SCIENCE NEWS of the week

Enzyme Structure Points to New Drugs

Enzymes work as chemical traffic cops, keeping the body's metabolic pathways flowing. They convert inactive substances into essential ones and render dangerous substances harmless. Now, advances in understanding a bacterial enzyme suggest a new mechanism for controlling human blood pressure.

For the first time, two crystallographers have figured out the three-dimensional structure of a short-chain dehydrogenase, an enzyme belonging to a widespread class of compounds that regulate levels of sugars, prostaglandins, alcohols and other important substances. The bacterial enzyme closely resembles its human counterpart, report William L. Duax and Debashis Ghosh of the Medical Foundation of Buffalo (N.Y.), Inc. They described their findings this week at the annual meeting of the American Crystallographic Association in Toledo, Ohio.

By controlling kidney levels of natural steroids, the human enzyme figures importantly in regulating blood pressure and plays a key role in the established link between licorice and hypertension. "Maybe there is a way to manipulate this enzyme to bring blood pressure down," Duax says.

Licorice contains an ingredient that prevents the human enzyme from converting the steroid hormone cortisol into cortisone. High levels of cortisol affect the body's salt balance and can cause blood pressure to rise, sometimes to dangerously high levels. Babies born without the ability to make the enzyme develop life-threatening hypertension.

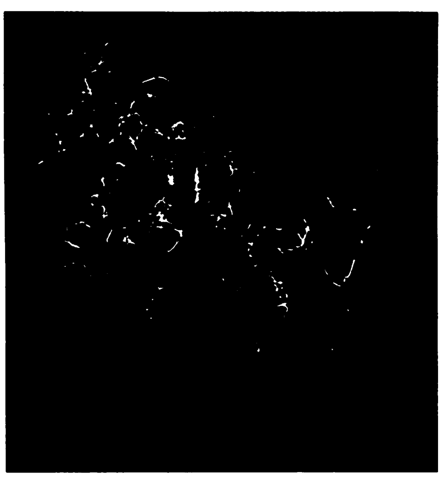
Licorice also inhibits the bacterial enzyme, the Buffalo researchers found. In addition, the amino acid sequences in the two versions look alike, even though they do not match those of longer, more intensively studied dehydrogenases containing 350 amino acids, Duax says. These similarities suggest that the bacterial enzyme can serve as a useful surrogate for the human version, which is difficult to obtain in large quantities, he says.

"We're hoping that by studying this [bacterial] enzyme we can gain some insight into how our [own] enzyme is working," says Carl Monder, an endocrinologist at the Population Council Center for Biomedical Research in New York City. That insight, he says, might suggest ways to alter the enzyme's activity to control blood pressure — and in other instances, to prolong the effects of steroidal medications.

The active form of the bacterial enzyme consists of four enzyme subunits that twist together into an asymmetric molecule. Using X-ray diffraction, Ghosh and Duax pinpointed the "handcuffs" used by this chemical cop — the twists and kinks in its molecular structure that temporarily snare steroid molecules and a "cofactor" compound necessary to metabolize them. Each of the four enzyme components contains about 250 amino acid building blocks, but most of these serve only as scaffolding to hold a few key amino acids in the proper position to create the handcuffs, Duax explains.

Its seems that a cortisol molecule nestles into one fold of the bacterial enzyme, and a cofactor molecule fits into another spot nearby. Then one of the amino acids, arginine, deactivates the cortisol by transferring a hydrogen from the steroid to the cofactor. "The enzyme is there to expedite the removal of the hydrogen," says Duax.

These findings may help pharmacologists create new drug compounds. "If you know the topology of the active site, then it should be possible to design chemical agents that fit into the active site and inhibit the enzyme," Monder says. He envisions drugs that could slow the deactivation of steroid drugs, prolonging their anti-inflammatory effects. As for hypertension, Monder says, "by knowing the [enzyme's] three-dimensional structure, we possibly gain some insight on how to enhance [its] activity." — *E. Pennisi*



Ghosh, Duax/Medical Foundation of Buffalo

Four subunits (shown in different colors) make up this bacterial dehydrogenase, which transfers hydrogen from a steroid molecule to a cofactor (both in pink).

