

of a snail, not living but made by living cells so as to protect them against an unfavorable environment." During the 1970s, NASA considered the possibility of making the planet Mars suitable for human life which included: providing water, oxygen, moderate temperatures, and protection from ultraviolet radiation. The conclusion was that Mars could be made habitable only through the progressive introduction of living species capable of creating, over an immense period of time, more and more complex ecosystems similar to the ones that have evolved on Earth during more than 3 billion years. This analysis has helped us recognize the profound and innumerable changes that life had to bring about on the surface of primitive Earth to create, for present living things, the fitness of the terrestrial environment that L. J. Henderson had taken as the normal state of affairs.

According to the Gaia hypothesis, the Earth's biosphere, atmosphere, oceans, and soil constitute a feedback or cybernetic system that seeks an optimal physical and chemical environment for life. At any given time, this system results in a relative constancy both in the composition of the environment and in the characteristics of living things. Lovelock refers to this equilibrium situation as "homeostasis," a word invented by the Harvard physiologist Walter B. Cannon to denote the remarkable state of constancy in which living things can maintain themselves despite changes in their environment.

The word *homeostasis*, however, does not do full justice to the Gaia concept, which implies in addition that living things have profoundly transformed the surface of the Earth while themselves undergoing continuous changes, in a co-evolutionary process. Practically all the examples that Lovelock discusses refer, in fact, to creative evolution rather than to homeostatic reaction. For example, the accumulation of oxygen in the air which became significant two billion years ago (a result of biological photosynthetic activities) probably destroyed many forms of life for which this gas was poisonous, but species emerged that were capable of living in the presence of oxygen and of using it for the production of energy. In Lovelock's words, "Ingenuity triumphed and the danger was overcome, not in the human way by restoring the old order, but in the flexible Gaian way by adapting to change and converting a murderous intruder into a powerful friend." In this case, as in most other environmental changes, the Gaian way was not an automatic homeostatic reaction but a creative co-evolutionary response.

It seems worth considering that the Gaian control results in global homeostasis only over a period of time that is short on the evolutionary scale. One figure will suffice to illustrate the magnitude of the terrestrial changes that are continuously caused by

life. In their aggregate, all the green plants now fix approximately 840 trillion kilowatt hours of solar energy per year in the form of biomass. This is more than 10 times the amount of energy that all of humankind uses annually, even with its most extravagant technologies. Who can doubt that this continuous turn-over of organic matter and energy must have modified and goes on changing the surface of the Earth. Lovelock predicts that the process of change may pick up speed and complexity as a result of human interventions, and he quotes René Dubos in stating that, on a local level, profound co-evolutionary changes have occurred in certain terrestrial environments and in their biological systems during historical times.

In the last chapter of his book, Lovelock explores the relevance of the Gaian hypothesis to the effects of human interventions into nature. He agrees with René Dubos that environmentalists often aim at wrong targets because the resiliency of the Earth, considered as an organism, probably makes ecosystems more resistant to pollution than commonly believed.

The Gaia hypothesis has not only homeostatic aspects but also creative aspects. This is emphasized by Lovelock's statement that the Gaia concept is an alternative to the "depressing picture of our planet as a demented spaceship, forever traveling driverless and purposeless, around an inner circle of the sun."

RENÉ DUBOS

(EDITED BY RUTH A. EBLEN)

For Further Reading: J. E. Lovelock, *GAIA: A New Look at Life on Earth* (1987); J. E. Lovelock *Healing GAIA: Practical Medicine for the Planet* (1991); Norman Myers, ed., *GAIA: An Atlas of Planet Management* (1993).
See also *Atmosphere; Ecological Stability; Remote Sensing; Space Environment.*

GARBAGE

See *Waste, Municipal Solid.*

GENETIC ENGINEERING

See *Biotechnology, Agricultural; Biotechnology, Medical.*

GENETICS

Genetics is the science of inheritance. Geneticists seek to understand the mechanisms that underlie two of the most curious phenomena of the living world: the preservation of species over many generations, and the

slow but steady appearance of new species. Together these have covered the Earth with an astonishing diversity of living organisms. Aspects of quantitative genetics are related to molecular biology, biotechnology, evolution, and biodiversity.

