NONLINEAR OPTICS

Transmuting Light Into X-rays

Despite all the recent advances in laser technology, one dream device remains elusive: No one has yet figured out how to make a tabletop instrument that can pump out a beam of high-intensity, coherent x-rays. Such a device would give researchers Superman-like eyes to peer into living cells or catch the swift dances of molecules during a chemical reaction. Now researchers have the beginnings of such a tool. A report on page 1412 describes a trick for boosting visible laser light efficiently into the soft x-ray range.

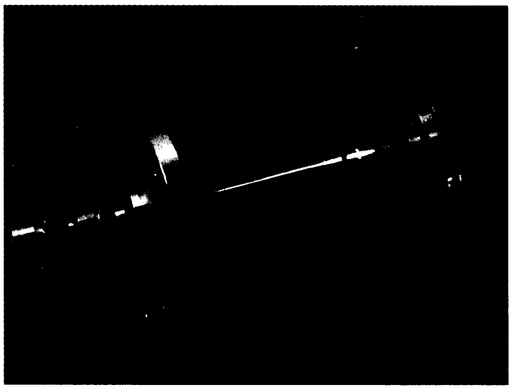
In principle, making a laserlike beam of x-rays, whose waves march in lockstep with each other, is straightforward: Start with a visible light laser, then use a series of crystals to double the frequency of the light, boosting its energy until it reaches the x-ray range. The technique works well for reaching ultraviolet frequencies, but unfortunately, standard frequency-doubling crystals are opaque to x-ray light. So scientists have had to look elsewhere for the energy kick, and most have focused on replacing the crystal with a gas that can more easily transmit x-rays.

When a laser plows into gas, it ionizes most of the atoms, creating a storm of free electrons. But occasionally, says Henry Kapteyn, a physicist at the University of Michigan, Ann Arbor, the laser can pull an electron far out of its orbit and then "slam it back down onto the same atom." When that happens, the atom shoots out a photon that can pack several hundred times the energy of an individual photon in the original laser beam. The process, harmonic conversion, can generate photons in the x-ray range.

But harmonic conversion is horribly inefficient, in part because the gas tends to slow down the laser light much more than it does x-rays. So if the laser blasts through a long volume of gas (which would be necessary to produce a significant quantity of x-rays), the x-rays generated at the front are out of step with those made further back. "[The x-rays] tend to cancel each other out," says physicist Margaret Murnane, also at Michigan.

Murnane, Kapteyn, and their colleagues found a way around this problem by equalizing the speed of the laser light and the x-rays in the gas. First they put the gas, argon in this case, in a precisely machined glass tube that acts as a "waveguide." The waveguide corrals and speeds up the laser light as it zigzags through but doesn't disturb the higher frequency x-rays. Then the team adjusted the pressure of the gas, which fine-tunes the velocity of the two beams, until they marched along at the same pace.

At a "magic pressure of 30 torr," says physicist Andy Rundquist, x-rays shot out of the 3-centimeter-long tube with a surprising intensity when the team blasted the gas with light from a titanium-doped sapphire laser. "At 2:00 in the morning, I was yelling and screaming in the lab," he recalls. Roughly one in 100,000 photons made the jump to x-rays, at least 100 times the proportion seen before, he says. The device, which emits x-ray pulses lasting just 20 femtoseconds, is "the first practical, coherent soft x-ray source," says Kapteyn.



WILLIAM PELLETIER / PHOTO SERVICES

Blue lightning. A 3-centimeter glass waveguide boosts the conversion of laser light to x-rays.

That has some researchers itching to build one of their own. "This will be a wonderful new tool," says Ken Kulander, a physicist at Lawrence Livermore National Laboratory in California, who hopes to use it to excite molecules and watch how they fall apart. "You could even think of using [such] lasers to manipulate [or control] chemistry." Visible-light lasers can drive reactions, he says, "but this opens up a whole new set of states that you can probe."

The technique is "very clever," agrees Janos Kirz, a physicist at the State University of New York, Stony Brook. But he points out that it's not yet capable of making the higher energy x-rays needed for imaging cells. "What everyone wants," he says, is x-rays of wavelengths between 2.3 and 4.3 nanometers, a region called the "water window." In this range, x-rays can slip undisturbed through water and scatter off very small objects, allowing scientists to make detailed images of tiny structures in live cells, which are mostly water.

