BIOCHEMISTRY

Getting All Turned Around Over The Origins of Life on Earth

"To everything, turn, turn, turn," goes a piece of folk wisdom. But which way? And why? That's the crux of a scientific mystery: Why do the sugar molecules in DNA and RNA twist to the right in all known organisms? Similarly, all of the amino acids from which proteins are formed twist to the left. The reason these molecules have such uniform handedness, or "chirality," is not known, but there is no shortage of theories on the subject. And, as was clear at a recent meeting on the topic in Los Angeles, there is also no shortage of passion, which is understandable, because the question of homochirality speaks to the mother of all scientific mysteries: the origin of life.

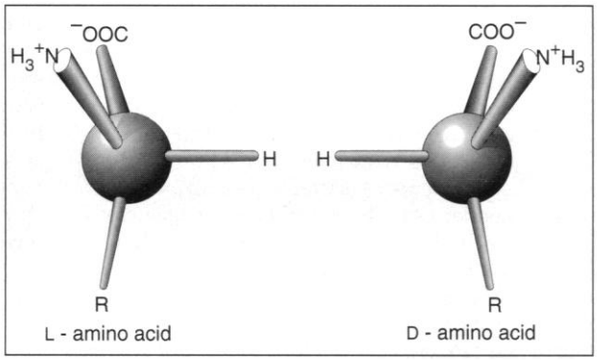
Two dozen physicists, chemists, and astronomers journeyed from around the world to attend the 3-day meeting on "The Origin of Homochirality in Life,"* which several said was the first gathering devoted to the subject. "It's an idea whose time has come," said David Cline, a physicist at the University of California, Los Angeles, who organized the meeting. "There is more and more interest in interdisciplinary ideas."

The meeting participants did agree on one thing: Homochirality—the total predominance of one chiral form, or "enantiomer"—is necessary for present-day life because the cellular machinery that has evolved to keep organisms alive and replicating, from microorganisms to humans, is built around the fact that genetic material veers right and amino acids veer left. But they didn't agree about much else.

They were sharply divided, for example, about the origin of this remarkable uniformity of twist. One division came over a question that resembles the chicken-or-the-egg riddle: What came first, homochirality or life? Organic chemist William Bonner, professor emeritus at Stanford University, argued that homochirality must have preceded life. "There's a huge [intellectual] gap between the origin of homochirality and the origin of life—a huge gap," said Bonner. "I happen to think that you have to understand the origin of homochirality before you can bridge that gap. Stepwise, one has to deal with the origin of homochirality first, and then how do you get to living organisms?"

Bonner argued that homochirality is essential for life because without it, genetic material could not copy itself. Specifically, studies have shown that the two complementary strands of genetic material that make up DNA cannot bind with each other if they are in a "racemic" mixture, a state in which there is an equilibrium of left-handed and right-handed enantiomers. Bonner dismissed the point of view that homochirality did not precede the origin of life as "believing in the tooth fairy or magic wands."

Scientists on the other side weren't about to be dismissed, however. They rolled their eyes at Bonner's views and those of his like-minded colleagues. Chemist Stanley Miller of the University of California, San Diego, contended that the homochirality-first group is "barking up the wrong tree." Chemist Jeffrey Bada of the Scripps Institution of Oceanography, who collaborates with Miller in studies of the origin of life, agreed: "Homochirality is probably an artifact of life rather than a precursor of life."



Mirror, mirror. Both left-handed (L) and right-handed (D) amino acids exist, but life only uses one type—left-handed.

Miller, who gained fame (with Harold Urey) in a classic 1953 experiment showing that organic compounds can be created in a flask by electrically zapping a mixture of gases presumed to exist on the prebiotic Earth, sketched a scenario for the origin of life that does not require homochirality. He believes there must have been a precursor to DNA or RNA. DNA and RNA have backbones of phosphate units linked to sugars, and Miller pointed out that the sugars decompose rapidly. This makes it highly likely, argued Miller, that the sugars would have decomposed before joining with phosphates and forming backbones. "The essential issue is: What was the backbone of the first macromolecule?" he said.

