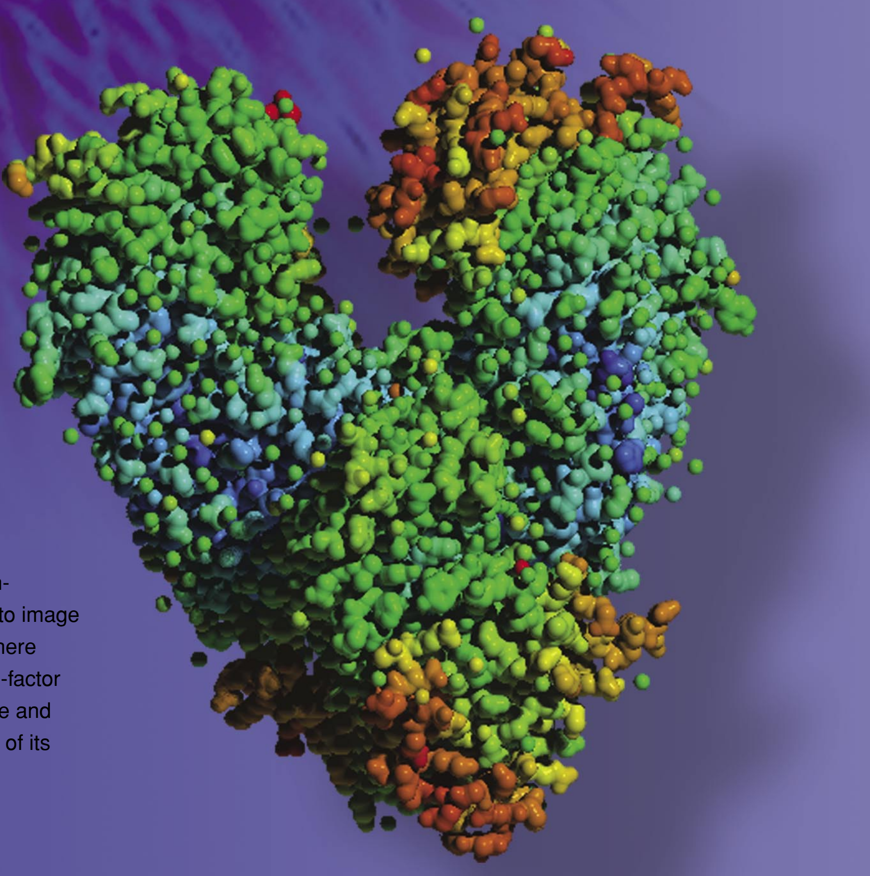
An Extraordinarily

Livermore researchers are part of the design team for the first large-scale x-ray laser.



The goal of the new fourth-generation light source is to image single molecules. Shown here are (foreground) the lethal-factor protein of an anthrax spore and (background) a simulation of its diffraction pattern.

Bright Idea

ITS short, intense pulses of x rays will reveal for the first time the structure and dynamic behavior of many proteins and viruses at atomic resolution and in three dimensions. It will unlock the secrets of high-energy-density plasmas, which are of interest to the nation's Stockpile Stewardship Program. And it will create the hot, dense matter believed to exist in the center of large planets.

It's the Linac Coherent Light Source (LCLS), the world's first large-scale x-ray laser, being designed for installation at the Stanford Linear Accelerator Center (SLAC). "The immense power of its short-pulse, laserlike x rays will create a revolution in science," says Alan Wootton, chief scientist for Livermore's Physics and Advanced Technologies Directorate.

The heart of the LCLS is a free-electron laser that produces beams of coherent, high-energy x rays. Coherence—the phenomenon of all photons in a beam acting together in perfect lockstep—makes laser light far brighter than ordinary light. Think of a 10-watt night light; then compare its brightness with that from a 10-watt laser—a beam so bright it can cut metal. Because x-ray photons at the LCLS will be coherent, the resulting beam of light will be as much as 10 billion times brighter than any other x-ray light source available today.

