up in an intellecually challenging environment has a higher probability of being more intelligent than one whose surroundings do not pose such challenges. Yet, the idea that mental faculties are genetically determined floated in the air, and in spite of being debunked by many scientists, still remains current in modern society.

It is also to be noted that genetics has made spectacular progress by taking a reductionist approach like other natural sciences. Any organism is broken up unto constituent parts, and each part is studied in details. We studied cells, then its nucleus, then its chromosome, then the nucleic acid, and finally the properties of individual genes. But, it has been shown in many areas of science that the whole may be more than the sum of the parts. At some point we'll need to put the pieces together to study the emergent property of the whole.

(*To be continued.*)

* Past installments of this article are available in our homepage www.breakthrough-india.org in the link → Breakthrough magazine → Archive.

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