The Handedness of the Universe

From atoms to human beings, nature is asymmetric with respect to chirality, or left- and right-handedness. Clues are beginning to emerge that connect chirality on different levels

by Roger A. Hegstrom and Dilip K. Kondepudi

In 1848 Louis Pasteur, examining a certain salt of tartaric acid under a microscope, noticed that it formed two types of crystals, each one a mirror image of the other. He separated the two, dissolved each in water to form two solutions and shined a light beam through each. To his great surprise, one solution rotated polarized light clockwise, the other counterclockwise.

This beautiful discovery, which he made at the age of 25, led Pasteur to develop a theory of molecular structure. Little was known then about the structure of matter on such a small scale; Pasteur postulated that the two distinct shapes of the salt crystals and their ability to rotate light differently were derived from the fact that the molecules making up the salt were themselves of two types, one "right-handed" and the other "left-handed."

His research along these lines paved the way for another remarkable discovery in 1857. One day Pasteur found that molds had grown in a dish containing an optically inactive solution, one that did not rotate light. Instead of simply throwing away the "contaminated" solution—the common practice—Pasteur checked its effect on a light beam. The contaminated solution rotated light! Microorganisms had changed an optically inactive solution to an optically active one.

On the basis of his molecular theory, Pasteur reasoned that the original solution was optically inactive because it contained equal numbers of right- and left-handed molecules. The molds had reacted chemically with only one type, leaving the solution with a relatively large amount of the other. The imbalance made the solution optically active.

Thus, Pasteur realized that the chemistry of life has a preferred handedness. He came to view handedness as one of the clearest distinctions between living and dead matter and ultimately proclaimed it to be a profound fact of nature that went far beyond the chemistry of life. "Life as manifested to us," Pasteur wrote, "is a function of the asymmetry of the universe and of the consequences of this fact." Later, before the French Academy of Sciences, he made the grand conjecture, "*L'univers est dissymétrique.*"

Pasteur's conjecture turned out to be true to an extent that no one, perhaps even he, imagined. Modern science has revealed that mirror symmetry is often absent in nature: the universe is *dissymétrique* at all levels, from the subatomic to the macroscopic. Many questions about how this asymmetry arises remain unanswered, but in the past few decades some understanding has been gained as to how handedness at one level may give rise to handedness at another. In order to describe what is known and what is not, it is convenient to begin at the scale of everyday objects.

Chiral Asymmetry

Most objects found in nature are not identical with their mirror images and therefore are said to possess chirality, or handedness. To distinguish the two forms, they are often designated right-handed or left-handed. In the case of some familiar chiral entities—hands or screws, for instance—the meaning of right- and left-handed is clear, but for objects such as an elm tree with many branches or for generally irregularly shaped things, the designation is somewhat arbitrary. When certain very simple objects such as spheres or triangles are reflected in a mirror, the resulting image is indistinguishable from the original object. Objects that are identical to their mirror images are termed achiral.

Not only objects but also processes, such as chemical reactions, may exhibit chirality. Certain atomic and nuclear interactions, for instance, display a preference for left or right. If all processes were chirally symmetric, one would observe in the real world an equal number of mirror-image systems displaying opposite preferences. That we do not is evidence that some processes in nature are asymmetric.

Although a chiral object and its mirror image are obviously different, there is no a priori reason that one should be superior to the other. Yet the real world usually does display a preference for one kind of chirality over another. This is strikingly demonstrated in the case of living organisms. Human beings, for instance, are structurally chiral: the heart is to the left of center, the liver to the right. People also display functional chirality. For example, although there is no apparent intrinsic advantage to either the left or the right hand, few people are ambidextrous. Why do individuals generally prefer one hand over the other? Many reasons can be postulated, but the correct one probably is not yet known.

Given that humans generally are not ambidextrous, the next question is: Why are most people right-handed? The dominance of the right hand over the left is universal, independent of race and culture. There would be no apparent disadvantages if most people were left-handed. The greater

ROGER A. HEGSTROM and DILIP K. KONDEPUDI work in the department of chemistry at Wake Forest University. Hegstrom received his B.A. from St. Olaf College in 1963 and his Ph.D. from Harvard University in 1968. His theoretical research has concentrated on the effects of electromagnetic and weak interactions in atoms and molecules. Kondepudi received a B.Sc. from the University of Madras in 1971, an M.Sc. from the Indian Institute of Technology, Bombay, in 1973 and a Ph.D. from the Center for Statistical Mechanics at the University of Texas at Austin in 1979. His interest in the origin of order and complexity has taken him through the disciplines of physics, chemistry and biology.

number of right-handed people seems to be just an accident. One might also ask why right- and left-handed persons are not born in equal numbers. Again, the answer is not known with any certainty, although it is plausible to argue that handedness is an inherited trait: once right-handedness became dominant, for whatever reason, it remained so.

There are other, less prominent examples of chiral asymmetry in organisms. Helical seashells spiral either like a right-handed screw or like a left-handed screw. Right-handed, or dextral, shells dominate—on both sides of the Equator. Among these right-dominated animals, left-handed individuals exist only as a result of mutations, which appear with a frequency ranging from about one in hundreds to one in millions, depending on the species. This "right-hand rule" is not universal, however: certain species—for example, the lightning whelk of the Atlantic coast—are predominantly left-handed, or sinistral. In rare instances left- and right-handed individuals occur in a species in almost equal numbers; the Cuban tree snail, *Liguus poeyanus,* is an example.

Like animals, most types of plants exhibit a preferred chirality. Bindweed winds as a right-handed helix, whereas honeysuckle grows as a left-handed helix. Helical structure in organisms also has been found on the smaller scale of bacteria. Since the 1970's Neil H. Mendelson and his co-workers at the University of Arizona have investigated the bacterium *Bacillus subtilis,* which usually forms right-handed spiral colonies. Remarkably, as the temperature increases, the spiral becomes left-handed!