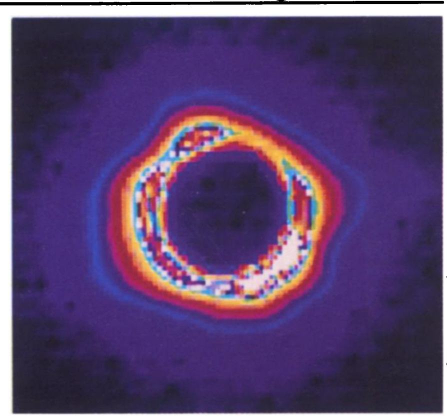
Out of the shadows: An illuminating eclipse

From the mountaintop vantage point of Mauna Kea, Hawaii, some of the world's largest and most powerful telescopes witnessed July 11's total eclipse of the sun. Using infrared, visible-light and radio-wave detectors, scientists took advantage of the event to study features of the solar atmosphere that show up clearly only when the moon blocks the brilliant light of the solar disk.

While the results remain preliminary, they have already yielded several new insights.

One set of Mauna Kea observations, made with a spectrograph attached to NASA's infrared telescope, pinpointed the location of a key spectral line of magnesium at one edge of the sun. Scientists use this infrared emission line, which splits into three components in the presence of a strong magnetic field, to gauge magnetic activity in the solar atmosphere. But uncertainties regarding the line's exact altitude have limited its usefulness, notes Donald Jennings of NASA's Goddard Space Flight Center in Greenbelt, Md. Ever since astronomers discovered the line in the early 1980s, they have debated whether it lies in the upper photosphere — a region at or just above the visible surface of the solar disk — or in a region just beyond the photosphere, called the lower chromosphere.

Two weeks ago, as the moon swept across the face of the sun like a giant shutter, Jennings and his colleagues measured the time interval between the moment when the moon first blocked the solar disk and when it later obscured the magnesium line as it moved across the sun. They then used the known velocity of the moon to calculate the altitude of the magnesium emission. The team, headed by Drake Deming of Goddard, discovered that the bulk of the emission occurs in the upper photosphere, just a few hundred kilometers above the solar surface, Jennings told SCIENCE NEWS. The



Smithsonian Astrophysical Observatory/Amber Engineering

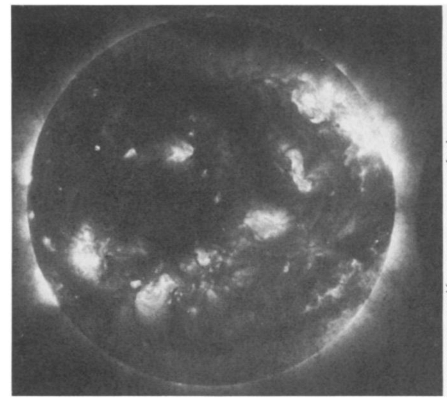
First infrared image of a solar eclipse shows corona surrounding darkened solar disk. White denotes highest intensity; blue denotes lowest.

finding provides a reference point that will help scientists "stitch together" the magnetic activity on the sun's surface with that in the solar atmosphere.

Other research teams at Mauna Kea examined solar features with wide-field infrared cameras, capturing the first infrared pictures of the sun during an eclipse. Astronomers had hoped the images would reveal whether a ring of dust or rocky material circles the sun thousands of kilometers above the solar surface. Such a ring might arise from dust shed by comets passing near the sun or from rocky material left over from the solar system's formation, says Eric Tollestrup of the Harvard-Smithsonian Center for Astrophysics in Cambridge, Mass. The preliminary images show no evidence of a ring, but this doesn't necessarily rule out its existence. The brightness of the corona – the outermost layer of the solar atmosphere – may have obscured the relatively dim glow of sun-warmed rocks or vaporized dust, Tollestrup says. If so, further processing to subtract the coronal background from the images might yet reveal the ring.

The preliminary pictures do show other key features of the solar atmosphere, Tollestrup says. These include bulges in the region surrounding the eclipsed solar disk, which depict long extensions of the corona called streamers; and white areas that indicate solar prominences – elongated gas clouds held intact by magnetic fields.

Some Mauna Kea observers are collaborating with researchers who imaged the sun at the same time from other sites. In one such project, astronomers plan to match visible-light features in the solar atmosphere observed from Hawaii with X-ray images taken simultaneously above White Sands, N.M., where the eclipse had not yet occurred. Comparing the X-ray images of the full solar disk with the eclipse photographs of the corona should help astronomers trace the path of magnetic field lines from the surface of the sun to its outer atmosphere, explains Leon Golub of the Harvard-Smithsonian Center for Astrophysics, who made the White Sands observations with colleagues from IBM in Yorktown Heights, N.Y. The X-ray images themselves, he says, may feature the highest resolution of any such photos of the sun (SN: 9/30/89, p.223). The bright areas of these pictures reveal elongated, magnetically confined regions of hot plasma – structures that did not show up clearly in previous X-ray images, Golub says.



