

Left and Right

Assemblage on corresponding crystal faces of enantiomorphic pairs of crystals, such as right-hand and left-hand quartz crystals, would provide us with a most simple and direct possibility of localized separate assemblage of right- and left-hand asymmetric molecules.

Victor M. Goldschmidt, 1952

Prebiotic processes produced a bewildering diversity of molecules. Some of those organic molecules were poised to serve as the essential starting materials of life—amino acids, sugars, lipids, and more. But most of that molecular jumble played no role whatsoever in the dawn of life. The emergence of concentrated suites of just the right mix remains a central puzzle in origin-of-life research.

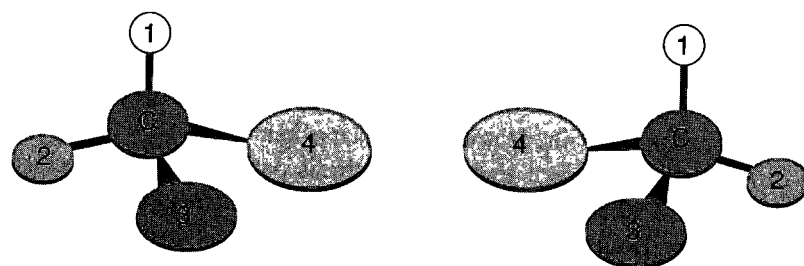
One of the stages of life's emergence—an early and confounding one at that—must have been the incorporation of handedness. Many of the most important biomolecules, amino acids and sugars included, come in mirror-image pairs: something like your two hands, which have the exact same structure, but can't be exactly superimposed. In the same way, pairs of these so-called chiral molecules have the exact same composition and structure, and many of the same physical properties, but they are mirror images of each other.

Virtually all known prebiotic synthesis pathways produce chiral molecules in 50:50 mixtures. No obvious inherent reason exists why left or right should be preferred. And yet living cells display the most exquisite selectivity, choosing right-handed sugars over left and left-handed amino acids over right. In spite of a century and a half of study, the origin of this biochemical "homochirality" remains a central mystery of life's emergence.

THE HANDEDNESS OF LIFE

Molecular chirality arises from a common circumstance of organic molecules. In many molecules, one carbon atom forms four bonds to four *different* groups of atoms. The amino acid alanine, for example, has a central carbon atom linked to one NH_2 molecule (an amino group), one COOH molecule (a carboxyl group), one CH_3 molecule (a methyl group), and one lone hydrogen atom. If you orient the hydrogen atom up and look down on the molecule, there are two ways to arrange the remaining three components. So-called "right-handed" or D-alanine has a clockwise arrangement of carboxyl–amine–methyl groups. Chemists employ the letter "D" after the Greek "dextro" for "right" (though the designation of molecular "right" vs. "left" is a completely arbitrary convention.) Alternatively, "left-handed" or L-alanine features a clockwise arrangement of amine–carboxyl–methyl groups. In this case the "L" comes from the Greek "levo," for "left."

For reasons that are still not well understood, life selects L-amino acids and D-sugars almost exclusively over D-amino acids and L-sugars. One critical consequence of this selection is that our cells often respond very differently to other kinds of chiral molecules. The familiar flavoring limonene, for example, tastes like lemons in its right-handed form, but like oranges in the left-handed variant. More sinister is the behavior of the infamous drug thalidomide: The left-handed form cures morning sickness, while the right-handed form induces birth defects. Consequently, the Food and Drug Administration demands



Many biomolecules occur in both left-handed and right-handed variants, which are mirror images of each other. This situation arises when a central carbon atom is linked to four different groups of atoms—groups that can be arranged clockwise or counterclockwise.

chiral purity in many pharmaceuticals—a difficult processing step that adds more than \$100 billion annually to our drug costs.

Chirality is an essential, diagnostic characteristic of cellular life. But how did this selectivity emerge in the seemingly random prebiotic world? A dozen theories, from the mundane to the exotic, have been proposed, but all ideas fall into one of two general categories.