Chirality in Molecules

As Pasteur found, molecules can also be chiral. Chemists refer to mirror-image molecules as L-enantiomers and D-enantiomers; L and D stand for levo (left) and dextro (right), a relic from Pasteur's studies of optical rotation of light. Enantiomeric forms are found in many organic and inorganic substances and in essentially all molecules crucial for the development of life—specifically proteins, which are responsible for the structure and chemical regulation of living cells, and DNA, the molecule that carries genetic information.

A protein molecule is a polymer, that is, a long chain of smaller molecules—in this case, a chain of ami-no acids. Although several hundred amino acids exist, all proteins are made from the same 20 amino acids. All the amino acids but one (glycine) are chiral, having L- and D-enantiomers. Strangely enough, proteins are made exclusively of L-amino acids. (In very rare cases short strings of amino acids—polypeptides—that contain D-amino acids serve a specialized biological role.)

The main function of certain proteins, called enzymes, is to catalyze biomolecular reactions, including the synthesis of other proteins. The catalytic ability of enzymes depends crucially on their three-dimensional structure, which in turn depends on their L-amino acid sequence. Synthetic chains of amino acids made of both L- and D-enantiomers do not twist in the way necessary for efficient catalytic activity; they cannot form the regular winding structure, called the alpha helix, that is present in most enzymes.
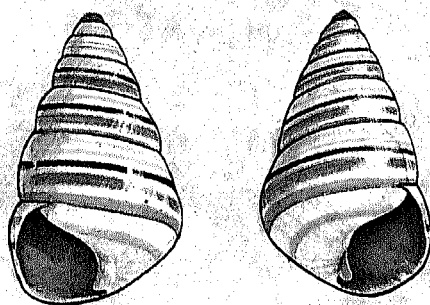
Because of the chirality of its key molecules, human chemistry is highly sensitive to enantiomeric differences. An extreme example came to light in 1963 when horrible birth defects were induced by thalidomide. The defects were caused by the fact that whereas one enantiomer of this chiral com-
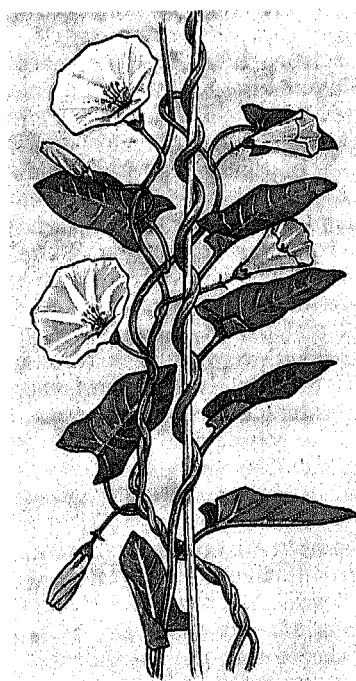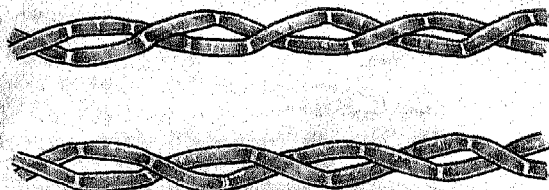

LIGUUS VIRGINEUS

CONVOLVULUS ARVENSIS   *LONICERA SEMPERVIRENS*   *BACILLUS SUBTILIS*

PREFERRED HANDEDNESS is a common trait of living things. Trumpet honeysuckle, *Lonicera sempervirens,* winds to the left; bindweed, such as *Convolvulus arvensis,* winds to the right— like the majority of helical plants. Snails, such as *Liguus virgineus,* are generally right-handed, but within a species, left-hand- ed versions appear owing to mutations. The bacterium *Bacillus subtilis* normally forms right-handed spiral colonies; when heated, these change to left-handed. Atoms and molecules also are asymmetric with respect to left and right, but this has not yet been plausibly linked to the handedness of living objects.
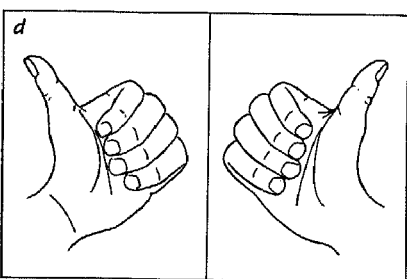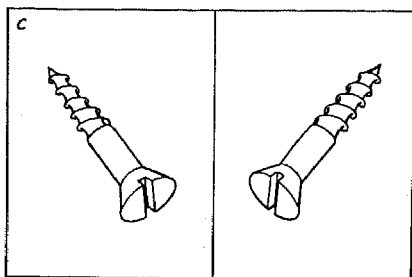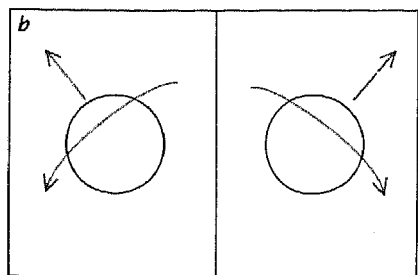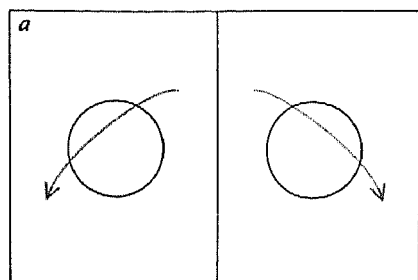
CHIRALITY manifests itself in the distinction between left and right. Objects that cannot be superposed on their mirror images are termed chiral. A stationary sphere is identical with its mirror image and is said to be achiral; even if a sphere is spinning (a), its mirror image can be superposed on the original object by turning it upside down, and so a spinning sphere is also achiral. If the sphere is moving along its spin axis (b), the mirror image cannot be superposed on the original, and the object becomes chiral. By convention, if a spinning object behaves like a right-handed screw as it moves, it is termed right-handed; if it behaves like a left-handed screw, it is termed left-handed (c). The direction of spin is defined by the "right-hand rule": curl the fingers of the right hand in the sense of rotation; the thumb points in the direction of the spin axis (d). (Hands and screws are chiral objects and cannot be superposed on their mirror images.)

pound cured morning sickness, the other caused birth defects. Today the pharmaceutical industry pays careful attention to the separation of enantiomers. A less morbid case of enantiomeric sensitivity involves limonene, a compound found in lemons, oranges and perfumes. Here one can smell the difference: one enantiomer smells like lemons, the other like oranges.