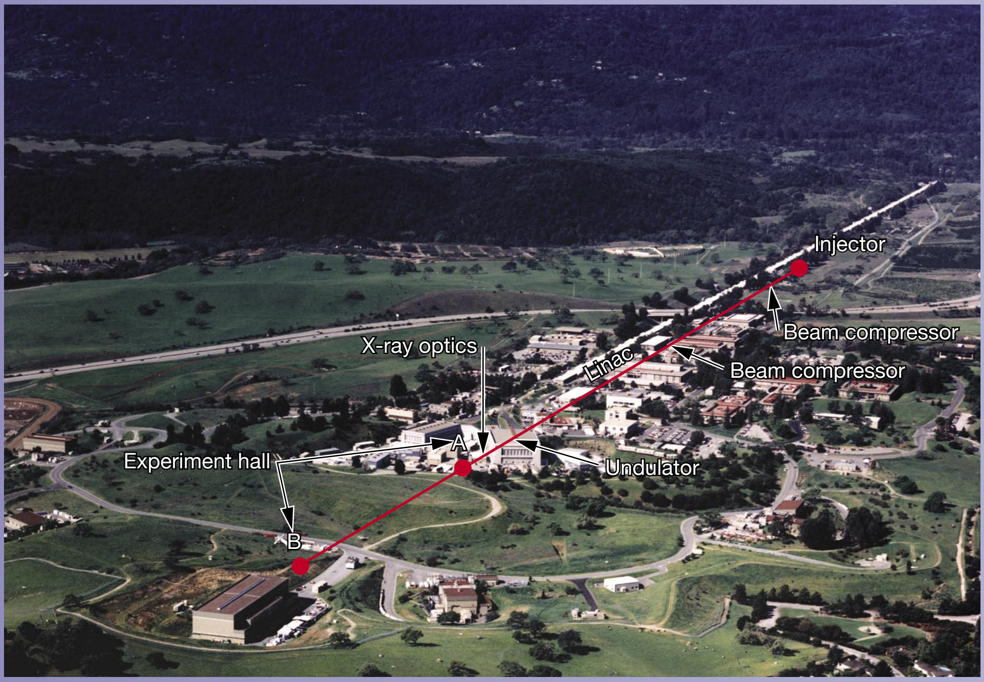
The LCLS, and a cousin planned in Germany, will improve on so-called third-generation light sources. The third-generation sources are circular, stadium-size synchrotrons, and they produce streams of incoherent x-ray photons. Because their pulses are long compared to the motion of electrons around an atom, synchrotron light sources cannot begin to explore the dynamic motion of molecules. The light from the fourth-generation LCLS will last for quadrillionths of a second, allowing its beam to capture such dynamic behavior.

Even determining the static structure of proteins and molecules will be easier and faster with the LCLS. Today, proteins and other macromolecules must be crystallized before their structure can be probed with synchrotron radiation. But not all proteins can be crystallized, and the crystallization process is long and involved. With the LCLS, a single powerful pulse will image one molecule with no prior crystallization required.

Lawrence Livermore is part of a SLAC-led consortium to plan, design, and build the LCLS. Other partners include the University of California at Los Angeles (UCLA) and Los Alamos, Brookhaven, and Argonne national laboratories.

Livermore's primary responsibility, under physicist Richard Bionta, is to design and fabricate the optics that will transport the x-ray beam to experimental chambers and to measure, or diagnose, the beam's condition. The extreme brilliance and ultrashort duration of the beam's pulses will give the beam a peak power of as much as 10 gigawatts. These features make designing optics a challenge because, says Bionta, "The energy of the beam can melt many materials in a single pulse."

Meanwhile, physicist Henry Chapman and other Livermore scientists are planning the first experiments at the LCLS and



The Linac Coherent Light Source will use the linear accelerator (linac) at the Stanford Linear Accelerator Center to create very bright, ultrashort pulses of laser radiation.

establishing the x-ray pulse parameters that are needed for various measurements.

"At the LCLS, we'll use lens-less imaging to determine the three-dimensional arrangement of atoms in a molecule," Chapman says. "We'll detect x rays scattered by a sample when the beam hits it and then examine the diffraction pattern." Radiation from the powerful beam will destroy each sample, but the beam's ultrashort pulse will generate diffraction data before that happens. "Every molecule has a unique diffraction pattern," says Chapman, "and that pattern depends on the molecule's structure."

Experiments at the LCLS will reveal protein structure, which determines protein function. Hence, the LCLS is expected to profoundly benefit structural biology and medical research. It could eventually help scientists solve the proteome—the entire system of proteins in the human genome.

