Magnets separate mirror-image molecules

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Spin, not shape, underlies a surprising new method for sorting biomolecules from their opposite-handed counterparts.

In the opening chapter of *Through the Looking-Glass*, as Alice imagines what life would be like on the other side of the drawing-room mirror, she wonders whether the milk there would be safe for her kitten to drink. Alice might not have known it, but by the time her story was published in 1871, chemists had already taken the first steps toward answering that question.

Nearly a quarter century previously, young Louis Pasteur—better known for his own work on making milk safe to drink—made the momentous discovery that crystals of sodium ammonium paratartrate came in two distinct shapes that were mirror images of each other. When he sorted the crystals by hand and dissolved each batch in water, he found that they induced opposite rotations on the polarization of incident light. Although little was known about chemical structures, Pasteur proposed that the asymmetry had a molecular basis.

He was right. Structural asymmetry, or chirality, is now known to be common among organic compounds. The amino acid cysteine, shown in figure 1, is chiral, as are all but one of the other amino acids that make up the proteins in both milk and kittens. Moreover, whenever a biomolecule can exist in distinct mirror-image forms, known as enantiomers, biology makes use of only one of them. Looking-glass milk is therefore chemically distinct from non-looking-glass milk—and because smell, taste, and digestion all involve interactions with receptors, enzymes, and other chiral structures in the body, it's probably not good for a non-looking-glass kitten to drink.

The different effects of enantiomers *in vivo* came to the fore in the wake of the thalidomide crisis of the 1950s and early 1960s. Like many other drugs, thalidomide is chiral. One of its enantiomers is a sedative that alleviates morning sickness in pregnant women; the other causes birth defects. The drug brought to the market was a mixture of the two forms, and thousands of children were afflicted. Unfortunately, the enantiomers easily interconvert—and some studies have suggested that both of them, in fact, cause birth defects—so an enantiomerically pure drug wouldn't have averted the tragedy. Still, the events spurred drug manufacturers to pay attention to chirality in the interest of reducing detrimental side effects. Plenty of other drugs, it turns out, can be made safer and more effective by enantiomeric purification.[1]

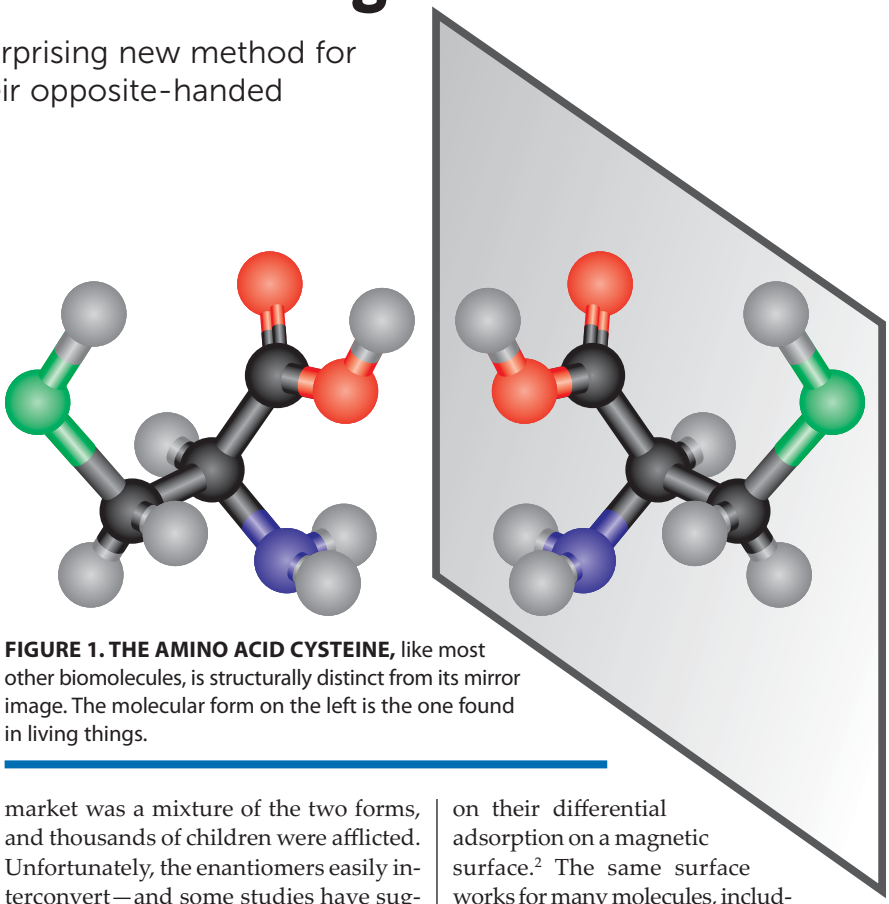

FIGURE 1. THE AMINO ACID CYSTEINE, like most other biomolecules, is structurally distinct from its mirror image. The molecular form on the left is the one found in living things.

Pasteur's paratartrate is one of only a few substances whose enantiomers self-segregate into crystals that can be distinguished by eye. More often, enantiomers can be separated through their interactions with other chiral substances, but the specific recipe and ingredients must be tailored, at considerable effort and expense, to the shape and properties of the molecule in question.

Now Ron Naaman of the Weizmann Institute of Science in Israel, Yossi Paltiel at the Hebrew University of Jerusalem, and their colleagues have discovered a new way to separate enantiomers based on their differential adsorption on a magnetic surface.[2] The same surface works for many molecules, including oligopeptides, short DNA strands, and single amino acids. And curiously, the surface itself is completely achiral.