Several other groups are beginning to see similar gains with waveguides and think a high-intensity x-ray beam in the water window may be in sight. "We could do it in a few years," says Eric Clement, a physicist at the University of Bordeaux in France. Christian Spielmann, a physicist at the University of California, San Diego, is more cautions. It will take a very high intensity laser to make enough x-rays in the water window to be of use, he points out. And such high intensities may, in turn, ionize so many atoms that it spoils the harmonic effect, he says: "This is a first step, but there are many more steps to go."

–**David Kestenbaum**

BEHAVIORAL GENETICS

New Clues to Alcoholism Risk

The going's been mighty slow, but the ardor for nailing down genes related to alcoholism continues undimmed. At a press conference held last week in Washington, D.C., researchers in the multicenter Collaborative Study on the Genetics of Alcoholism (COGA), now into its 10th year, reported what they called some "significant milestones." Those included debunking one candidate for an "alcoholism gene," coming up with some new hot spots in the human genome where such genes might be located, and firming up a link between alcoholism and a certain type of genetically influenced brain wave.

Looking ever more dubious, according to the COGA people, is the controversial hypothesis that a gene encoding a particular variant of a receptor for the neurotransmitter dopamine increases a person's risk of alcoholism and other addictions. Biologist Howard Edenberg of Indiana University School of Medicine in Indianapolis reported that "we found absolutely no evidence" for such a link. In 105 families of alcoholics, the suspect gene was not transmitted any more often to alcoholics than to nonalcoholics.

Psychiatrist Ernest Noble of the University of Texas Health Science Center in San Antonio, a leading proponent of the dopamine-receptor gene hypothesis, says he is undeterred by the findings. Family-based linkage studies—as opposed to association studies done in the general population—lack sufficient "power" to detect the effect, he says; and besides, the COGA researchers are looking only at alcoholism when the effect may not rise to significance unless other compulsive disorders are also taken into account.

COGA researchers have, however, found hints of other genes that might increase the risk of alcoholism. Psychiatrist Theodore Reich of Washington University School of Medicine in St. Louis described a linkage study in which researchers scanned 291 markers (segments of

DNA that vary from one person to another) in pairs of siblings—987 people in all—from 105 families. By identifying markers shared by alcoholic siblings, the researchers found "highly suggestive" evidence that chromosomes 1 and 7 carry alcoholism susceptibility genes, "modest" evidence for such genes on chromosome 2, and "suggestive" evidence for chromosome 4, said Reich.

A similar study by Jeffrey Long and David Goldman of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) on an entirely different population—a community of alcoholism-prone Southwest American Indians—confirmed that chromosome 4 may contain alcoholism susceptibility genes. The study also produced what Long called "strong suggestive evidence" of involvement by chromosome 11.

The DNA stretches implicated are already known to carry genes that could influence behavior, including pleasure seeking and compulsive overindulgence. The chromosome 2 region, for example, carries one gene related to the control of endogenous opioids and another that controls production of leptin, a peptide involved in appetite and obesity. The chromosome 11 area includes many genes that direct the production and metabolism of various brain chemicals.

Psychiatrist Henri Begleiter of the College of Medicine at the State University of New York Health Science Center at Brooklyn, COGA's principal investigator, noted that "it's a very long road from genes to behavior." But he reported progress in identifying what may be one point along that road: a genetically influenced brain wave, called the P3 wave. Visual or auditory stimuli evoke this oscillation in the brain's electrical activity, which is associated with recognition and attention, and Begleiter found deficits in the wave in alcoholics and in many close relatives of alcoholics. He also said that recent, soon-to-be-published research with adolescents by psychologist William Iacono of the University of Minnesota, Minneapolis, has shown that P3 deficits go not only with alcoholism and drug addiction but also with antisocial behavior and learning disorders. Begleiter says, "We have evidence that [P3 deficit] is a good index of central nervous system disinhibition," which characterizes all those conditions.

NIAAA director Enoch Gordis emphasized that we are far from the day when alcoholism genes could be useful as predictors for individual risk. The gene search is infinitely more difficult than that in a single-gene disease, he said: Alcoholism genes are multiple, they interact in unknown ways, and they have incomplete penetrance, which means you can have the genes but not be an alcoholic. As Gordis puts it, "these genes are for risk, not for destiny."