A Single Straight Shot

When the LCLS becomes operational, sometime in 2008, the free-electron laser's photoinjector will shoot electrons down part of the SLAC linear accelerator, or linac. The photoinjector will produce tiny bunches of electrons that travel in a narrow, bright beam at almost the speed of light. After the electrons enter the kilometer-long linac, compressors along the accelerator path reduce the length of each bunch by a factor of 30, which increases their peak current. Their energies may be pushed as high as 14 gigaelectronvolts, a value that will be adjusted from experiment to experiment to produce the desired range of x-ray frequencies.

The electrons then enter an undulator—a vacuum chamber just 5 millimeters across and about 125 meters long and lined with 7,000 magnets arranged in alternating poles. As the electron bunches move down this narrow channel, the magnetic fields push and pull on them, causing the bunches to emit x rays. The LCLS undulator is so tightly focused that x rays emitted by one electron interact with the electrons in front of it. This interaction causes the electrons to bunch more tightly, which generates more x rays.

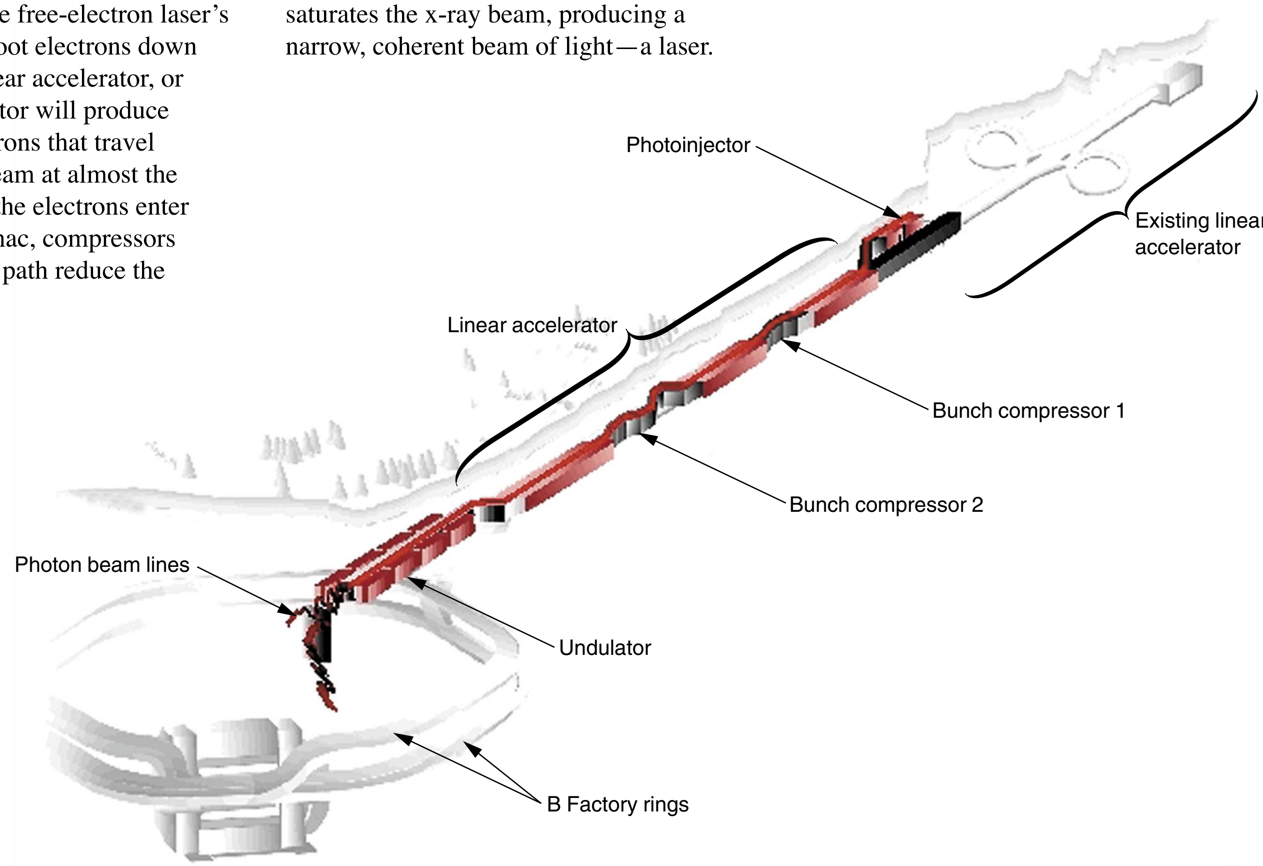
As the process repeats, the bunches become smaller and smaller. This chain reaction is called self-amplification of spontaneous emission, or SASE (pronounced "sassy"). SASE eventually saturates the x-ray beam, producing a narrow, coherent beam of light—a laser. Broadband spontaneous (not coherent) radiation about 10,000 times brighter than that from any other light source emerges from the undulator as well.