Quantitative genetics began with the controlled mating of pairs of inbred strains of garden peas that were identical except for single, discrete differences in appearance. From studies in the mid-1800s of the hybrid offspring of inbred strains of pea plants differing by single traits (yellow peas in the pods vs. green ones, for instance), the Moravian monk Gregor Mendel made two discoveries, and from these he was able to construct the first accurate model of inheritance. First, he found that the appearance, or phenotype, of the hybrid offspring was never an "average" or "mixture" of two parental phenotypes, but was always identical to the phenotype of one parent: this was named the dominant phenotype. The parental phenotype that disappeared from view in the hybrid plants was named recessive. Second, he found that although the recessive phenotype was invisible in the hybrid, hybrid plants mated to themselves gave rise to offspring of recessive as well as dominant phenotypes, and did so at a constant ratio of one recessive out of four offspring.

Building on these and other experimental results, Mendel's model for inheritance envisioned the presence in hybrid plants—and by extension in all living creatures—of particles of information encoding the various phenotypes that together make up the form and function of an organism, entities subsequently given the name *genes*. Pollen, sperm, and egg cells—all called gametes—are formed in the bodies of sexually mature individuals by a series of cell divisions called meiosis. In the Mendelian scheme, a complete set of genes is donated to each individual organism by each of its parents as the female parent's egg cell fuses with the male parent's pollen or sperm cell at the moment of fertilization, assuring that each adult organism contains two copies of each gene from the moment of conception. Recessive phenotypes result from the inheritance of two copies of the recessive version, or allele, of a gene. A dominant phenotype may result from two possible genotypes, or pairs of alleles: two copies of the dominant allele or one dominant and one recessive allele would each generate the dominant phenotype.

For this model to work, gametes must contain only one copy—not two—of each gene, and equal numbers of gametes formed in the body of a hybrid organism must contain each parental allele. Then, after the random union of pollen and egg at fertilization, the recessive genotype would occur, at random, one in four times, which was the observed ratio.

Mendel's model, which depended on the existence of

stable genes, was first reported in the 1860s but not recognized by European science until the beginning of the 20th century. Recessive alleles, no less than dominant ones, are stable through time. They need never be "diluted" away, even when they are not visible in the phenotype; a hybrid genotype can be inherited in any number of generations, each generation looking dominant but carrying, undiluted, the capacity to give rise to a recessive offspring. Mendel's insights remain valid today, and they provide clear evidence that earlier—but still prevalent—notions of inheritance operating through the "dilution" of "blood" or some other fluid, cannot be right.

Insightful as it was, the Mendelian paradigm of inheritance was limited in two ways by the laboratory systems in which it was first studied. First, students of population genetics soon showed that most phenotypes seen in nature are not the results of differences in single genes. The ones that are most interesting in humans, height or skin coloration for instance, result from the activities of dozens or hundreds of different genes, each of which might have two or more different possible functional alleles. Even for traits that are the result of a small number of genes, in nature it is usually the case that their gene(s) encode a range of responses to their environments, not an absolute phenotype: inadequate food over a lifetime will keep a person short regardless of whether he or she carries alleles for shorter or taller stature.

Second, Morgan and other geneticists working with simpler organisms like the fruit fly showed that genes are not marbles in a bag, autonomously passed from generation to generation by random assortment in gametes. Rather, they occupy specific positions in the chromosomes that fill the nucleus of each living cell. Thousands of genes on the same chromosome are linked to each other, but this linkage may be interrupted by crossing over during meiosis, so patterns of inheritance are not always as predictable in advance as the one-in-four ratio observed by Mendel.