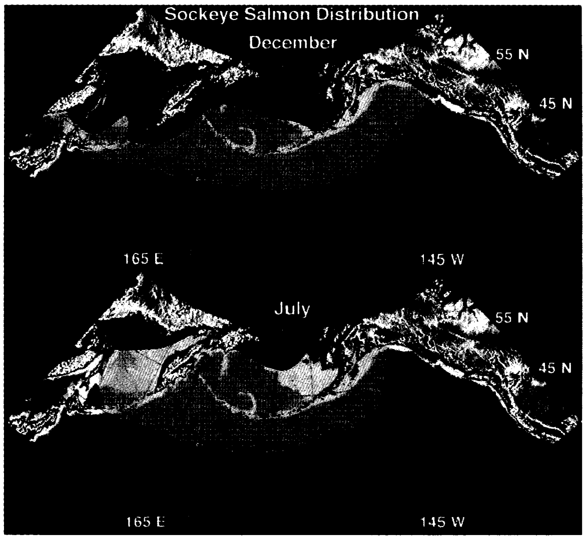
–Constance Holden

MARINE SCIENCE

Temperature Rise Could Squeeze Salmon

Modest rises in sea surface temperatures, in line with predictions of global warming over the next half-century, could make salmon disappear from much of the North Pacific Ocean. That possibility is suggested by a new review of a 40-year database that examines how fluctuating water temperatures affect the distribution of this commercially important fish. "This is a major study of enormous importance highlighting the need to study fish throughout their natural environments," says fisheries biologist John Everett, head of research at the U.S. National Marine Fisheries Service in Silver Spring, Maryland.

The study of sockeye salmon (*Oncorhynchus nerka*) appears in the April edition of the *Canadian Journal of Fisheries and Aquatic Science*. In it, David Welch of Canada's Department of Fisheries and Oceans in British Columbia and Japanese colleagues at the National Research Institute of Far Seas Fisheries in Shimizu in central Honshu mine data from major salmon surveys and sea-temperature measurements taken by the Japanese, Canadian, and U.S. governments going back to the mid-1950s. These data are equivalent to "29.1 years of continuous ship survey time," says Welch.



SOURCE: DAVID WELCH

In hot water. Warmer temperatures caused by a projected doubling of atmospheric carbon dioxide would shrink the current range of sockeye salmon (area north of the dark blue region) to the red zone.

Although laboratory experiments have shown that sockeye salmon are capable of surviving in waters warmer than 20 degrees Celsius, the study found that from November to March, the fish are only found in regions where the surface temperature is below 7 degrees Celsius. The maximum temperature rises to 15 degrees by August before dropping back to 7 degrees by November, the team finds. Such "sharp thermal limits," says Welch, are evident in all months (except October, for which data are lacking) and in all regions where sampling extended into sufficiently warm ocean regions. "Lethal limits for Pacific salmon are generally well above 20 degrees Celsius, so the remarkably low thermal limits observed result in sockeye salmon being excluded from vast areas of the North Pacific that are otherwise potentially habitable," says Welch.

These findings have led the authors to speculate that water temperatures interact with another factor—the need to minimize basic metabolic rates when food supplies are low—in shaping where the fish live. Laboratory studies have found that basal metabolic rates for cold-blooded animals rise exponentially with temperature. In other words, the fish may be avoiding warmer water because food supplies are insufficient to maintain such high metabolic rates.

The new studies also suggest a potentially devastating impact on salmon populations from predicted patterns of global warming caused by increasing concentrations of atmospheric CO_2. "A rise of 1 to 2 degrees Celsius in sea surface temperature in the Northern Pacific by the middle of the next century is a real possibility," says climate modeler Simon Tett at the Hadley Centre for Climate Change in Bracknell, U.K. Such a change could shrink the range of the salmon dramatically, largely restricting it to the Bering Sea. "Although much attention has been paid to the possibility that some stocks of salmon near the southern end of their range may be adversely affected by climate warming in fresh water, events happening in the marine phase could be even more disruptive," says Welch. In addition, he says, a northern shift in their ocean habitat would force the salmon to travel farther to reach their breeding rivers, resulting in smaller fish with fewer eggs.

The next step is to see whether other cold-blooded organisms display a similarly clear response to temperature variations. "So few studies have been done," says Everett. "We need urgently to know more about the effect of environmental temperatures on aquatic ecosytems."

–Nigel Williams