Some experts suspect that prebiotic synthesis was an inherently asymmetrical process, leading to an inevitable global excess of L- over D-amino acids on the prebiotic Earth. More than a century and a half ago, Louis Pasteur demonstrated that left- and right-handed crystals cause polarized light to be rotated in opposite directions. Conversely, the orientation of polarized light shining on a chemical-rich environment might influence the relative proportions of left- versus right-handed molecules, either by selective synthesis of L-amino acids, or by selective breakdown of D-amino acids. Though the effect is generally small, this kind of chiral-selective process might conceivably have occurred in deep space near a rapidly rotating neutron star, or perhaps on Earth's surface as the result of polarized sunlight reflected off the ocean surface. No one knows for sure what hundreds of millions of years of such processing might yield.

Other physicists echo this theme, but posit that asymmetric synthesis resulted from so-called parity violations that occur during radioactive beta decay. In physics, the parity principle states that physical processes appear exactly the same when viewed in a mirror. Beta decay, which occurs when an unstable radioactive atom loses an electron (or a positron) in the process of becoming a stable atom, is the only known physical event that violates this parity principle. Beta-decay events produce polarized radiation of only one handedness, and this chiral radiation, in turn, could have enhanced the synthesis of L- versus D-amino acids. One problem with these asymmetric processes is that they seem to yield only the slightest excess of one handedness over the other—generally less than a minuscule fraction of 1 percent. Such minute effects hardly seem sufficient to tip the global balance toward L-amino acids or D-sugars.

LOCAL SYMMETRY BREAKING

Many origin-of-life researchers (myself included) argue that chiral selectivity more likely occurred as the result of an asymmetric local, as

opposed to global, physical environment on Earth. After all, the emergence of life consisted of a series of chemical events, each of which occurred at a specific place and a specific time. It is very possible that those emergent steps were repeated countless millions of times across the globe, but each individual emergent event was local: It occurred at specific location with specific molecules. Consequently, if the local environment where a reaction occurred was strongly chiral, then chiral molecules might have emerged.

The chemical process of life's origin is in some respects like the formation of a crystal. In life, as in crystals, two essential and largely independent steps are necessary. The first step in crystal formation, nucleation, requires the precise organization of a relatively small number of atoms or molecules into a "seed." This seed might by chance have either a D or L character. Then comes growth, as the original seed provides a template for the ordered assembly of more atoms and molecules. Each step in the chemical origin of life must also have required nucleation, followed by growth.

In life, as in crystal formation, these two stages usually proceed at very different rates. Nucleation may take place with ease, while growth is slow. Such a situation leads to the myriad microscopic crystallites that give colorful agates and frosted glass their distinctive translucent optical properties. If, on the other hand, nucleation is rare while growth is rapid, then a single large crystal may form.

Since life is vastly more complex than any crystal, it is reasonable to think that nucleation—the self-organization of molecules into a replicating entity—is relatively rare, perhaps even a singular event in Earth's history (though that is by no means a certainty). But, once formed, this protolife must have grown rapidly, in the process consuming every available molecular feedstock and frustrating further origin events. If that life-form was by chance homochiral, D or L, then that handedness would be passed on to subsequent generations. All it takes is an initial local chiral environment.

We now realize that such local environments abounded on the prebiotic Earth. Indeed, every chiral molecule is itself a tiny local chiral environment that might select other molecules of similar handedness. The pioneering chirality studies of Louis Pasteur relied on this characteristic: When he evaporated a 50:50 solution of D- and L-tartaric acid, the mixture spontaneously divided into pure D and pure L crystals. Such

a circumstance arises because D-D or L-L pairs of tartaric acid molecules happen to fit together more easily than D-L pairs.