Like proteins, the nucleic acids DNA and RNA are polymers that exist in nature in only one chirality. Each is composed of four types of subunits, each of which incorporates a chiral sugar group. Only the D-enantiomer of the sugar is present in nucleic acids. DNA and RNA ordinarily form right-handed helixes as a result of the exclusive presence of D-sugars. The proper replication of nucleic acids depends on the activity of proteins made of L-amino acids, and so the relative chiralities of proteins and nucleic acids are intimately connected.

The great preference in the chemistry of life for L-amino acids and D-sugars over their mirror-image counterparts is peculiar for two reasons. First, except for extremely minor differences to be discussed later, the chemical properties of the L- and D-enantiomers are essentially mirror-symmetric. Second, when chiral molecules are synthesized in the laboratory from achiral building blocks, equal amounts of L- and D-enantiomers are produced unless painstaking care is taken to introduce an asymmetric agent during the synthesis.

There is a fundamental underlying reason for this symmetry: chemical reactions are essentially a result of the electromagnetic interaction of atoms. The electromagnetic force behaves in such a way that if a given process takes place, the mirror image of that process occurs with equal probability. Any force that gives rise to both a process and its mirror image with equal probability is termed parity-conserving. Because the electromagnetic force conserves parity, one would expect equal numbers of L- and D-enantiomers to inhabit the world. Why is this not so? We shall return to this question after examining chirality at the subnuclear scale.

Four Forces

All known elementary particles interact with one another through four types of forces: gravity, the electromagnetic force (responsible for ordinary chemical reactions), the strong nuclear force (which holds atomic nuclei together) and the less well-known

weak nuclear force. Until 1957 it was thought that nature was chirally symmetric at the scale of elementary particles—that is, that the four forces were parity-conserving. In that year it was discovered that the weak nuclear force does not conserve parity.

As its name implies, the weak force is relatively feeble, about 1,000 times less powerful than the electromagnetic force and 100,000 times less powerful than the strong nuclear force. The most familiar effect governed by the weak force is the production of beta rays in radioactive decay. Beta rays are actually energetic electrons and their antimatter twins, positrons. These particles have an intrinsic spin and hence, when they are moving along or against their spin axes, can be classified as either left- or right-handed. The surprising and now famous 1957 discovery of parity violation by Chien-Shiung Wu and her colleagues at Columbia University led to the recognition that beta particles emitted from radioactive nuclei have a definite chiral asymmetry: left-handed electrons far outnumber right-handed ones.

Further investigations of beta decay led to the discovery of the neutrino and antineutrino, electrically neutral particles that are also emitted in beta decay and that always travel at the speed of light. Like the electron, the antineutrino emitted by radioactive matter has a spin; unlike the electron, it exists only in the right-handed form. No one knows why chiral asymmetry exists at such a fundamental level. Radioactive antimatter emits an excess of right-handed positrons (antielectrons) and only left-handed neutrinos. Right-handed neutrinos and left-handed antineutrinos seem not to exist in the universe.

For the next decade or so it was believed that parity nonconservation was confined to nuclear reactions. Phenomena such as chemical reactions or interactions between atoms and light, which depend on the electromagnetic force, appeared to conserve parity. In the late 1960's, however, Steven Weinberg, now at the University of Texas at Austin, Abdus Salam of the International Centre for Theoretical Physics in Trieste and Sheldon L. Glashow of Harvard University developed a theory that unified the weak and electromagnetic forces [see "Unified Theories of Elementary-Particle Interaction," by Steven Weinberg; SCIENTIFIC AMERICAN, July, 1974]. Their theory predicted a new "electroweak" force between an atom's electrons and the protons and neutrons in its nucleus. The existence of this force, which

does not conserve parity, was confirmed in the 1970's.

Because the electroweak force distinguishes between left and right, atoms and molecules that were previously thought to be achiral must be chiral in some way. Furthermore, enantiomers such as L- and D-amino acids must differ with regard to physical properties, such as energy, that depend on their handedness.

It is now evident that the world is chirally asymmetric at all scales, from the scale of elementary particles upward. How do the asymmetries arise? Are chiral symmetries at one level linked to those at another, or are they independent? We shall attempt to answer these questions, insofar as it is possible to answer them, beginning at the scale of elementary particles.

Chirality of Elementary Particles

At rest, an elementary particle such as an electron or a positron is spherically symmetric and hence achiral. But if a spinning particle is moving in either direction along its spin axis, it becomes chiral. If it behaves like a right-handed screw as it moves, it is said to be right-handed; if it behaves like a left-handed screw, it is said to be left-handed.