Molecular Genetics

Genes and genotypes remained mathematical abstractions linked in an obscure way to chromosomes, and the way in which genes and chromosomes were copied at each generation remained a complete mystery, until the mid-1940s, when Oswald Avery at the Rockefeller Institute for Medical Research showed that a bacterial gene was made of the long polymer DNA. Within a decade, in 1953, James Watson and Francis Crick had shown that DNA was a double-stranded helix of indefinite but enormous length, a twisted ladder made of four different kinds of rungs called base-pairs, held in a fixed sequence by two stretches of repeating sugar-phosphate groups. They also showed that while the

outer contour of a DNA molecule was an information-free repeat of these simple sugar-phosphate groups, the four different sorts of inside "rungs" or base-pairs could appear in any order, and that the genetic information of a DNA molecule was contained within its sequence of base-pairs. Finally, and all within a single, 900-word paper in the scientific journal *Nature*, they presented a model for DNA's ability to replicate itself, showing that DNA met this requirement of the genetic material. When one molecule of DNA unzips by the separation of base-pairs, each single-strand of DNA can serve as a template for the synthesis of a new, double-stranded DNA whose base-pair sequence will be identical to the parent model. As they put it:

The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined. . . . It has not escaped our notice that the specific pairing we have postulated immediately suggests a copying mechanism for the genetic material.

Within another decade scientists had worked out the RNA-based mechanisms and the genetic code used by cells to read the genetic information in a stretch of DNA and translate it into sets of proteins, the molecular machines that create the phenotypes we see. From this work the four great generalities of molecular biology arose: first, that the mechanisms of DNA replication and translation into protein were common to the cells of all living things; second, that a gene could be redefined as a stretch of DNA that encoded a protein; third, that each gene was surrounded by regulatory DNA sequences that did not encode protein but rather determined whether or not the protein encoded by that gene would be synthesized in a given cell; and fourth, that changes in DNA base sequence—even as small a change as one base-pair—were the cause of the sudden appearance of stable differences in genotype and phenotype called mutations.

Evolutionary Genetics

The genetic explanation for the universality of basic molecular mechanisms is the simplest: given a common ancestry of all living things, these mechanisms would have been active in the last common ancestor of us all. Then, providing that mutation did not cause their loss, they would be retained in all living things to this day. The notion of evolution, that all living species share a common ancestor, was not first generated by molecular biology. The living world today is separated into tens of millions of populations that are reproductively isolated and genetically distinct, populations we call species. In 1859, the same decade as

Mendel reported on his work with peas, Charles Darwin published *The Origin of Species*, his observations on the universality of variation from individual to individual within a species, and his model of natural selection. In this model, new species may arise from isolated groups of variant individuals within an old species, but only if they have a greater than average capacity to generate offspring and carry them to an age where these can, in turn, inherit variant skills or strengths—called adaptations—and pass them on to yet another generation.

Natural selection requires an environment of limited resources, and a great deal of time so that many generations can be subject to its force. Darwin, working in the absence of information about genes and mutations, and with a very much foreshortened time scale for natural selection (millions of years, versus the 3 billion years life actually has been present on Earth), could not explain how adaptive variations arose, and posited that stress and deprivation may have generated them. There is no conclusive evidence for the notion, also championed by Jean Lamarck, that adaptive mutations can be induced to order by manipulation of an organism's environment. Rather, mutations—even those induced by chemical mutagens—occur at random in any sequence of DNA, and many more variant phenotypes are generated at random than can possibly be adaptive for survival in any set of circumstances.

Darwin also presumed that natural selection would be uniform and gradual in its effects. Today it appears that in more than one instance many species arose rather rapidly (in only a few million years) soon after mass extinction of a fair percentage of all large living creatures. Evidence is increasing that these rare events resulted from impacts of large asteroids. The most recent of these mass extinctions occurred at the Tertiary-Cretaceous boundary about 65 million years ago, killing dinosaurs and other large animals and plants, and allowing the rapid radiation of new species of birds and mammals, including the shrew-like animals that were our earliest mammalian ancestors.

Darwin's original model lacked any mechanism for either the generation of variation or its persistence through inheritance. Mendel's genes provided the latter, and the discovery of mutations—sudden changes in genotype that expressed themselves as new, stably inherited phenotypes—provided the former, at the turn of the century. Mutations occurring at random sometimes generate diversity of phenotype, but always create new alleles. New alleles that are adaptive in a given environment, and those that are merely neutral and not detrimental, will survive over time. As first shown by Ernst Mayr, natural selection can be understood to work by changing the frequency of survival of alleles in small, isolated populations within a species. Mem-

bers of a species may become the genetically isolated precursors of a new species either through physical isolation, or by the inheritance of physiological or behavior barriers to successful mating with other members of their species, or by a mixture of both isolating mechanisms.