Polarization

The search for a relationship between chirality and magnetism has a long and storied history. Pasteur himself tried and failed to induce a preference for one enantiomer by performing chemical reactions under a magnetic field. Pierre Curie proposed using a combination of electric and magnetic fields; Pierre-Gilles de Gennes determined theoretically that that might work, but only if nonequilibrium states are involved. A 1994 paper purporting to show enantiomer selectivity in a static magnetic field made a brief splash in the chiral chemistry community before it was revealed that one of the coauthors had faked the experimental results.[3]

The new work is different in that it capitalizes not on the magnetic field but on the electron spin polarization of the

magnetic material itself. Suppose, for example, that the surface is magnetized in the spin-up direction. Because the Pauli exclusion principle prevents two parallel-spin fermions from occupying the same quantum state, a molecule with an excess of spin-up electrons would have more trouble sticking to the surface than one with a net downward spin. The same thing can happen when molecules have a net spin of zero but a nontrivial spin distribution: An excess of spin-up electrons at the end of the molecule most likely to bind to the surface—and a spin-down excess elsewhere in the molecule—still inhibits adsorption.

Chiral molecules don't—indeed, can't—have permanent enantiomer-dependent spin polarizations. But they can acquire a temporary polarization through an effect that Naaman and colleagues first noticed two decades ago.

Selectivity

In 1998 Naaman and his group were studying the possible damage electrons can inflict on DNA. They created a thin DNA film on a gold surface and used a laser to liberate electrons from the gold. When the laser light was circularly polarized—and the photoelectrons therefore spin polarized—the polarization direction had a strong influence on how many electrons were transmitted through the DNA film. When the researchers replaced the DNA with a film of stearoyl lysine, another chiral molecule, the effect persisted.[4]

Further work confirmed that when electrons move in a given direction through chiral molecules, their transport is spin dependent, with spin-up electrons preferentially passing through one enantiomer and spin-down electrons moving more freely through the other. Although the theoretical details are still being worked out, the effect has been attributed to coupling between spin and orbital angular momentum. Spin–orbit coupling is a well-known phenomenon in materials with heavy atoms or unpaired electrons, but organic chiral molecules, which have neither, are an unexpected venue for it, and just how the coupling becomes strong enough to explain the observed results is unclear.[5]

Nevertheless, the experiments unambiguously show spin-dependent transport in organic molecules, and the effect has been explored for applications in spin filters and other spintronic devices. But that's not all. Chirality influences the transport of not only external electrons passing through but also a molecule's own electrons as they're pushed and pulled among different parts of the molecule. That pushing and pulling can result from the approach of another molecule, perhaps in the beginning stages of a chemical reaction. Or it can be caused by proximity to a surface—in this case, the very surface to which the molecules are trying to adsorb.

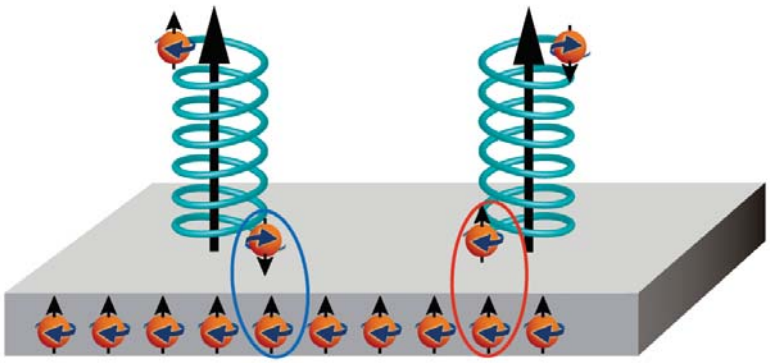

FIGURE 2. AS MIRROR-IMAGE MOLECULES (light blue spirals) approach a magnetized substrate, they temporarily take on equal and opposite spin distributions induced by the internal flow of electrons. When the molecular spin nearest the surface is antiparallel to the substrate spins, as shown in the blue oval, the molecule easily adsorbs. When the spins are parallel (red oval), adsorption is inhibited by the Pauli exclusion principle. (Adapted from ref. 2.)

As the molecules near the surface, their internal electron motion creates a temporary spin polarization: an excess of one spin state at the end of the molecule nearest the surface, and an excess of the other at the far end. Which spin state is which depends on the handedness of the molecule, as shown in figure 2. One enantiomer, as a result, brings the antiparallel spin into contact with the magnetized substrate, as shown by the blue oval; the other brings the parallel spin, shown by the red oval. The Pauli exclusion principle causes the antiparallel-spin enantiomer to have a much easier time approaching and sticking to the surface.

Separation

Naaman, Paltiel, and colleagues devised several experiments to demonstrate the differential adsorption in action. In some, they started with a solution of just one enantiomer and exposed it in turn to surfaces magnetized in opposite directions; they then used either fluorescence measurements or scanning electron microscopy to determine how many molecules stuck to each surface. In other experiments, the researchers started with an equal mixture of enantiomers, brought it in contact with a magnet, and analyzed the composition of the remaining solution using either measurements of circular dichroism (the differential absorption of left- and right-circularly-polarized light) or conventional enantiomer separation techniques. The molecules they studied included cysteine (shown in figure 1), two different amino-acid chains, and a short DNA strand.

In each case, the spin-favored enantiomer adsorbed more frequently than its mirror image, by up to a factor of eight. Because the molecular spin polarization is only temporary, however, the effect is transient: When the solution is left in contact with the magnet for more than a few minutes, both enantiomers adsorb in equal amounts.

Naaman, Paltiel, and their colleagues are working on fleshing out their understanding of the separation mechanism by studying how it depends on the specific magnetic substrate and on molecular properties such as polarizability, length, and charge; the goal is to develop it into a general technique to completely separate the enantiomers of any molecule.

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