Livermore-designed optical devices, placed beyond the undulator, will manipulate the direction, size, energy spread, and duration of the x-ray beam. They also will diagnose the beam and direct x rays to one of two halls for use in experiments.

The experimental halls, A and B, are located 50 and 400 meters downstream from the end of the undulator. Experiments requiring a very narrow, high-energy-density beam will use facilities in Hall A, while Hall B will house experiments that require lower energy densities.

Optics Bear the Brunt

All the diagnostic equipment on the LCLS is designed to minimize interference with the beam. "Because the beam is so



Layout of the Linac Coherent Light Source at the Stanford Linear Accelerator Center. Experimental halls A and B will be to the left, beyond the photon beam lines.

powerful," says Bionta, "our goal is to not put anything in its path, except a gas attenuator."

A mask, valves, and movable jawlike slits just beyond the undulator intercept most of the spontaneous radiation that accompanies the beam. These devices are designed so that they do not block the narrow, intensely coherent x-ray beam.

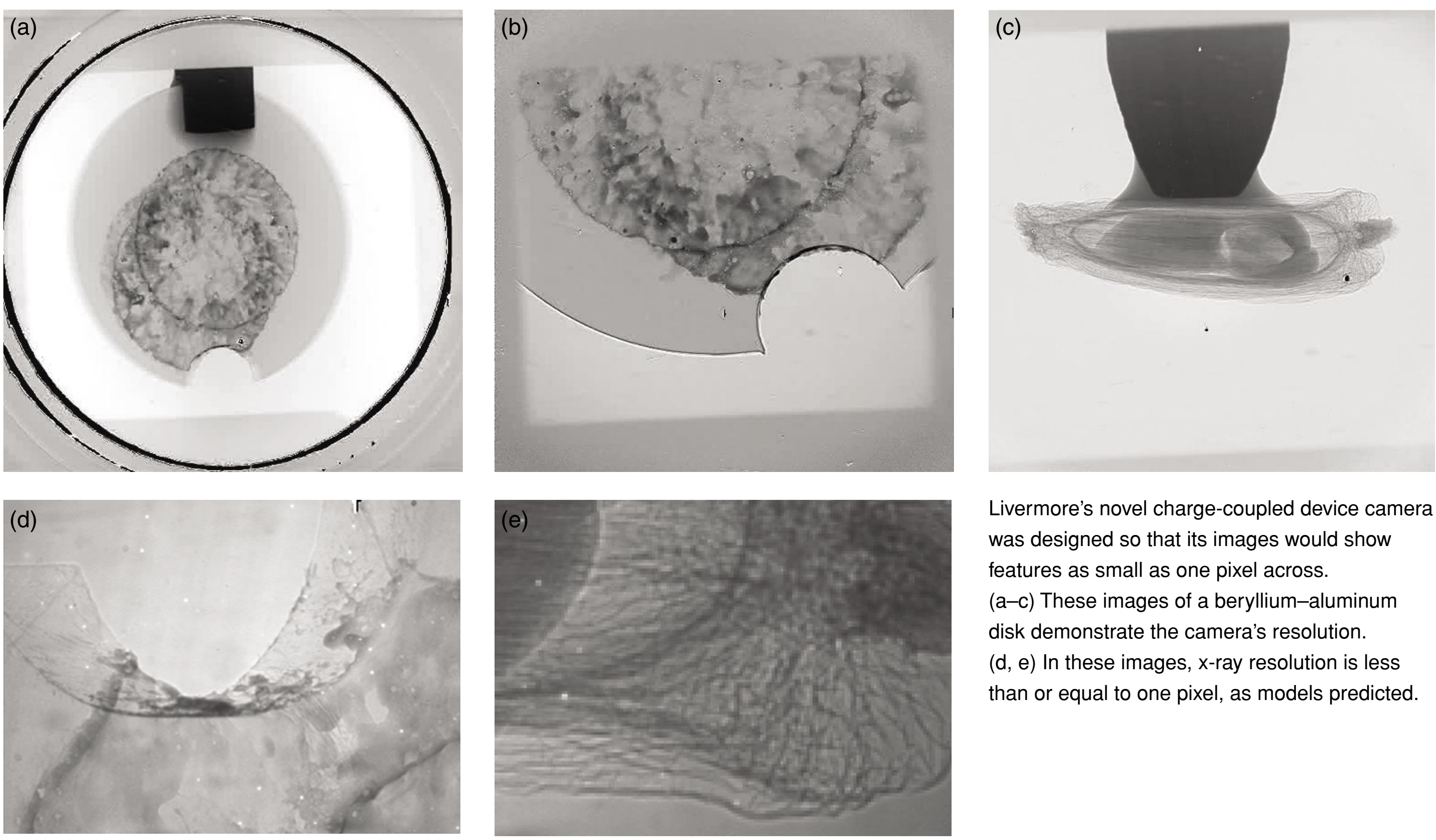
Livermore researchers have been working for several years to understand the damage that occurs when an LCLS beam encounters optics, diagnostics, and targets. Several types of simulations, including Monte Carlo and wave models, helped them fully characterize the x-ray beam. Armed with these data, Wootton, Bionta, and others began to develop schemes for imaging such a bright beam.