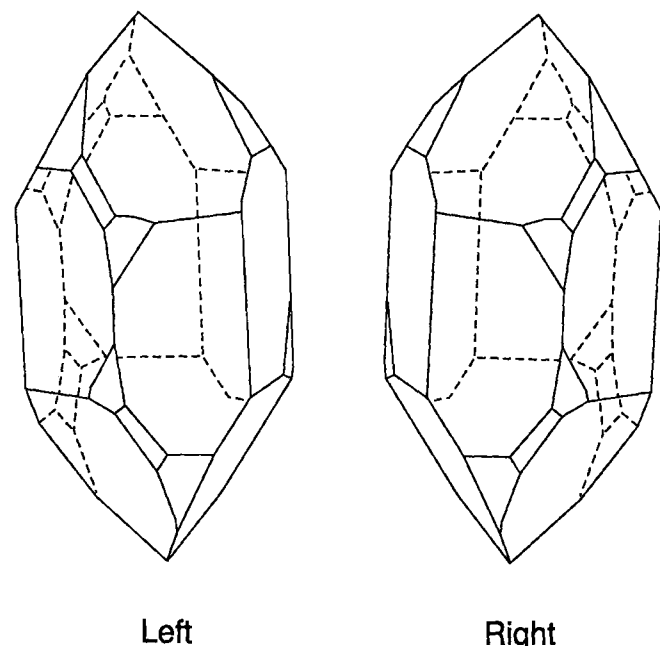
Might prebiotic organic molecules have displayed the same behavior? Evidence is still spotty, but a few experiments do reveal a strong tendency for chiral self-selection in certain polymers. The Swiss chemist Albert Eschenmoser, who explored the stabilities of more than a dozen variants of RNA with modified sugar-phosphate backbones, has found that some (but not all) of these molecular chains grow spontaneously with greater than 90 percent chiral purity. Perhaps prebiotic polymers became homochiral by a similar self-selection process.

One caveat: In a dilute, complex primordial broth, the chances of linking together *any* two types of molecule, much less two useful monomers of the same handedness, would have been exceedingly small. That's why James Ferris, Leslie Orgel, Graham Cairns-Smith, and others have resorted to mineral surfaces, which induce polymerization by concentrating and aligning desirable molecules. But some mineral surfaces have an added advantage. Every rock, every grain of sand or particle of silt also has the potential to offer chiral environments, in the form of asymmetric mineral surfaces. Left- and right-handed mineral surfaces might provide the perfect solution for concentrating and separating a 50:50 mixture of L and D molecules.

Minerals often display beautiful crystal faces, which might have provided ideal templates for the assembly of life's molecules. A few minerals, most notably quartz (the commonest grains of beach sand), occur in both right-handed and left-handed structural variants. The quartz structure features helices of atoms that in some crystals spiral to the left and in other crystals to the right. Every grain of beach sand thus provides a chiral environment.

But even though the vast majority of minerals are "centrosymmetric," and thus not inherently handed, their crystals commonly feature pairs of faces whose surface structures are mirror images of each other. Like quartz, these chiral surfaces have arrangements of atoms that are ideally suited to select and concentrate L versus D molecules, such as amino acids or sugars.

Natural left- and right-handed surfaces occur in roughly equal numbers, so there's not much chance of chiral selection occurring on a global scale. But, once again, here's the key: The chemical origin of life was not a global event. The first common ancestor—the precursor to



The common mineral quartz forms both left-handed and right-handed crystals.

all of the varied life-forms we see on Earth today—arose as a bundle of self-replicating chemicals at a specific place and time. Once that chiral system began making copies of itself, the handedness of life was fixed. To many experts in the field, the choice of L- versus D-amino acids seems to have been a one-time, chance event, and that scenario points to a simple mineralogical mechanism for chiral selection.

CHIRAL MINERAL SURFACES

As a mineralogist for more than a quarter of a century, I love the idea that crystals may have played a central role in life's beginnings. For a time, the question of origins took me away from minerals, but they have called me back to some of the most delightful experiments of my career.

The chirality problem represents a particularly puzzling aspect of the more general question of molecular selection, but it's also an as-

pect that can be studied with well-controlled experiments. We know that prebiotic synthesis processes yield huge numbers of different molecules, of which life uses relatively few. It would be impossible to study that full range of prebiotic products in one experiment. But using pairs of chiral molecules makes things a lot easier: Because all known prebiotic syntheses result in equal amounts of left- and right-handed molecules, it's relatively easy to design an experiment that starts with a 50:50 mix and looks for environments that separate left from right. If we can discover the processes by which handed molecules were selected and concentrated, then there's hope that we can solve the more general selection problem as well.

For most of the twentieth century, scientists have recognized the power of minerals to select molecules—processes in which one kind of molecule sticks more strongly to a surface than another. If two molecules differ significantly in size and shape, then such selection is easy to comprehend; it's just a matter of which molecule fits best. But selection between two mirror-image molecules is more difficult. Such pairs of molecules are chemically identical, so each type of molecule forms exactly the same kinds of bonds with the mineral surface. The only way for chiral selection to occur is for the molecule to form *three* separate points of attachment, and those three bonds can't be in a straight line. You've experienced this kind of selection process if you've ever gone bowling. The ball has three holes, for your thumb and second and third fingers. A left-handed bowler can't use a right-handed ball and vice versa, because the three holes aren't in a line.

