

With Mirrors and Finesse, Labs Domesticate the X-ray Laser

Space beam weapons and unlimited energy from fusion may have been pipe dreams of the 1980s. But today these dreams are giving birth to practical laboratory tools: tabletop x-ray lasers that may open up whole new areas of chemistry and biology. The first x-ray lasers were energized by nuclear explosions or jolts of light from giant glass lasers built for fusion experiments—hardly bench-top equipment. Now, says Joseph Nilsen, a physicist at Lawrence Livermore National Laboratory (LLNL), “several small university-size places are actually making a lot of progress toward tabletop lasers people can use every day.”

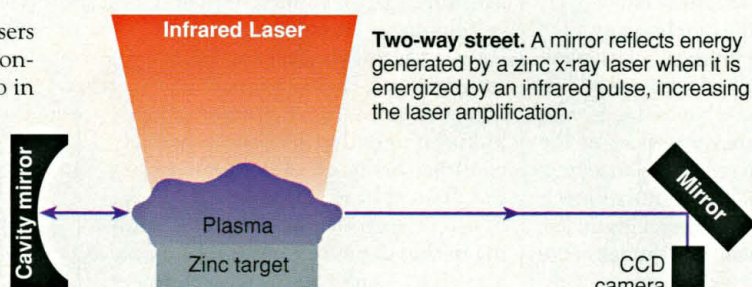
Although cheap, ubiquitous x-ray lasers aren't here yet, the 5th International Conference on X-ray Lasers, held 3 weeks ago in Lund, Sweden, highlighted some remarkable progress. “The big push at this meeting was to make them less and less expensive, and to go to shorter wavelengths that aren't accessible with other sources,” says David Eder of LLNL. To shrink their devices, investigators are substituting electric discharges and lower powered optical lasers for the brute-force pumping techniques of the first x-ray lasers. And they are boosting efficiency by reflecting the x-rays back and forth through the laser medium to extract more of its energy. All of which is raising expectations that the intense, coherent, short-wavelength pulses from bench-top x-ray lasers will soon be opening windows on the dynamics of chemical reactions or allowing investigators to make holograms of living cells.

In principle, x-ray lasers are no different from lasers at other wavelengths. They extract photons from a medium that has been jolted into what is called a population inversion: a state in which many of the atoms have been boosted to energy levels from which they can emit a photon when another photon of the same wavelength brushes past—a process called stimulated emission. The net result, two photons instead of one, both traveling in the same direction, is laser amplification.

The shorter the wavelength emitted by the laser, the higher the energy level to which the atoms have to be boosted. And that's the challenge with x-ray lasers. To get a material—usually a metal such as selenium, zinc, or yttrium—to emit x-rays, it has to be heated to temperatures as high as millions of degrees centigrade, forming a plasma, or ionized gas. The plasma then has to be excited even further to create the population inversion. Of-

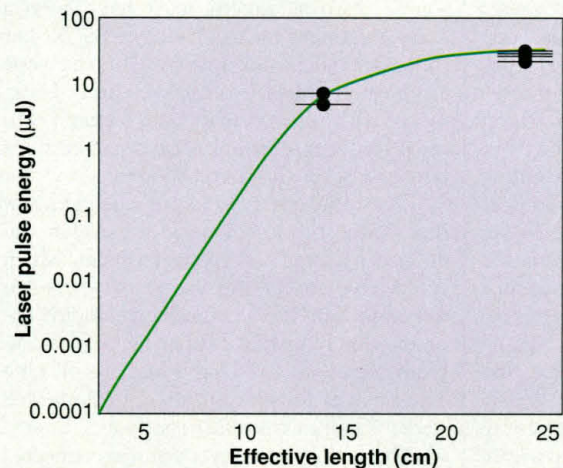
ten this is done by heating the plasma so rapidly that the free electrons become much hotter than the positively charged ions and kick the ions into higher energy states.

The traditional way of pumping in all this energy—with a single jolt from a powerful infrared laser like the building-sized Nova laser at LLNL—stands in the way of making x-ray lasers into tabletop instruments. Lasers like Nova are not only big and costly but also have to cool down after each “shot,” limiting the repetition rate of x-ray pulses to once every 20 minutes at best. “The bigger the ma-



chine, and the older the technology, the longer it takes to wait for the next shot,” says Pierre Jaeglé of Paris University at Orsay.