The concept they selected uses a camera that will be one of the first diagnostic devices beyond the undulator. In this setup, a small fraction of the beam's light is directly reflected off a thin, polished beryllium foil. Beryllium was chosen for the foil because it has a low electron density and tends to absorb few x rays. Beryllium also will be used for many of the reflective optics at the front end of the system where photon densities are highest.

When the beam reflects off the foil, it strikes the surface of a 100-micrometer-thick lutetium oxyorthosilicate (LSO) crystal doped with a 5-micrometer-thick scintillating layer of cerium. "The LSO crystal is designed to reflect just one-ten-thousandth of the total light from the beam," says Bionta. Reflected visible light is collected by a microscope lens and forms a magnified image on a charge-coupled device (CCD) camera. The images of a beryllium–aluminum disk shown below demonstrate the fine resolution of the camera.

Using the CCD camera, the team has studied how photons from short-pulse lasers at various wavelengths interact with different materials. For example, silicon was irreversibly damaged even at low energy densities using a laser in the visible wavelength and pulse lengths similar to those of the LCLS.

Focusing the LCLS's high-energy beam will be a challenge. The Livermore researchers are developing a new class of tubular optical devices in which the x-ray beam reflects off the inside wall. The slight grazing incidence of the beam on the wall of the lens reduces the absorbed energy considerably. X rays enter the tube at one end and are reflected once by the highly reflective interior surface. They then exit from the other end of the tube, but now the



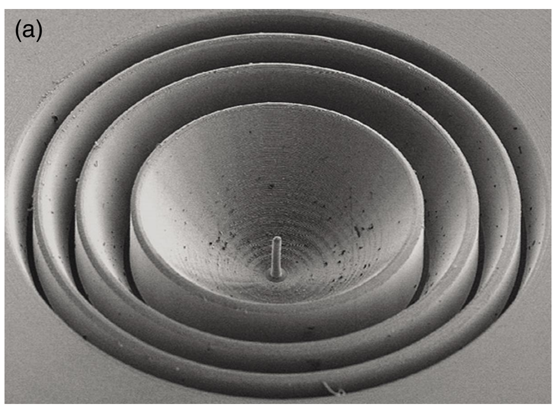
Livermore's novel charge-coupled device camera was designed so that its images would show features as small as one pixel across.
(a–c) These images of a beryllium–aluminum disk demonstrate the camera's resolution.
(d, e) In these images, x-ray resolution is less than or equal to one pixel, as models predicted.