Miller offered one possibility. Peptide nucleic acid (PNA), a potential prebiotic DNA precursor discovered by the University of Copenhagen's Peter Nielsen and co-workers and described in a paper in *Science* in 1991, binds to itself more strongly than the complementary strands of DNA do to each other. This feature means that PNA provides a more stable backbone than DNA. Another intriguing aspect of the pairing of two strands of PNA is that the double helixes show no chirality, presumably because each molecule continuously switches from a right-handed to a left-handed helix, much in the way you could twist a rubber band one way and then the other. "This is just the sort of thing needed for a nonhomochiral origin of life," said Miller.

Nielsen, who also presented at the meeting, detailed a key step that could have taken a racemized mixture of PNA helixes toward homochirality. As Nielsen and colleagues reported last year in *Nature*, adding a left-handed or a right-handed lysine, an amino acid, to the end of PNA strands fixes the chirality of its helix as right or left. Theoretically, homochirality of genetic material could have occurred if amino acids first made chiral PNA and then one enantiomer had a selective advantage. For example, said Miller, if PNA, like RNA, has enzymatic activity, one enantiomer of PNA might have helped the molecule copy itself more efficiently. Over time, this could have led to homochirality of that enantiomer.

This chicken-and-egg dispute wasn't the only divisive issue. Scientists at the meeting also fell into two camps over where life began, a mystery that some tied tightly to the origin of homochirality. While Miller and Bada believe life began on Earth, Bonner and many of the physicists at the meeting suspect it originated in space. "I spent 25 years looking for terrestrial mechanisms for homochirality and trying to experimentally investigate them and didn't find any supporting evidence," said Bonner. "Terrestrial explanations are impotent or nonviable."

The heart of the extraterrestrial camp's misgivings about a terrestrial origin is that entropy drives molecules into racemic mixtures. Scientists therefore have hunted for physical forces on Earth—as opposed to evolutionary forces, such as the selective pressure driven by an enzyme—that could satisfactorily explain how one enantiomer could come to dominate.

In controlled experiments, researchers have investigated whether electric, magnetic, or gravitational fields could have created enantiomeric excesses. Roger Hegstrom of Wake Forest University in Winston-Salem, North Carolina, noted that physicists in particular have become interested to know if

*"The Origin of Homochirality in Life," 15–17 February, Santa Monica, California.

biological homochirality is linked to the fact that "fundamental forces in nature are chiral." For example, the electrons and positrons that are produced by a form of radioactive decay called β decay, which is governed by the so-called weak force, can exhibit a chirality themselves by spinning either to the left or the right, respectively; several theoreticians and experimentalists have asked whether a bombardment by such rays could have induced homochiral biomolecules. But none of this work, said Bonner, has yielded convincing conclusions.

That failure leads Bonner to speculate that homochiral molecules came to Earth from an extraterrestrial source. Perhaps, he suggested, a remnant of a supernova known as a neutron star emitted radiation that included circularly polarized light (CPL), an electromagnetic wave that spirals clockwise or counterclockwise. These CPL waves, in turn, might have led to an enantiomeric excess of organic molecules in space.

This idea was most fervently promoted at the meeting by Mayo Greenberg from the University of Leiden in the Netherlands. Greenberg theorized more than a decade ago that comets are composed of interstellar dust containing organic material. Building on Bonner's hypothesis, Greenberg presented evidence that he could get enantiomeric excesses of the amino acid tryptophan in a laboratory experiment that mimicked CPL from a neutron star. "If a comet could have provided a local concentration [of homochiral biomolecules], you could have a head start" for the origin of life, said Greenberg.

Although many of the theories about the origin of homochirality can never satisfactorily be proved or disproved, the comet theory may be put to the test. In 2003, the National Aeronautics and Space Administration will launch its Rosetta mission, a spacecraft that will orbit the comet Wirtanen and send two smaller spacecraft to land on it and perform experiments. Walter Huebner, a visiting NASA scientist who attended the meeting, is working to include a device on one of the crafts to assess whether homochiral molecules are present on the comet.

Although Scripps's Bada is designing a device that could measure homochirality in extraterrestrial settings—he's particularly interested in Mars—he strongly doubts that they'll find homochiral molecules in a comet. "If the Earth was seeded with homochirals, we should see it happening today," said Bada, who has analyzed amino acids in meteorites and found them to be racemic.

Greenberg took the counterarguments in stride. "It's a continuing story," he said of the search for homochirality's origin. And, like a racemized mix of molecules, scientists will surely have opposite spins on the story for years to come.

