ASTRONOMY

Could Stellar Ash Revise Cosmic Ages?

Start talking about how particles can escape from the deep nuclear furnaces of red giant stars and reach their surfaces, and researchers who build computer models of stars get uncomfortable. Their computer codes imply that the giants' layered structure includes a version of the windless doldrums at sea: a quiet "radiative" boundary that prevents the ash from their deep hydrogen-burning regions from reaching their churning, convective outer layers. But somehow the ash blows through—and the consequences could say something about an issue as grand as the age of the oldest objects in the universe, astronomer Allen Sweigart argues in a paper to appear in the 1 January issue of *The Astrophysical Journal*.

Astronomers had already noticed that carbon, oxygen, and aluminum—the ash of nuclear burning in the core of a star—do end up in the surface layers of aging red giant stars, becoming more abundant in older stars. Now Sweigart, a stellar modeler at NASA's Goddard Space Flight Center in Greenbelt, Maryland, has computed the consequences of this mixing and come to some startling conclusions. His calculations show, for example, that dredged-up nuclear ash could brighten the nests of very old stars in the Milky Way's halo called globular clusters. That could lower the estimated age of these stars, which—at 15 billion years or so—has been out of step with other indicators of the age of the universe such as its expansion rate, which tend to give ages of 8 billion to 12 billion years. The moral of Sweigart's work, says David Schramm of the University of Chicago, is that stellar mixing casts "a big question mark" over the age estimates.

According to standard models of giant stars, "there's absolutely no way you should be dredging material from that deep [inside a star]," says Michael Bolte of the Lick Observatory at the University of California, Santa Cruz. So in spite of the signs that mixing takes place, modelers computing how red giants evolve had assumed that their surface compositions stay constant, untainted by the nuclear alchemy taking place below. Sweigart, however, decided to take a hard look at the consequences of the mixing, which he and others have suggested might somehow be driven by a star's spin.

Along with carbon, oxygen, and aluminum, Sweigart realized, the mixing would also stir up large amounts of helium ash—which is much more difficult to observe. Sweigart then added the extra helium, which is less opaque and more massive than the hydrogen in a star's outer layers, to his stellar-evolution codes. He found that it causes red giants to contract and heat up, burning a bit brighter and bluer than they would without the mixing.

The astrophysical consequences of this extra brightness would emerge in a later stage of the stars' lives, when some of them pass through a so-called RR Lyrae phase. RR Lyraes are identified by their pulsations, and they all have about the same brightness. Astronomers use them as one of their "standard candles" for working out the absolute brightnesses of other stars in globular clusters.

The stars' pattern of brightnesses, in turn, holds a clue to a cluster's age. When stars deplete the hydrogen fuel at their cores, they move off the main sequence of a Hertzsprung-Russell diagram—a graph of stars' luminosity versus color—and toward the red giant branch. More massive and luminous stars reach this turnoff point sooner than do their dimmer cousins. By working out the brightness of stars reaching the turnoff in a particular cluster, astronomers can fix its age. If the RR Lyrae stars are brighter than assumed, the turnoff luminosity goes up, and the age estimate for the clusters drops.

Sweigart has not yet calculated just how much this effect might lower the ages of the clusters. But he notes that a tiny increase in the RR Lyrae brightness would trim up to 1.5 billion years from the cosmic age inferred from the oldest clusters. His calculations could also have implications for the timing of events in our own galaxy. Astronomers have assumed that otherwise similar clusters whose very old stars differ in color also differ in age by a few billion years. To some theorists, this age spread implies that the Milky Way's halo—its oldest part—was gradually assembled from smaller pieces. But if the apparent age differences are due instead to different amounts of mixing, says Sweigart, "the halo may have formed more quickly."

One question he's not tackling yet is just how giant stars churn up the ash in the first place. By the time the models have an answer, Sweigart jokes, the stars will have gone dark.

–James Glanz

ENDOCRINE DISRUPTERS

Scientists Angle for Answers

A few years ago, British biologists noticed something odd about the fish they pulled from the sewage-laced River Lee near London: The testes of males were laden with eggs. Scientists suspected that something in the water was acting like a sex hormone, skewing reproductive development. And soon, the gender-bent fish became one of the poster species in the still-unfolding controversy over "hormone disrupters," chemicals thought to derail developmental processes in wildlife and perhaps even humans.