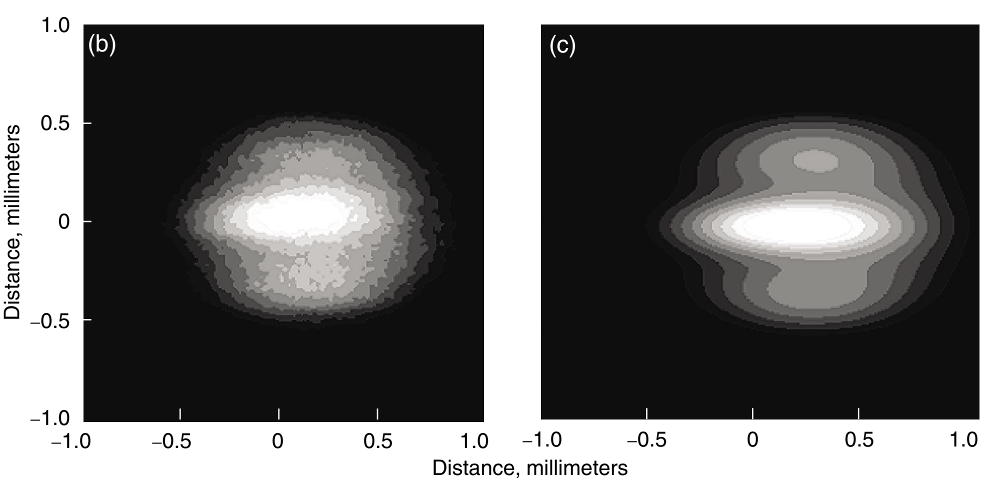
x rays are traveling in a slightly different direction.

A special focusing element has also been designed for the warm, dense matter experiments that will take place in Hall A. Warm, dense matter is an energetic plasma whose density is almost that of a solid, but it may be as hot as 10,000 kelvins. Scientists believe this matter may exist in the centers of large planets, such as Jupiter, and its properties are important to astrophysics and relevant to the production of inertially confined fusion reactions. Warm, dense matter will be created in the laboratory by focusing the x-ray laser's beam to a 2-micrometer spot in the center of a sample of solid matter.

The focusing element will be a blazed phase lens, as shown in the top image below. The lens is made of carbon, which has low x-ray absorption characteristics. Although carbon is not as resistant as beryllium is to the intense power of the LCLS, it has a higher refractive power and is easier to machine precisely, allowing more interesting optical designs. To test the lens design, the research team had a prototype machined at Livermore's Large Optics Diamond Turning Machine (LODTM).

The prototype lens is made from a thin disk of aluminum, which has the same optical properties as carbon. The aluminum lens was tested at the Stanford Synchrotron Radiation Laboratory. Although lens performance was limited by the material chosen and the geometry of the experiment was not ideal, the measured performance closely matched predictions from simulations.





(a) A prototype blazed phase lens made of pure aluminum. The pattern was carved using Livermore's Large Optics Diamond Turning Machine. Each groove is 18.7 micrometers deep, and the final thickness of the disk is 79 micrometers. In tests of the lens at the Stanford Synchrotron Radiation Laboratory, (b) measured images closely matched (c) simulations.

Precision machinists at the LODTM are trying to make lenses from blocks of pure beryllium. Beryllium is a challenge to machine because of its grain structure and because it's a hazardous material. In fact, Livermore's LODTM is one of the few facilities in the nation authorized to work with it.

Perhaps the most challenging LCLS diagnostic will be measuring the 230-femtosecond pulse length. Streak cameras are not an option because they measure down only to 500 femtoseconds. One potential device is a fiber-optic interferometer developed by Livermore photonics experts. The interferometer uses the beam from a continuous-wave laser to monitor the electronic state of a tiny waveguide inserted across its measurement arm.

"When we tested the interferometer at Stanford's synchrotron," says Bionta, "it was sensitive to x rays perturbing the waveguide. In fact, its response was faster than we could measure with the synchrotron beam." Further experiments will be conducted with shorter-pulse x-ray sources at Livermore and SLAC, to determine if the device is really fast enough to measure the 230-femtosecond LCLS pulse.

Technologies for Experiments

Two general classes of experiments have been proposed for the LCLS. In the first class, the x-ray beam will be used to probe the sample without modifying it, which is the current practice for most experiments with synchrotron sources. For example, scientists can use the x-ray laser to determine the dynamic behavior of chemical interactions, essentially by watching the interaction occur on a femtosecond scale, which has never been possible before.

In the second class of experiments, the LCLS beam will induce nonlinear photoprocesses, or it will create matter in extreme conditions. These experiments include creating warm, condensed matter, as previously described, and determining the structure of macromolecules, by recording crucial information about a molecule before it is vaporized.