Chiral asymmetry at the subatomic level is fundamentally connected to parity nonconservation. According to the Standard Model of elementary particles propounded by Weinberg, Salam and Glashow, the electroweak force distinguishes between left and right through "weak charged currents" and "weak neutral currents." The strength of these currents—referred to as the W and Z forces—between any two elementary particles depends on the distance between the particles and on their "charges."
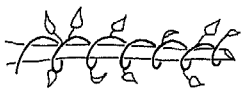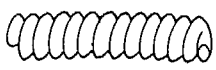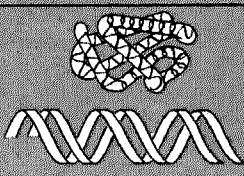
We use the term charge here in analogy to electricity. The electron has a negative electric charge, and the electrical force between any two electrons is repulsive. In contrast, the weak W charge is nonzero for a left-handed electron but zero for a right-handed one. Therefore, a right-handed electron simply does not "feel" the W force. This is considered a fundamental property of the weak force; at present there is no deeper understanding of it. One result of this asymmetry is that nuclear beta decay, which is governed by the W force, produces mostly left-handed electrons.
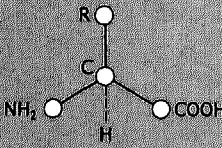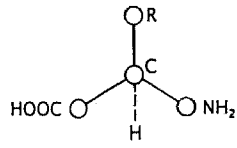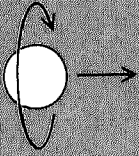
As for the Z force, left- and right-handed electrons have Z charges of opposite signs and approximately equal magnitudes. The difference in sign causes right-handed electrons to be attracted to the nucleus by the Z force and left-handed ones to be repelled. (These statements about the effects of the W and Z charges on chiral electrons are strictly valid only when the electrons are at high energies, traveling near the speed of light. The concepts are nonetheless useful for understanding the chiral asymmetries in low-energy electrons.)

In a looking-glass world, beta decay would produce right-handed electrons, and the Z force would attract left-handed electrons to the nucleus. These processes are not observed in the real world, however, which is another way of stating that the weak

HELICAL SEASHELLS		
HELICAL PLANTS		
HELICAL BACTERIA		
PROTEINS AND DNA	VERY RARE IN NATURE	
AMINO ACIDS		
CHIRAL CURRENTS IN ATOMS	NOT FOUND IN NATURE	
HELICAL NEUTRINO		NOT FOUND IN NATURE

PREFERENCE between left and right is displayed by nature on many levels. Colored boxes indicate the predominant handedness. Most helical seashells are right-handed, but some left-handed species and mutants exist. Winding plants are also predominantly right-handed. Helical bacteria come in right- and left-handed versions. Ordinarily, proteins and DNA wind in right-handed helixes; left-handed versions are rare, and true mirror-image versions do not appear in nature. Right- and left-handed amino acid molecules exist at different energy levels as a result of the asymmetric weak nuclear force; those in organisms are almost always left-handed. The weak force also affects the way electrons orbit the nucleus and so causes atoms in general to become right-handed. The elementary particle known as the neutrino exists only as a left-handed object: its direction of spin points contrary to its direction of motion.

force is chirally asymmetric and that parity is not conserved.

Atoms and Molecules

An important consequence of the weak Z force between electrons and nuclei is that all atoms are chiral. Because of the Z force, when an electron is near the nucleus, its direction of motion is partially aligned with its spin axis, which makes it right-handed [see illustration below]. This means that the electron orbit, which would be circular in the absence of the Z force, becomes a right-handed helix in the vicinity of the nucleus. Because the interaction that causes the helical electron motion does not conserve parity, the mirror-image atom with a left-handed helical electron flow does not exist in nature.

Given the extremely low strength of the weak force, one might expect this helical motion to be unmeasurable. For instance, the Standard Model predicts that in the most favorable experimental setup, light passing through an atomic gas should be rotated by a scant 10^{-5} degree—the angle subtended by a hand at a distance of roughly 1,000 kilometers. And yet during the past decade experimental support for the chirality of atoms has been obtained, including the observation of rotations of the predicted amount [see "An Atomic Preference between Left and Right," by Marie-Anne Bouchiat and Lionel Pottier; SCIENTIFIC AMERICAN, June, 1984]. Here is one clear instance in which a chiral asymmetry at the level of elementary particles *causes* a chiral asymmetry at the higher level of atoms.

On a slightly larger scale, the Z force causes a chiral molecule to exist in a higher- or lower-energy state than that of its enantiomer. The split comes about in a subtle way. First, suppose that one models the chiral molecule as a helix, and imagine the Z force to be "turned off." If an electron with spin "up" is moving "up" the helix, it will be right-handed; if a spin-up electron is moving "down" the helix, it will be left-handed. Because probabilistically equal numbers of electrons in a molecule are moving up and down, one would expect the average electron chirality to be zero.

The ordinary parity-conserving electromagnetic forces between the electrons and the nuclei in the molecule, however, tend to align the axis of each electron's orbit against its axis of spin; this phenomenon is referred to as spin-orbit coupling. For a right-handed helical molecule, spin-orbit coupling favors down-spiraling for spin-up electrons and up-spiraling for spin-down electrons. In either case the spin axis of the electron tends to be aligned against the electron's direction of motion, so that in a molecule shaped as a right-handed helix, spin-orbit coupling produces predominantly left-handed electrons. In regions where the molecule is shaped as a left-handed helix, right-handed electrons predominate. As a result, molecules display regions of differing electron chirality [see illustration on opposite page].

Now switch on the Z force. Because the Z force interacts in different ways with right- and left-handed electrons, it produces an energy shift in the molecules: the energy of one enantiomer is increased and that of the other is decreased.