While the detailed mechanism of species formation remains incompletely understood, the current vast diversity of living forms is clearly the result of millions of years of differential reproduction of genetic change in isolated groups of interbreeding individuals. Darwin's major insight, that all living creatures are related to each other by descent from common ancestors, remains as valid today as it was 140 years—or 3 billion years—ago.

Genetics and Biotechnology

Just as the discovery of a common genetic code and a common genetic molecule—DNA—shows that all living species are linked to each other through long-lost common ancestors, so the tools developed to manipulate DNA allow genes of all living species to be shuffled into combinations never seen in any ancestral organism. Novel assortments of DNA sequences from different species are called recombinant DNA molecules, and the assembly of them is called gene splicing. The tools and techniques scientists use to carry out gene splicing collectively amount to a molecular form of "word processing." Here the "text" is DNA, a long stretch of information in the form of a unique sequence of base-pairs. The molecular versions of "cut" and "paste" keys are restriction enzymes and hybridization. Restriction enzymes find specific sequences and cut the DNA at precise points, generating short DNA fragments with identical, defined ends. Hybridization of single-stranded DNA re-zips two strands into one double-stranded DNA when the two strands can form an uninterrupted run of proper base-pairs.

The molecular word processor's "software" comes from bacteria and the viruses that live within them. These microbes were discovered relatively recently, not long before Mendel's discovery of stable recessive alleles. Only a century ago the notion that a disease might be the result of a microscopic organism growing inside of people had the same novelty that the notion of a disease caused by a latent allele has today. But current biotechnology uses microbes to carry and reproduce novel genes and the proteins they encode. Molecular engineers "search," "cut," and "paste" DNA sequences by using hybridization to find a gene, then splicing it into a bacterial chromosome for propagation as a recombinant DNA. To learn how genes work, scientists can get them into a fertilized egg cell so that they will be replicated into every cell of an embryo, and their effects over the organism's lifetime can be

observed. Recombinant genes that reach this state are called transgenes.

The polymerase chain reaction, or PCR, "copies" long pieces of DNA that lie between two short, known sequences, generating billions of identical copies of the entire sequence between the two known ends. The root of a hair or the tiniest drop of blood has many copies of an animal's or a person's entire genome and much more to tell—with hybridization and PCR—than a fingerprint. PCR has also democratized the genome. Once a pair of short sequences bracketing a gene are published, anyone can synthesize them at relatively low cost and then use PCR to pull as many copies of the entire gene out of a chromosome, as might be needed for any purpose.

Genetics and Biodiversity

Biodiversity is greatest in the tropical forests, and these are disappearing at an alarming rate. Only a small fraction of all species are known to humankind; humans are killing off species faster than we can even identify them. In a rearguard action, DNA technology can be used to save the genomes of animals, plants, and microorganisms even as the living creatures are killed off. Gene banks, as they are called, are but a pale shadow of the real species, but they are better than nothing, and they will give scientists of the future a chance to reconstruct at least a partial record of the disappearing species. Museums of science and natural history are now being rediscovered as libraries of ancient species, as DNA from preserved specimens and even from fossils is amplified and recovered by PCR. The oldest DNA recovered from a fossil so far is from a plant that lived about 250 million years ago; the oldest animal DNA is from a termite that lived about 30 million years ago. It is sadly ironic that the technology of DNA research has used the universality of this molecule to generate powerful new ways of examining the genes of all species, just as other human technologies are destroying species at an ever-increasing rate. This is a problem the next generation of geneticists must confront.

ROBERT E. POLLACK

For Further Reading: Horace F. Judson, *The Eighth Day of Creation: The Makers of the Revolution in Biology* (1979); Robert E. Pollack, *Signs of Life: The Language and Meanings of DNA* (1994); James D. Watson, *The Double Helix: A Personal Account of the Discovery of the Structure of DNA* (1968).

See also Biodiversity; Biotechnology, Agricultural; Biotechnology, Environmental; Biotechnology, Medical; Darwin, Charles; DNA; Evolution; Mendel, Gregor.