It is in biology that the hard x rays of the free-electron laser are expected to have the biggest effect. No technique available today can image the interior of micrometer-size particles in three dimensions at high resolution. With the LCLS, scientists will be able to analyze very small samples, from tens of micrometers down to single molecules.

With third-generation synchrotrons, the low-intensity x rays can diffract to atomic resolution only when a molecule has been crystallized. Once a protein has been crystallized, scientists can't study its interactions with other biological molecules. Nuclear magnetic resonance spectroscopy is used to overcome these shortcomings of x-ray crystallography, but it does not work for larger proteins. With the LCLS, researchers can study proteins that can't be crystallized, such as proteins linked to lipids (fats) and embedded in cell membranes. The short pulses of the LCLS will also reveal how some molecules change shape in just a few femtoseconds.

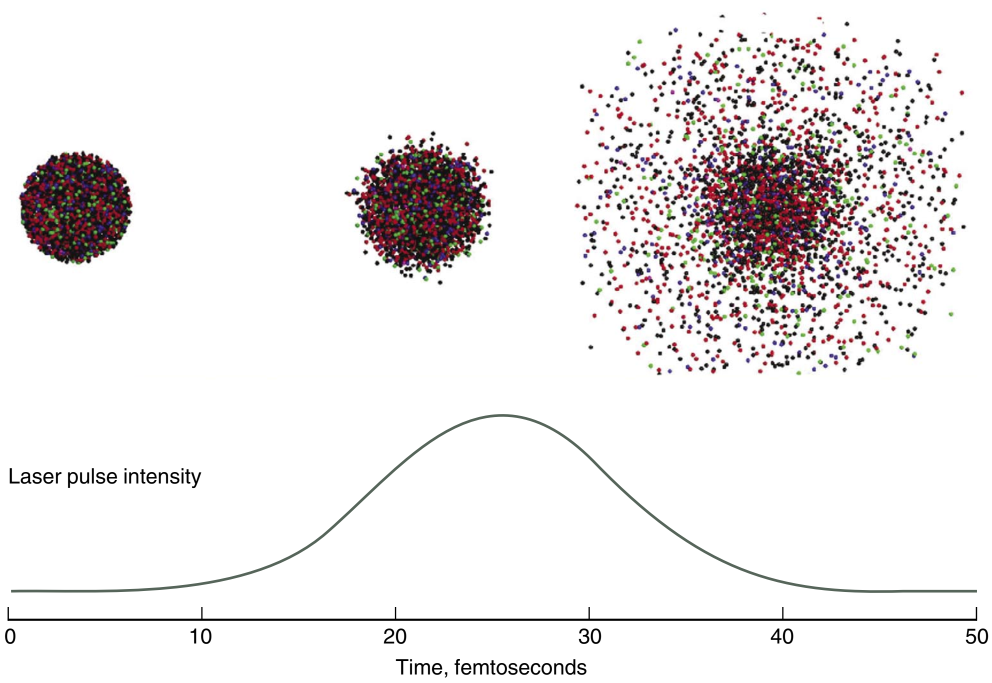
Recording the diffraction pattern before the molecules blow up is critical. X-ray pulses are diffracted by electrons orbiting the atoms in molecules. By studying the patterns made by these diffracted rays, biologists can deduce the structure of the molecule under analysis. Team members have developed a hydrodynamic model to understand the various interactions between the x-ray beam and the sample and to verify that the beam's pulse will end before the sample begins to be torn apart. The figure to the right shows results from simulations of a 20-nanometer protein molecule when it's hit by an x-ray free-electron laser. Models also indicate that a water tamper will suppress the explosion, extending the time range of the diffraction process. Researchers have used simulations to establish the minimum photon density required to classify diffraction and have determined that the necessary pulse durations range from 10 to 30 femtoseconds.

Experiments to verify the timing of the explosion will be performed at the Tesla Test Facility (TTF), the proving ground for the TESLA x-ray free-electron laser that is being designed in Germany. "The TTF is the only place we have now for testing any of these simulations experimentally," says Chapman. "Its wavelength is longer than the LCLS's will be, so we can't get to atomic resolution. But we can begin to understand how and when damage occurs."

The team is also exploring ways to get samples into the beam's path. "Molecules will be just a few billionths of a meter wide," says Wootton. "Somehow, we have to get them lined up with a beam that's only slightly larger, a few millionths of a meter wide and running at the speed of light."