Smithsonian Astrophysical Observatory/IBM Research

A rocket-borne telescope flying over White Sands, N.M., captured this X-ray image just minutes before the moon passed in front of the sun. The picture may represent the sharpest X-ray image yet of solar-disk features. The moon looms at right.

– *R. Cowen*

Wavering radio signals hint at an unseen planet orbiting a pulsar

British astronomers have found tantalizing evidence that a planet-sized object orbits a pulsar some 33,000 light-years from Earth. If their finding proves correct, it will mark the first detection of a planet outside the solar system. A confirmation of this provocative result would also challenge accepted theories about the formation of pulsars.

Previous reports of planets orbiting stars other than the sun have not withstood further scrutiny. But the British team maintains that the long-term consistent nature of their data bolsters their finding.

Early last year, Andrew G. Lyne and his colleagues noticed a peculiar, periodic pattern in the arrival times of radio emissions from PSR1829-10, a Milky Way pulsar they had discovered in 1985. In reexamining earlier data, they discovered that the timing of radio signals from this star, unlike that of the 39 other pulsars they had identified, had fluctuated about every six months since close monitoring of PSR1829-10 began in 1987.

Six weeks ago – after Lyne and his coworkers at the University of Manchester rejected other explanations for the star's variability – they arrived at a startling conclusion: The emission pattern indicates that the pulsar and a much smaller body orbit each other, and that the "companion" object meets the criteria for a planet. The unseen object, perhaps only 10 to 15 times the mass of the Earth, follows a nearly circular path about 105 million kilometers from the pulsar – roughly the distance between Venus and the sun – and each orbit takes six months to complete, the researchers report in the July 25 NATURE.

"If there is a companion, the work ... will challenge some, perhaps several, fundamental aspects of our view of the evolution of stellar and planetary systems," writes David Black, of the Lunar and Planetary Institute in Houston, in an accompanying commentary.

The pulsar and its planetary companion, Lyne says, would orbit around a common center close to the pulsar, as is the case with Earth and the sun. When the pulsar travels on the far side of its orbit, its radio pulses take longer to reach Earth; on the near side, they arrive sooner. This hypothetical scenario, Lyne asserts, would account for the six-month changes in the timing of the signals.

While the discovery of a possible planet outside our solar system seems dramatic in itself, the presence of a planet near a pulsar poses a special puzzle, Lyne says, particularly if the planet predated the pulsar's explosive birth. According to standard theory, the catastrophic events leading to the formation of a pulsar – a rotating neutron star – should destroy a planet or eject it from the star's gravitational grasp.

For example, if the red giant star that likely gave rise to the pulsar suddenly shed more than half its mass to form the new pulsar, the planet could not remain bound. In any case, the ensuing shock wave spewed out by the collapsing red giant would blow the planet apart. But Lyne and his colleagues suggest that the pulsar may have formed more slowly and less violently than the standard theory permits, and that this would enable the planet to remain intact. "If this 'kinder, gentler' process works, the new discovery will have led to a revolution in [pulsar] astrophysics," writes Black.

Lyne and his colleagues have also developed an alternative theory, which assumes that the planet did not predate the pulsar. In this model, which Black calls "more likely and equally intriguing," a neutron star spinning especially rapidly would slow down by forming a disk around its equator, and material in the disk could condense into a planet. Researchers believe the solar system planets arose from a disk that once surrounded the sun. A planet that formed in this way could have several features similar to those of the object inferred by the British team, Black says.

Direct observations of the proposed planet seem unlikely, since the object probably reflects light dimly at all wavelengths, Lyne says. Black says he's reluctant to call the object a planet, because this substellar mass and its environment would bear little, if any, resemblance to known planets.

Lyne says his group will continue monitoring PSR1829-10 to corroborate their findings and to examine whether subtler changes in the radio emissions indicate the presence of a second, more massive planet. The team will also look for periodicity in emissions from other pulsars in the hope of uncovering evidence of other planet-like objects. – *R. Cowen*