The Z force is so small that its effect on the chemical properties of molecules has not been observed. An interesting theoretical result, however, has been obtained by Stephen F. Mason and George E. Tranter of Kings College, London. Between 1983 and 1986 they performed detailed calculations of the energies of several L- and D-amino acids, taking into account the

COULOMB FORCE

Z FORCE

COULOMB FORCE

Z FORCE

MIRROR WORLD

REAL WORLD
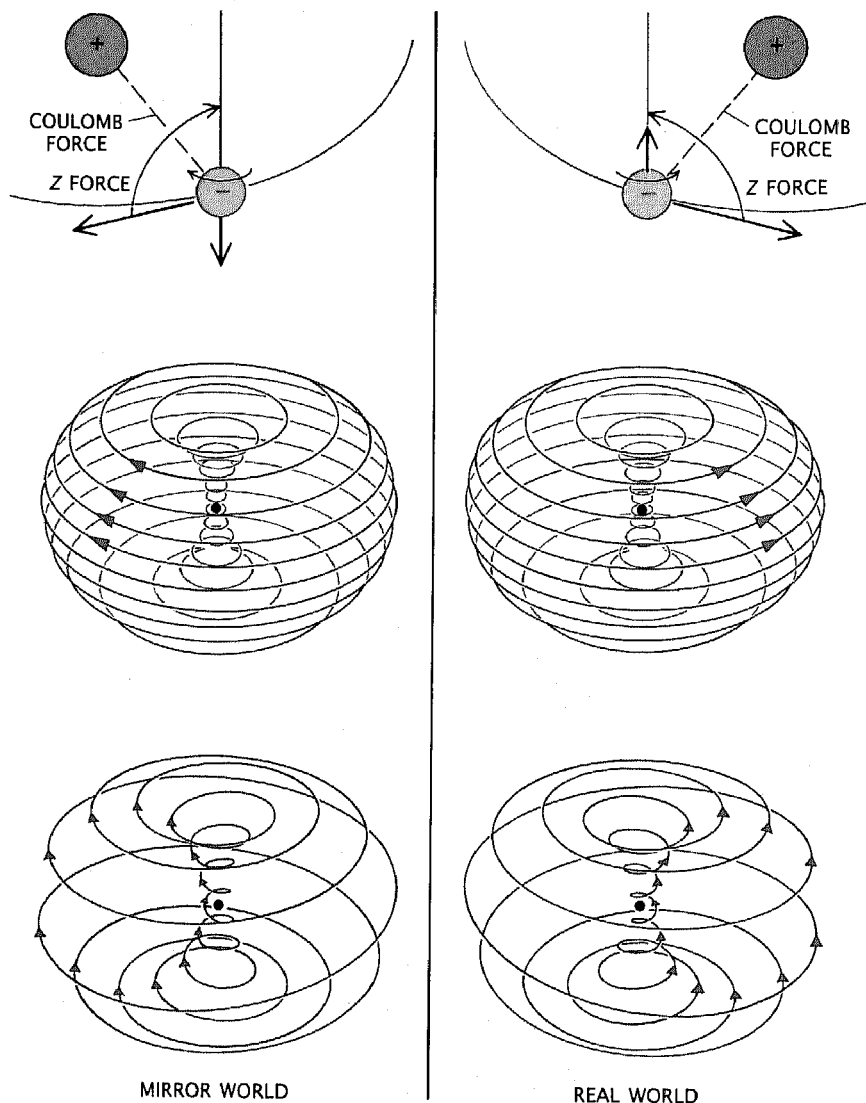
ATOMS become chiral under the action of the weak nuclear Z force. At the top right an electron with spin "up" is shown in orbit around a nucleus; its mirror image is at the top left. Without the Z force, the paths of the electron flow would resemble those in the middle drawings. The nucleus is at the centroid of each atom. If the mirror image is flipped upside down, the new electron paths can be superposed on the original ones, and so these paths are achiral. With the Z force present, the direction of the electron's motion tends to align with the direction of its spin. The result is shown at the bottom right. The paths are now chiral: the electrons travel up along the inner, right-handed helix and down along the outer, left-handed helix. The mirror-image atom, shown at the bottom left, does not exist in the real world. For this drawing the effect of the Z force was magnified by a factor of 10^{10}.

asymmetric Z force. The expected energy split between the enantiomers emerged; curiously, in all cases the biologically dominant L-enantiomer was found to have the lower energy.

Basic principles of statistical mechanics require that in any equilibrium situation the lower-energy form should be more abundant than the higher-energy form. Mason and Tranter showed that L-amino acids should outnumber D-amino acids by one part in 10^{17}. Such an infinitesimal difference explains why L- and D-enantiomers are found in the laboratory in essentially equal numbers. Still, one cannot help but wonder whether this minute difference, caused by the weak nuclear force, is somehow connected with the dominance of L-amino acids and D-sugars.

Chiral Symmetry in Life

So little is known about the origin of life that one cannot speculate about its causes with any confidence, but since the first experiments of Stanley L. Miller of the University of Chicago in the 1950's, scientists have developed a good picture of how a variety of biologically significant molecules could have arisen on the primitive earth. Somewhere in the course of the chemical evolution that led from atoms to life, the chiral asymmetry of biomolecules was established.

This raises three important questions. How could biomolecules with a chiral preference have arisen from chemical reactions that are identical for the two enantiomers? Is the dominance of L-amino acids and D-sugars over their mirror images in any way linked to the weak force? Was chiral asymmetry a precondition without which life could not have arisen, or did the asymmetry arise later—as a consequence of biological, rather than chemical, evolution? We shall address these questions one by one.

Paradoxical though it may seem, mirror-symmetric chemical reactions can produce unequal amounts of L- and D-amino acids through a phenomenon called spontaneous symmetry breaking. In this case, a symmetric state is one with equal numbers of L- and D-forms; the asymmetric state is one in which one form dominates. Spontaneous symmetry breaking is a mechanism by which a system "spontaneously" goes from a symmetric state to an asymmetric one.