By the 1930s, scientists in Greece and in Japan had applied these ideas and tried separating left- and right-handed molecules by pouring D- and L-solutions over left- or right-handed quartz. During the next half-century, a dozen similar experiments were attempted. The basic idea was sound: Different-handed molecules do have the potential to stick selectively to different-handed surfaces. Nevertheless, these early experiments were flawed. In an effort to maximize the surface area of interaction, and thus the magnitude of the desired effect, the scientists ground their beautiful quartz crystals into fine powder. Powdering increases the surface area of a peanut-sized crystal a thousand times or more, but it destroys the flat crystal surfaces that might promote selection. A powder displays every possible crystal surface simultaneously. Some of these surfaces may very well select L-amino acids with great efficiency, but surfaces with a different exposed atomic

structure might just as likely select D-amino acids. Even if an experiment revealed a small preference for L or D molecules, there would be no hope at all of determining which crystal surface was doing the selecting.

I decided to try a different approach.



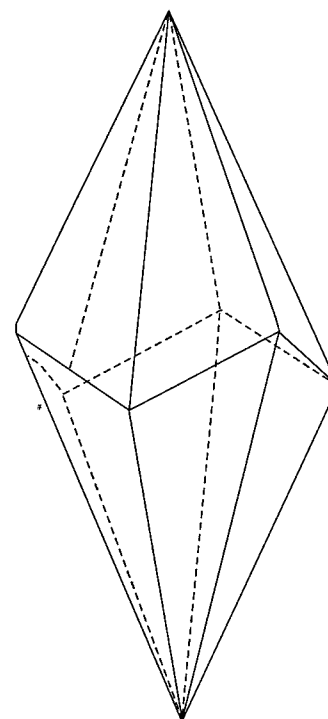
Big crystals are the key—fist-sized crystals with fine flat faces. That's the only way to understand the atomic-scale interaction between molecule and crystal. But what mineral fits the bill?

My crystals had to be big because a layer of molecules adsorbed onto a surface an inch square weighs at most a few billionths of a gram—a daunting analytical challenge. To measure that effect, I had to find crystals with faces at least a few square inches in area. Big crystals of most minerals tend to be astronomically expensive, thanks to the voracious appetite of mineral collectors; so I had to find a common rock-forming mineral that collectors don't covet. As an added benefit, the commonest minerals are also likely to be the most relevant to origin scenarios. Most important, the crystals had to possess faces with surface structures that lack mirror symmetry. Only a chiral face could accomplish the chiral selection task.

I thumbed through my favorite mineralogy book, a frayed, dog-eared copy of Edward Dana's *A Textbook of Mineralogy*, purchased at the American Museum of Natural History when I was 14. Classic line drawings of crystal forms decorate almost every page. The vast majority of crystal faces, I realized, aren't chiral. Many of the commonest minerals—garnet, olivine, mica, pyrite—won't do.

Then I turned to page 512—calcite, an abundant mineral and the one most closely associated with life. Calcite is the mineral of clamshells and snail shells, of pearls and coral. Lo and behold, its commonest crystal faces are chiral. Most calcite crystals feature a graceful, six-sided, pointed form with the fancy scientific name of scalenohedron. Everybody in the business calls it a dogtooth.

A quick search of eBay confirmed that dogtooth calcite crystals are both common and cheap. I bid on three pretty specimens from the then thriving (but now defunct) Elmwood lead-zinc mine outside Carthage, Tennessee. A week and \$40 later I had the beginnings of what



The commonest crystal shape of the mineral calcite is the so-called "dogtooth." All 12 faces of this form are chiral.

has become a sizable calcite crystal collection. Now to design an experiment.



I wanted to find out whether chiral crystal surfaces would selectively attract chiral molecules. I had fist-sized calcite crystals with left- and right-handed faces, and I had D- and L-amino acids. Would D- or L-amino acids attach themselves preferentially to left- or right-handed calcite faces?

Seventy years of false claims and ambiguous results had set the bar high; a casual, sloppy experiment wouldn't do. I knew that many previous authors had started with concentrated D- or L-molecules, and then looked for a difference in behavior as those molecules interacted with a chiral crystal (usually quartz). That experimental path was fraught with