But recently scientists have realized that if they create and excite the plasma with several ultrashort pulses, lasting just a few trillionths of second each, rather than a single longer one, they can get away with a smaller pumping laser. Explains Ernst Fill of the Max Planck Institute for Quantum Optics in Garching, Germany, “A prepulse creates the plasma, and then the main pulse heats it in such a short time that you get an overshoot”—



Pushing the limit. By increasing the travel of x-rays through a tabletop laser, a mirror saturates its energy output (dots).

a state, far from equilibrium, in which superheated electrons pummel the cooler ions, efficiently creating the population inversion.

At the meeting, Peter Nickles and his team at the Max Born Institute in Berlin described how they exploited this multiple-pulse approach, which was pioneered at LLNL. With a prepulse of 5 joules and a main pulse of 3 joules, Nickles's group was able to spark x-ray lasing in titanium vapor—a feat requiring a 200-joule pulse at Nova. Although the Berlin group's pumping laser still sprawls across three 10-meter tables, researchers say that transforming it into a tabletop device should be a straightforward engineering task. “This is a very exciting result, leading the way to tabletop lasers,” says Fill.

Another way to cut x-ray lasers down to size is to eliminate the pumping laser altogether, and find a completely different way to create and excite a plasma. Jorge Rocca and

his team at Colorado State University in Fort Collins took that tack 2 years ago, when they used a powerful electric discharge to create a plasma confined in a narrow capillary. The result was a bench-top device that generated and amplified

“soft,” or low-energy, x-rays at a wavelength of 47 nanometers (*Science*, 4 November 1994, p. 732). Now Rocca has vastly improved the efficiency of his device. At the meeting he and his colleagues were one of two groups reporting that they had extracted the maximum possible amount of energy from the excited plasma.

Optical lasers reach this state, known as “saturation,” with the aid of mirrors at either end of the lasing medium that reflect the light back and forth through it. This step is key for a practical laser, because it's only at saturation that a laser produces truly coherent radiation—

radiation at which the wave motions of all the photons are in step. Coherence, in turn, makes the laser light suitable for a host of applications such as holography or interferometry.

Saturation has been difficult to achieve for x-ray lasers, in part because the population inversion often lasts no more than a few tens of picoseconds—time for the x-rays to travel only a few centimeters. But Rocca found that placing an x-ray mirror at one end of the plasma lengthened the x-rays' travel enough to achieve saturation. With the help of the mirror, his small discharge-pumped laser yielded an amplification of 63-fold.

Jaeglé's group also reached saturation in their device, which is pumped by a large infrared laser. "It was a surprising discovery that with a mirror that reflects only over a few centimeters we could multiply by a factor of 100 the intensity of the radiation," he says.

The feat takes Rocca's tabletop laser closer to practical application. For the first time, he and his colleagues announced, they could measure "a substantial energy output from such a tabletop device." The result has excited a community of potential users, he says. "We have been approached by a very large group of people who either are starting up experiments or are planning to start experiments."

Although Rocca's laser looks a lot like the tabletop device researchers dream of, its soft x-rays have wavelengths a little too long for some tastes. "If he would get down to [10 or 20 nanometers], his x-ray laser would catch on much faster," says Dennis Matthews of LLNL, who developed the first x-ray laser with substantial amplification in the early 1980s. "Then you would be doing things people travel to synchrotrons for." Synchrotrons, massive electron-storage rings, are currently researchers' only source of nearly coherent x-rays. Rocca is also trying to boost his machine's repetition rate, now at one shot per minute. If he could achieve his goal of one shot per second, says Matthews, his laser "would put out as much energy per second as you normally get on a beam line on a large synchrotron."

There are plenty of other obstacles standing in the way of a practical x-ray laser. Current x-ray mirrors—complex structures typically consisting of 800 to 1200 molybdenum carbide and silicon layers half a wavelength thick—don't stand up well to the harsh conditions of the hot plasma and the intense radiation, and most of them last just one shot. But a group led by Troy Barbee Jr. of LLNL reported at the meeting that by building multilayer mirrors from new materials—using silicon carbide in place of silicon, for instance—they improved the structures' heat resistance enough to withstand a few shots. These new mirrors should not only improve the lasers themselves but also make it easier to harness the x-rays they produce. "We can do interferometry and various kinds of imaging, a whole variety of things that you couldn't possibly do 2 years ago," says Barbee.

X-ray laser researchers believe that their devices are now in the stage that optical lasers reached in the early 1960s, when they ceased being laboratory curiosities and began opening up a huge variety of applications. Says Jaeglé, "We have reached a turning point: The x-ray laser leaves the area of the study of plasmas to become a laboratory source."