Spontaneous symmetry breaking occurs only under specific physical conditions. It cannot occur in a system closed to the inflow of energy and
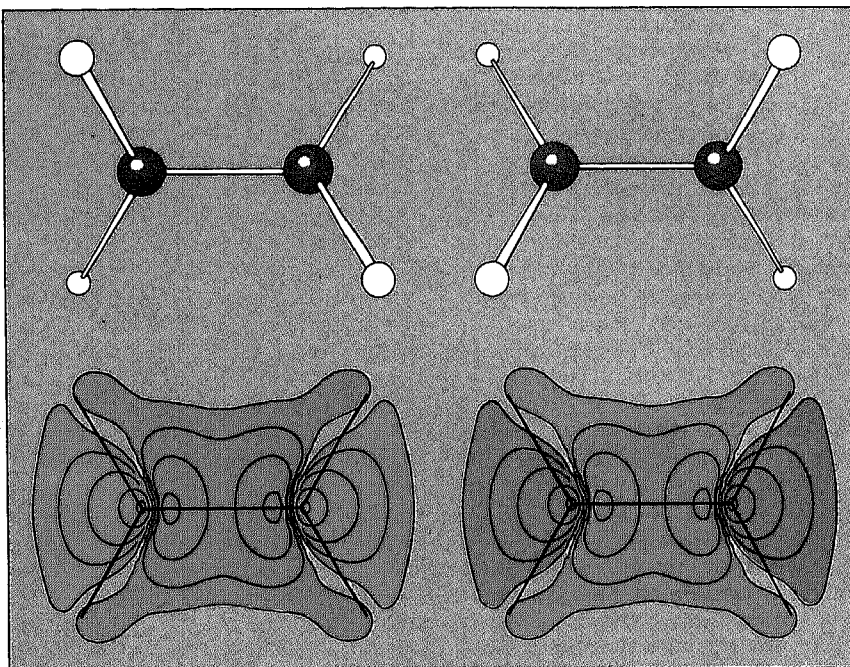
TWISTED ETHYLENE is a simple chiral molecule consisting of two carbon atoms and four hydrogen atoms (C_2H_4). The top drawings show the D- and L-enantiomers at the right and the left, respectively. In ethylene a phenomenon known as spin-orbit coupling, which tends to align an electron's spin against its orbital angular momentum, produces regions of differing electron chirality. The bottom drawings, based on calculations by one of the authors (Hegstrom) and his student Melinda S. Montgomery at Wake Forest University, show these regions as viewed from "above" the line connecting the two carbon atoms. Red shading indicates the regions where the electrons are right-handed, blue shading the regions where they are left-handed. Mirror reflection reverses the regions of chirality. The weak Z force acts in an opposite way on left- and right-handed electrons, so that the mirror reflections are subtly different: the L-enantiomer of ethylene has a lower energy than the D-enantiomer.

matter. Such a system will proceed toward thermodynamic equilibrium, a state in which the concentration of a molecule depends only on that molecule's energy and entropy. Because the energies of L- and D-enantiomers are equal (ignoring the tiny energy difference caused by the Z force), in this state the numbers of L- and D-enantiomers will be equal, and the state will be chirally symmetric.

If the system is open to the inflow of energy or matter, however, it is no longer in thermodynamic equilibrium. Spontaneous symmetry breaking then can become operative and can throw the system into a chirally asymmetric state, one that has unequal amounts of the enantiomers.

In 1953 Sir Frederick Charles Frank of the University of Bristol developed a simple model to illustrate how spontaneous symmetry breaking might operate in a chemical system consisting of two molecular species. Frank's model assumes that each species is capable of replication and that the presence of one diminishes the population growth rate of the other; that is, they compete. The replication rates

for the species are identical, as is each one's effect on the other. Nevertheless, as soon as one species becomes slightly more numerous than the other (for example, by means of a random statistical fluctuation), the more numerous species quickly becomes completely dominant. The symmetric balance between the two types of molecules is unstable and spontaneously evolves into an asymmetric state in which one type dominates.

It is easy to imagine how this would work on a biological level. Even if the mirror image of life as we know it once existed on the earth, competition between the two types might have resulted in the extinction of looking-glass life. Frank's model shows that this is also possible on the molecular scale, thereby demonstrating how an excess of L-amino acids or D-sugars could have arisen from a primordial soup in which both enantiomers were initially on an equal footing.

The Weak Force Again

We now turn to the second question: Is it possible that the weak nuclear

force is responsible for the dominance of L-amino acids and D-sugars? Ever since the discovery of parity violation, there have been attempts to invoke beta decay and related phenomena as mechanisms that could lead to an excess of one enantiomer. Frederic Vester and Tilo L. V. Ulbricht, who were at Yale University in 1957 when parity violation was discovered, noted that beta electrons, because they are predominantly left-handed, emit predominantly left-handed electromagnetic radiation (radiation that is polarized and rotated to the left). Vester and Ulbricht proposed that left-handed radiation decomposes one enantiomer preferentially, leaving a net excess of its mirror image. The expected asymmetry produced by the Vester-Ulbricht process, however, is extremely small and has yet to be detected experimentally.

Beta particles can also decompose chiral molecules directly. One of us (Hegstrom) has calculated that the relative difference in the rates of such decomposition for L- and D-enantiomers is about one part in 10^{11}. Experiments by Arthur Rich, James C. Vanhouse and their co-workers at the University of Michigan have found that the difference is indeed less than one part in 10^9.

Yet another candidate is the Z force itself, which can affect the production rates of L- and D-amino acids. As previously noted, however, the effect of the

Z force is so minuscule that the expected difference would be about one part in 10^{17}. For such a small asymmetry to have produced the observed dominance of L-amino acids and D-sugars, some amplification mechanism must have been operating.