But now two studies are shedding new light on the hermaphroditic fish. One, a survey sponsored by the U.S. Geological Survey (USGS), finds that fish from many streams across the United States also appear to have unusual levels of sex hormones. The other, by British researchers, suggests that, in many cases, natural hormones in women's urine—not industrial chemicals—may be disrupting fishes' reproductive health.

Presented last month at the Society of Environmental Toxicology and Chemistry meeting in Washington, D.C., both sets of results bolster concerns that hormonelike chemicals may be harming aquatic ecosystems on a broad scale. But the fact that natural substances have been fingered also sounds a cautionary note to investigators. Says John Sumpter, an endocrinologist at Brunel University in Uxbridge and a member of the British team, "It's a very good example of 'Don't have a preconceived idea of what the result should be.' "

The USGS researchers analyzed more than 600 carp from 25 study sites in the basins of 11 major rivers, including the Hudson, Mississippi, and Columbia. Water quality at the sites ranged from nearly pristine to highly polluted, with many streams contaminated by agricultural runoff, urban sewage, or polychlorinated biphenyls from industrial dumping. Collaborators at the University of Florida analyzed the fishes' blood for the female sex hormone 17β-estradiol and the male hormone 11-ketotestosterone. Although their results are still preliminary, the researchers found that fish at polluted sites tended to have abnormal hormone levels when compared to fish from cleaner sites. In a more intensive study at sewage-contaminated parts of Lake Mead near Las Vegas, the researchers also found unusually high levels in male fish of vitellogenin, a protein in-

Confused carp. Fish with unusual levels of sex hormones are turning up in the United States.

volved in egg-laying that normally is only found in females.

Project manager Tom Muir cautions that the various soups of chemicals at the sites seem to produce a wide range of effects. "There's a lot of fuzziness to the national data set," Muir says. In some rivers, for instance, female fish had high levels of 11-ketotestosterone, while in others, both sexes had depressed levels of male and female hormones. More research is needed to establish cause-and-effect relationships, Muir adds.

That's just what the British study, sponsored by the U.K. Environment Agency, set out to do. The research followed on earlier work by Sumpter's group, which had shown that male rainbow trout kept in cages near sewage outfall pipes produced high levels of vitellogenin. To tease out what compounds might be responsible, researchers collected sewage effluent from three treatment plants and, using a variety of analytic techniques, isolated compounds that were likely to act like estrogen in the fish.

To their surprise, the researchers discovered that the estrogenic compounds were not industrial pollutants but three hormones found in women—17β-estradiol, estrone, and ethynyl estradiol. The last, which was present in vanishingly small amounts, is a potent synthetic hormone in birth control pills. One reason the researchers didn't expect to find these substances in the water is that before they are excreted in urine, the kidneys tack on a chemical group—a glucoronide or sulfate—that renders the compounds biologically inactive. Sumpter speculates that during sewage treatment, enzymes from bacteria may be clipping off the chemical group. The researchers then showed in the lab that the tiny amounts of hormones found in the effluent can cause male fish to produce vitellogenin. They are now exposing young fish to effluent to see whether it will cause them to develop into hermaphrodites.

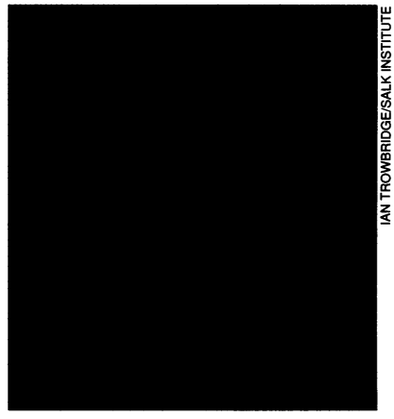
Sumpter says their result doesn't mean industrial chemicals aren't also harming fish in some heavily polluted rivers. For example, he believes that high vitellogenin levels found in male fish in some U.K. rivers will turn out to be caused primarily by nonylphenol, a chemical discharged by textile factories. But, he says, because sewage is the dominant source of pollution in U.K. rivers, these substances in urine are probably largely responsible for the country's hermaphroditic fish. And that's a lesson for other researchers studying endocrine disrupters, Sumpter says: "I would almost certainly have voted for synthetic man-made chemicals, and that would have turned out to be wrong." Toxicologist Steven Safe of Texas A&M University in College Station agrees: "This points out that we have to be pretty careful in jumping to conclusions."