–Jon Cohen

PHYSICS

A New Accelerator Explores The Social Life of Quarks

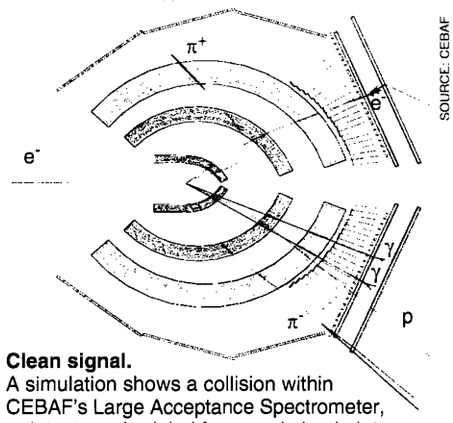
On a large scale, matter may seem inert, but zooming in on a single atom reveals a beehive of activity. The quarks that inhabit the nucleus cluster in small groups to form protons and neutrons, but they don't stay put—hopping restlessly from one group to another and sometimes summoning up companions from the vacuum. This picture of ceaseless motion, however, is just a rough interpretation, based on tantalizing observations and on the formidable mathematics describing quark behavior. "The situation today in the study of the nucleus is similar to what scientists faced in the 1920s with the study of the atom," says physicist Nathan Isgur.

"We don't get to see quarks as they live, inside the nucleus," adds Jack Lightbody, a physicist at the National Science Foundation. Part of the problem is that Lightbody and his colleagues just haven't had the right tools. The traditional way to observe the smallest units of matter is to smash protons or smaller particles together in a mammoth machine. This brute-force approach can flush out individual quarks and gluons, particles that carry the "strong" force that binds quarks together. But high energies and showers of debris can obliterate the subtle patterns that reveal the society of quarks in their natural habitat, the atomic nucleus. Probing the nucleus with a lighter touch is the goal of the Continuous Electron Beam Accelerator Facility (CEBAF), a new particle accelerator in Newport News, Virginia. Built by the Southeastern Universities Research Association with funding from the Department of Energy, CEBAF was completed last summer—on time and on budget, its managers boast—and is set to begin taking data this spring.

Rather than colliding bursts of high-energy particles, the $515 million accelerator probes nuclei in fixed targets with a steady stream of electrons. The subtler approach, says physicist Elizabeth Beise of the University of Maryland, should allow her and her colleagues to observe the strong force as it normally behaves in the nucleus. At CEBAF, they hope to study the paradoxical tendency of the strong force to increase as quarks are separated; they would also like to observe it conjure up new quarks from apparently empty space and find out how it seeps out of individual protons and neutrons to form the glue that holds the nucleus together.

To be sure, descriptions of all these behaviors are to be found in the theory of the strong force, called quantum chromodynamics (QCD). Yet under the conditions of ordinary matter, the equations of QCD become an impenetrable thicket. CEBAF, says Isgur, head of the theory group there, is designed to probe that thicket.

To do so, CEBAF uses chains of superconducting accelerating cavities to hurl electrons around an oblong racetrack with a long axis of 500 meters. After five circuits, the beam smashes into a fixed target, where the electrons collide with nuclei in a variety of materials. Using a fixed target rather than colliding two oppositely directed beams, as many accelerators do, sacrifices collision energy. Indeed, CEBAF's 4 billion electron volts is several hundred times lower than the energy of colliders such as HERA, in Hamburg, or the Fermi National Accelerator Laboratory's Tevatron. But high collision energy isn't critical for subtle exploration of the nucleus. CEBAF's design allows experimenters to vary the target to study nuclei of various types, and it generates far more collisions than can be achieved by aiming two hairsbreadth beams of particles at each other.



SOURCE: CEBAF

Clean signal. A simulation shows a collision within CEBAF's Large Acceptance Spectrometer, a detector scheduled for completion in late 1996. An electron (e^-) collides with a proton (p), snapping a quark-quark bond and generating a quark-antiquark pair that decays into a sprinkle of pions (π) and a pair of gamma rays (γ).

What's more, unlike other accelerators, CEBAF produces these collisions continuously. Existing accelerators generate their high-energy particles in bursts, resulting in a boom-and-bust cycle of collisions. During a spate of collisions, says Isgur, "you are blinded by a burst of particles," making it impossible to sort out isolated collisions. In CEBAF, the electrons strike the target in smaller bunches, at a much higher rate.

Until a few years ago, this strategy was out of the question, says John Domingo, CEBAF's associate director for physics, be-