One of us (Kondepudi) and George W. Nelson, now at the Los Alamos National Laboratory, have shown theoretically that such a mechanism indeed exists in nonequilibrium chemical systems. It is referred to as noise averaging by communications engineers, who exploit it to extract a signal from a noisy background. Imagine a pool of water in which two enantiomers compete with each other, as in Frank's model. Many random influences will tend to favor the survival first of one enantiomer and then of the other. These fluctuations are much larger than the effect of the weak force, but because they are random, they tend to cancel out. Given enough time, the small systematic effect of the weak force will influence the handedness of the symmetry breaking and push the system to a dominance of one enantiomer over the other.
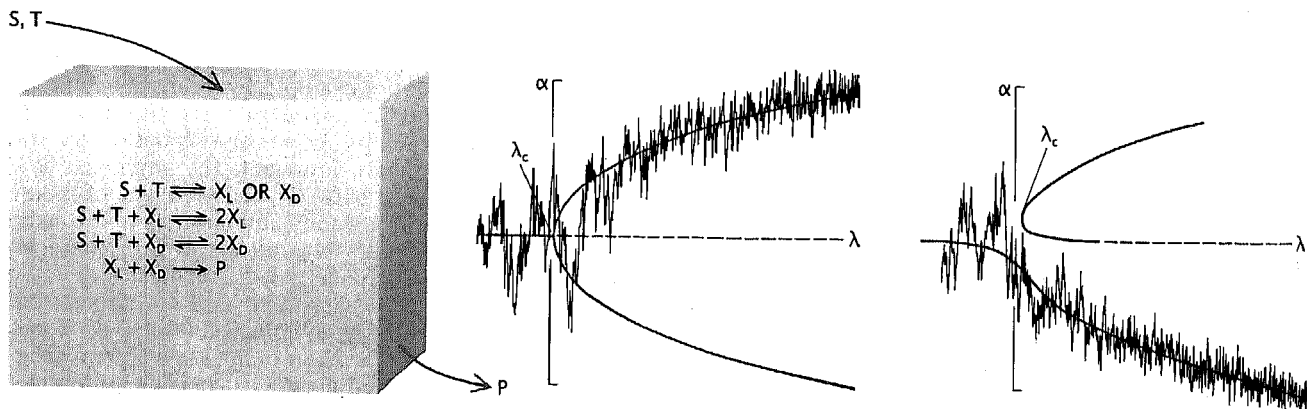
What conditions are necessary for the noise averaging to operate, and what time scales are involved? There should be a more or less constant flow into the pool of the achiral reactants needed to produce the enantiomers. The system will therefore be open and far from equilibrium, ensuring that

spontaneous symmetry breaking can take place. The reactants should produce enantiomers that replicate and compete with each other. And the pool should be large enough and sufficiently well mixed (over an area of about 10 square kilometers and a depth of several meters, roughly) to eliminate largely the net effect of random fluctuations. If these conditions are satisfied, the weak nuclear force should be capable, over a period of from 50,000 to 100,000 years, of strongly influencing the outcome of the symmetry-breaking process. After this time there is at least a 98 percent chance that nearly all the molecules—amino acids, in this instance—will be left-handed (assuming that the weak force favors L-enantiomers). In such an environment, chirally asymmetric life based on L-amino acids could evolve.

Such a slow chemical process is difficult to observe in the laboratory. An elegant electronic simulation by Frank E. Moss of the University of Missouri at St. Louis and Peter V. E. McClintock of the University of Lancaster has confirmed the existence of the predicted mechanism, but no such mechanism has yet been observed in a real chemical system.

Before or after Life?

We have presented several models to show how chiral asymmetry might have arisen in biomolecules. The fi-

S, T

$$S + T \rightleftharpoons X_L \text{ OR } X_D$$
$$S + T + X_L \rightleftharpoons 2X_L$$
$$S + T + X_D \rightleftharpoons 2X_D$$
$$X_L + X_D \longrightarrow P$$

P

α

λ_c

λ

α

λ_c

λ

AUTOCATALYSIS AND SYMMETRY BREAKING are demonstrated in a simple chemical model. Two achiral molecules, S and T, are pumped into a pool of water (*left*). They react to form the chiral molecule X in either of its enantiomeric forms, X_L or X_D. X may react again with S and T to produce a second X_L or X_D; this self-replication is termed autocatalysis. X_L and X_D may also annihilate each other by producing a product P. If none of these reactions favors the L- or the D-enantiomer, the concentrations of X_L and X_D should remain equal. The reaction-rate equations show, however, that the balance between autocatalysis and mutual annihilation is unstable. The critical parameter is lambda (λ), the product of the concentrations of S and T. When λ is increased past a critical value λ_c, the system will flop into a state where X_L or X_D is favored, although which state is chosen is entirely random. The symmetry between L and D is "broken spontaneously." Alpha (α), the difference between the concentrations of X_L and X_D, is a measure of this asymmetry. Frank E. Moss of the University of Missouri at St. Louis and Peter V. E. McClintock of the University of Lancaster simulated this model electronically. They found (*center*) that as λ increased, symmetry was broken and X_D became dominant, although the dominance of X_L was equally likely. They also altered the simulation to give a small systematic advantage to X_L, analogous to the possible effect of the Z force (*right*). As λ increased, the system almost always followed the lower branch, where X_L dominates; the upper branch, where X_D dominates, became an improbable outcome. Such a model may explain the dominance of L-amino acids over D-amino acids in nature.
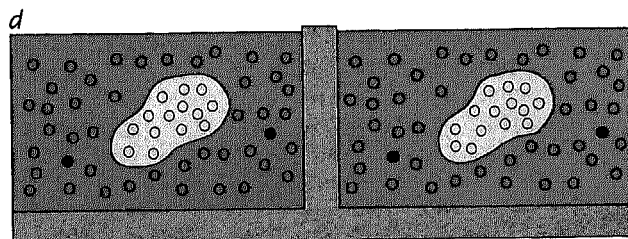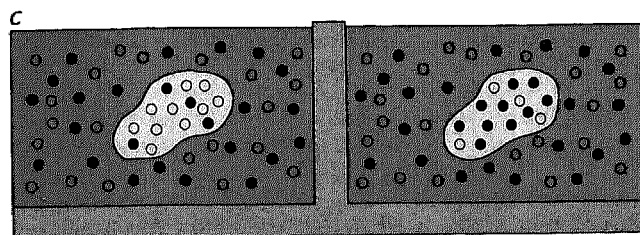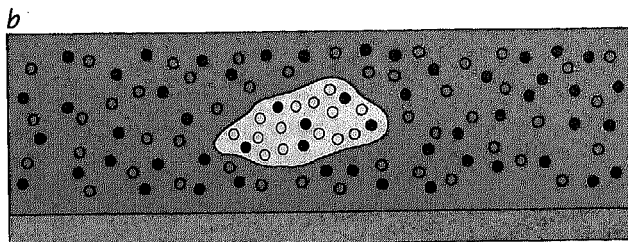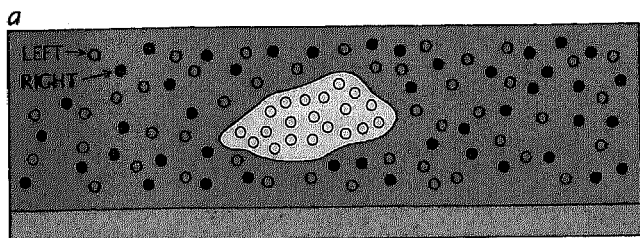
CHIRAL LIFE CHEMISTRY may be a relic of prebiotic conditions or an artifact of the life process. One theory holds that when life appeared in the primordial soup, the first cell formed containing all L-amino acids (a). This would have been extremely improbable, however, if the soup were composed of an equal mixture of left and right enantiomers. Another possibility is that the first cell randomly formed with a slight excess of L-amino acids (b), and evolutionary selection favored life based on just one enantiomer. Some have proposed that life arose in many places simultaneously in both L- and D-amino acid-based forms (c); these forms competed, and life based on D-amino acids became extinct. An alternative view, investigated by the authors, is that spontaneous symmetry breaking produced near chiral homogeneity in each of the many places where life appeared (d). The parity-violating weak force influenced the symmetry-breaking process in favor of L-amino acids.