–Jocelyn Kaiser

ALZHEIMER'S RESEARCH

Dissecting How Presenilins Function—and Malfunction

In Alzheimer's disease research, one small protein has long claimed a large share of attention. Known as β amyloid (Aβ), it is a major constituent of the abnormal structures called plaques that stud the brains of Alzheimer's patients, and mutations in the gene that produces it account for some inherited cases of the disease. But β amyloid is now having to share the stage with two other proteins, the presenilins, that play an even larger role in hereditary Alzheimer's. Discovered barely 2 months apart in 1995, the two presenilin genes, now called *Presenilin 1* and *-2* (*PS1* and *-2*), are mutated in about half of all inherited cases, compared to a few percent for the gene that makes Aβ. And now researchers are beginning to glimpse the normal roles of these proteins—and how they might go awry in the disease.



IAN TROWBRIDGE/SALK INSTITUTE

Localized. The yellow staining indicates that the presenilins are present in the endoplasmic reticulum and the Golgi.

New results, presented just last month at the annual meeting of the Society for Neuroscience in Washington, D.C., indicate that the protein produced by the *PS1* gene is apparently needed for the proper operation of a major developmental regulatory pathway. Known as the Notch pathway after a protein that is one of its key members, its jobs include transmitting the signals needed to make cell-fate decisions—such as whether to develop into nerve or muscle cells—in species ranging from the fruit fly to mammals. Just how the presenilin contributes to Notch signaling is unclear, but some researchers think it may play a role in the cell's internal protein-handling systems, helping bring Notch to its normal location, the external cell membrane.

If so, the finding would dovetail with other work, presented both at the neuroscience meeting and in a raft of recent publications. It suggests that the mutations in *PS1* and *PS2* somehow alter the way that cells handle another protein—the larger molecule from which Aβ is clipped—and thus cause increased production of a particular variant, called Aβ42 because it contains 42 amino acids, that is thought to be especially prone to forming plaques. "I think it's all really quite exciting. The amyloid work and the presenilin work are coming together rather nicely," says Alzheimer's researcher Dennis Selkoe of Harvard University. The hope is that if researchers can understand how the gene mutations lead to Alzheimer's, they will be that much closer to finding the causes of the much larger number of nonhereditary cases.

Selkoe cautions, however, that despite the rapid progress, some major gaps remain. Any role for the presenilins in protein trafficking is, for the moment, conjecture. But the work is telling researchers which aspects of cell physiology are likely to hold the answers, as well as providing a good model organism that ought to aid the studies. This is the tiny nematode, *Caenorhabditis elegans*, one of developmental biologists' favorite creatures, which turns out to have a presenilin of its own. Indeed, it was a discovery made about a year ago in *C. elegans* that originally tipped researchers off to the possibility that the presenilins might play a role in Notch signaling.

Molecular biologists Diane Levitan and Iva Greenwald of Columbia University College of Physicians and Surgeons were looking for mutations that suppress the effects of a mutation in a worm gene, called *lin-12*, that is the equivalent of the *Notch1* gene of the mouse. The idea was that any gene containing such a suppressor mutation might work in the same signaling pathway as *lin-12/Notch1*. Levitan and Greenwald found what they were looking for, and when they cloned one of the affected genes, which the researchers called *sel-12* (for *suppressor and/or enhancer of lin-12*), its sequence turned out to be 50% identical to that of *PS1*. That high degree of resemblance suggested that *PS1* might also be involved in Notch signaling. Further work in both *C. elegans* and mice has borne that out.

At the neuroscience meeting, Philip Wong, who works with Sam Sisodia at Johns Hopkins University School of Medicine, provided the first public description of a mouse in which the *PS1* gene has been knocked out. The disruption of the gene produced results much like those that Janet Rossant's team at Mount Sinai Hospital in Toronto found when