—Alexander Hellemans

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IMMUNOLOGY

Muscling Transplants Into Mice

Rejection threatens all tissue transplants, as the immune system seeks out and destroys foreign cells. Yet this threat does not exist everywhere in the body. Like safe havens for refugees, the body harbors protective pockets, in the eye and testis, for example, where transplants are safe from immunologic patrol. Creating similar "immune-privileged" pockets to protect a new heart, liver, or kidney graft has long been a transplant biologist's dream. Now researchers at Children's Hospital of Philadelphia have devised a way to do that by genetically engineering muscle cells to produce a key ingredient of immune privilege: a protein known as the Fas ligand, or FasL, that can induce immune cells to kill themselves.

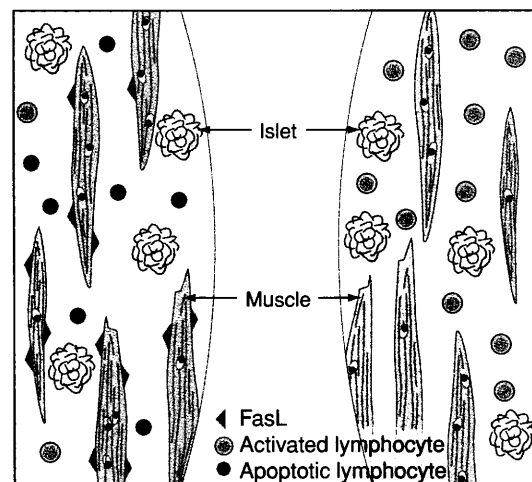
On page 109, transplant surgeon Henry Lau, molecular biologist Christian Stoeckert, and two colleagues report using their muscle-cell bodyguards to protect transplants of islet cells, the insulin-producing cells of the pancreas, in diabetic mice. "It's a stunning advance," says Douglas Green of the La Jolla Institute for Allergy and Immunology in California. "It's almost the Holy Grail of immunosuppression to restrict the suppression to the environment of the graft."

Richard Duke of the University of Colorado Health Sciences Center in Denver, whose team was the first to find a role for FasL in immune privilege, calls the work "a home run." The finding, Duke says, not only opens the door to a possible treatment for the 700,000 people in the United States with insulin-dependent diabetes, but also holds promise for people receiving other types of tissue and organ transplants who now must take immunosuppressive drugs, which often lead to infections and cancer.

In conceiving their islet-grafting strategy the Children's Hospital team took its cue from a great deal of work showing that FasL and its partner, a protein called Fas found on immune-cell surfaces, help shut down immune responses. They do this by inducing immune cells to kill themselves in a process called apoptosis. FasL sends the death signal by binding to its receptor, Fas, which transmits it to the cell interior. This interaction is also the basis for immune privilege, as Colorado's Duke and his colleague Donald Bellgrau showed last year for the testis (*Nature*, 19 October 1995, p. 630), while Thomas Ferguson's team at Washington University Medical School in St. Louis produced similar findings for the eye (*Science*, 17 November 1995, p. 1189).

Several researchers quickly began trying

to express FasL in a variety of tissues in hopes of using the molecule as a transplant tool, but Lau's is the first group to claim a victory. After showing that muscle cells genetically engineered to make FasL kill tumor cells expressing Fas in lab culture, they began the transplant studies. For these, the team transplanted islet tissue wrapped with the engineered muscle cells under the kidney capsules in 31 diabetic mice. They compared these to 16 control mice, including some who received only islets and others who received islets cloaked in unaltered



Muscular bodyguards. Muscle cells expressing FasL (left) protect islets by inducing immune-cell suicide.

muscle. Not only did the engineered muscle cells prolong survival of the islet-cell grafts compared to the controls, presumably by killing T cells before they got to the islet cells, they did so in a dose-dependent way: Transplanting 10,000 muscle cells lengthened average survival from 10 to 26 days, while transplanting 2 million muscle cells upped survival to more than 84 days.

The downside is that more than half the mice receiving the top dose lost their grafts within 80 days, in part because the muscle cells stopped expressing FasL. Thus, before any studies begin in humans, biologists must find a way to ensure long-term FasL expression. What's more, the experiment was done in mice with chemically induced diabetes, so the finding must be confirmed in mice with naturally occurring autoimmune diabetes. Still, researchers are confident that, as La Jolla's Green puts it, this FasL work represents "the beginning of a new era in transplantation."

—Ingrid Wickelgren

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