nal important question is whether this asymmetry arose before or after the appearance of the first primitive life, the "first cell." Based on current knowledge of the structure and function of biopolymers, it is difficult to understand how a protein or nucleic acid consisting of both L- and D-monomers could function. Experiments show that strings of amino acids containing both L- and D-acids do not correctly form the alpha helix shape that is crucial for the catalytic functions of proteins. Without homochirality (the situation in which all amino acids have the same handedness), the catalytic activity of proteins would have been extremely poor; it is hard to imagine how the complex structures of life could have evolved under such conditions. Similar observations apply to nucleic acids. It would appear, then, that homochirality in biomolecules must have arisen before life.

In support of this view, various autocatalytic, symmetry-breaking models, such as the Kondepudi-Nelson mechanism referred to previously, have been proposed. Yet no one has been able to pinpoint a particular set of prebiotic compounds that have all the properties required by such models. Some investigators consider this a serious difficulty; it is one of the main reasons they think chiral asymmetry must have arisen not before but after the first cell.

According to this view, the first cell developed as a singular event, and it did not possess the strongly chiral chemistry characteristic of mod-

ern life. The original "common ancestor" of all life was accidently created with a small excess of L-amino acids or D-sugars and so incorporated only a slight chiral asymmetry. Proteins made of only one enantiomer are better catalysts, nucleic acids made of only one enantiomer are more stable and L-proteins interact more efficiently with D-nucleic acids. Therefore, in a competitive environment, evolutionary refinement of succeeding generations gradually produced life with all L-proteins and all D-nucleic acids. There is still the problem of imagining a viable life-form—the original common ancestor—made of biopolymers that contain nearly equal numbers of L- and D-enantiomers. To avoid this difficulty, some students of the subject have proposed that, by chance, the first cell already had proteins composed entirely, or nearly entirely, of L-amino acids. By any reasonable estimate, however, the probability of this happening is extremely small.

Some have proposed a third possibility—that the appearance of life was not a singular event. Symmetry breaking occurred in many places randomly, without being influenced by the chirally asymmetric weak force. In places dominated by D-amino acids, "D life" arose, and in places dominated by L-amino acids, "L life" arose. The two forms competed, and D life vanished without a trace.

Clearly, the key questions about the origin of chiral asymmetry in life remain unanswered, as do questions concerning the origin of chiral asym-

metry on a macroscopic level. Although it is now evident that the weak force, acting on the level of elementary particles, can give rise to handedness and left-right asymmetry in atoms and molecules, it is not known if these characteristics are expressed at the level of plants and animals. The chiral asymmetry in snails' shells, for example, does not appear to be related in any way to the asymmetry incorporated in their DNA or proteins; the offspring of sinistral snails can be dextral. The answers to questions about handedness in snails, human beings, cabbages and kings will have to await further revelations from developmental and evolutionary biology.

FURTHER READING

THE AMBIDEXTROUS UNIVERSE: MIRROR ASYMMETRY AND TIME-REVERSED WORLDS. Second Revised and Updated Edition. Martin Gardner. Charles Scribner's Sons, 1979.
WEAK NEUTRAL CURRENTS AND THE ORIGIN OF BIOMOLECULAR CHIRALITY. D. K. Kondepudi and G. W. Nelson in Nature, Vol. 314, No. 6010, pages 438-441; April 14, 1985.
PARITY VIOLATION AND THE ORIGIN OF BIOMOLECULAR CHIRALITY. Dilip Kondepudi in Entropy, Information, and Evolution: New Perspectives on Physical and Biological Evolution. Edited by Bruce H. Weber, David J. Depew and James D. Smith. The MIT Press, 1988.
MAPPING THE WEAK CHIRALITY OF ATOMS. R. A. Hegstrom, J. P. Chamberlain, K. Seto and R. G. Watson in American Journal of Physics, Vol. 56, No. 12, pages 1086-1092; December, 1988.