Each pulse of the x-ray beam can hit just one sample in its path. Complete three-dimensional information about a molecule will then be collected by examining multiple, identical samples, one by one. One method for acquiring such data is to use some kind of "molecule gun" to feed samples into the beam path.

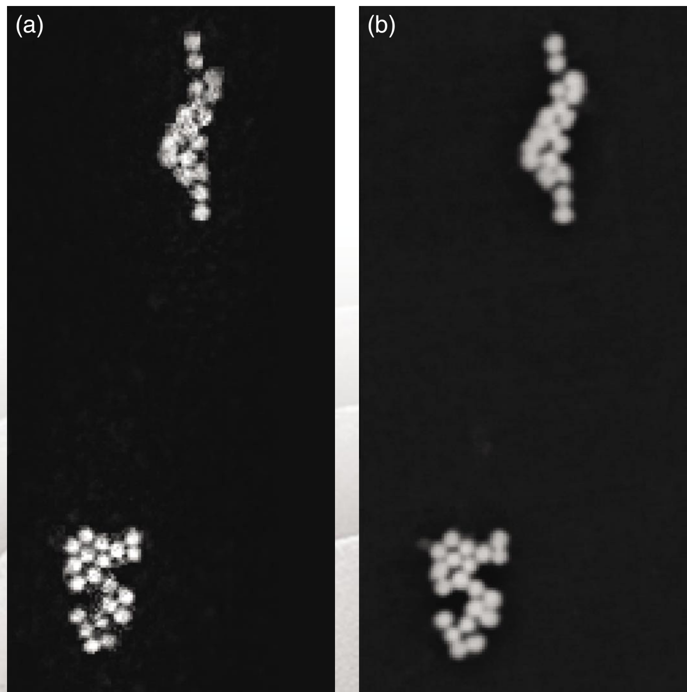
An alternative method is to tether several protein molecules to a membrane positioned in the beam's path. This option, in which the molecules are oriented the same way, requires a lower photon density. Says Chapman, "Because in this case we can now use a lower photon density, which will cause overall less damage, models show we can use longer pulses where the rate of damage is reduced." The team is



Atom trajectories computed by a hydrodynamic model show a 2-nanometer protein exploding after it is hit by a 20-femtosecond, 12-kiloelectronvolt x-ray pulse that is 0.1 micrometer wide. Models indicate that atomic-resolution imaging can be achieved with pulses shorter than 20 femtoseconds. They also show that a water tamper on the protein slows its destruction so that longer pulses could be used.

exploring whether dip-pen nanolithography can be used to produce this carefully oriented pattern of molecules. In dip-pen nanolithography, molecules of a protein or other organic material are deposited on a substrate in a regular pattern.

The Livermore researchers who are developing the algorithms to reconstruct diffraction patterns have been aided by experiments at the Advanced Light Source, a third-generation synchrotron at Lawrence Berkeley National Laboratory. One recent experiment, in collaboration with colleagues from Berkeley and Arizona State University, used a silicon nitride pyramid decorated with 50-nanometer gold spheres. These spheres were chosen because they could be well characterized by other, independent means. As shown below, a reconstructed image of gold ball clusters compares extremely well with an image obtained using a scanning electron microscope. “This reconstructed image is the first true lens-less x-ray image,” says Chapman.



Computer algorithms are being developed to use diffraction pattern data to reconstruct an image of the molecule under study. In experiments at Lawrence Berkeley National Laboratory’s Advanced Light Source, (a) a reconstructed x-ray image of gold ball clusters compares extremely well with (b) an image obtained using a field-emission scanning electron microscope.

Beyond the Tip of the Iceberg

Chapman’s team will also conduct experiments at the TTF in Germany. Those single-shot diffraction experiments will use samples mounted on a substrate and samples shot across the beam. Samples will include lithographic test patterns, diatoms, and wet cells.

“With these experiments, we’ll be able to achieve the long-sought goal of x-ray imaging at resolutions beyond the radiation-damage limit,” says Chapman. “We hope to get spectacular images. But they will be just the tip of the iceberg compared to what we will be able to achieve at the LCLS.”

—Katie Walter

Key Words: free-electron laser; Linac Coherent Light Source (LCLS); linear accelerator (linac); protein structure; Stanford Linear Accelerator Center (SLAC); x-ray laser; warm, condensed matter.

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