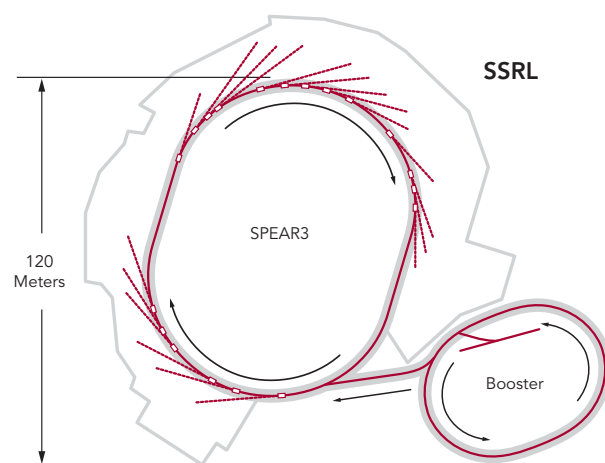


SSRL

At SSRL, electrons accelerate around a ring to produce beams of bright X-ray light for probing matter at the atomic and molecular level, enabling advances in biology, medicine and many other fields.

Nine of SSRL's 33 experimental stations host biological structure experiments, and about 40 percent of scientists using SSRL work in bioscience or biomedicine. Automation allows them to load samples and collect data remotely. An additional beamline will soon be available for higher-throughput, higher-resolution studies of proteins, viruses and other biological samples.

- 27 beamlines can be operated simultaneously
- 33 experimental stations; about 12 are specialized for biological or biomedical studies
- About 40 percent of scientists using it are in bioscience or medical disciplines
- New beamline under development will allow state-of-the-art structural biology studies
- Companies have used SSRL for drug development research



Electrons are accelerated in the 90-meters-wide SPEAR3 ring at SLAC's SSRL. The electrons rounding this ring, which are supplemented by a booster ring that also feeds bunches of high-energy electrons, emit X-rays millions of times brighter than dental X-rays. The X-rays are streamed into dozens of beamlines, allowing simultaneous experiments. Some of these beamlines are equipped with a sequence of magnets to create even brighter X-ray light.

SLAC is operated by Stanford University for the U.S. Department of Energy Office of Science.

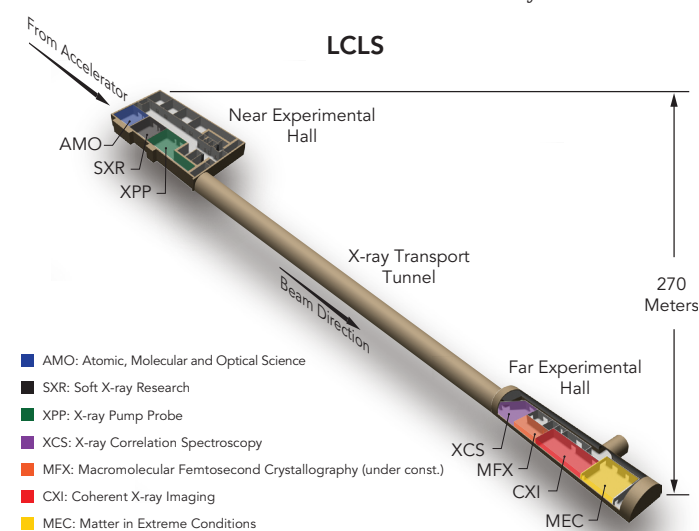
LCLS

LCLS produces the world's brightest X-ray pulses. Like a high-speed camera with an incredibly bright flash, it takes X-ray snapshots of atoms and molecules at work, revealing never-before-seen details in biological samples.

One-quarter of scientists who use LCLS work in bioscience or biomedicine, and about 40 percent of the experimental proposals at LCLS are biology-focused. The number and variety of these studies is set to grow with the addition of a unique experimental station currently in development and a planned LCLS upgrade.

Increasingly, researchers are using both LCLS and SSRL to study the same samples in different ways, which can validate new experimental techniques and provide more robust results.

- Can study nanoscale crystals, living cells, intact viruses in very natural conditions
- Six experimental stations, including one that specializes in protein studies
- One additional experimental station, under construction, will be optimized for biological samples
- About 25 percent of scientists using LCLS are in bioscience or medical disciplines
- A planned upgrade will significantly increase the capacity for experiments and add new capabilities to remain at the international forefront of X-ray laser science



In the 1.3-mile LCLS X-ray laser, bunches of electrons that are amplified and sped up in a two-thirds-mile segment of SLAC's linear accelerator (not shown) are wiggled in a sequence of powerful magnets called an undulator, which causes them to emit ultrabright X-rays that arrive at experimental stations at a rate of 120 pulses per second.

New Frontiers in Biomedical Research at SLAC's SSRL and LCLS

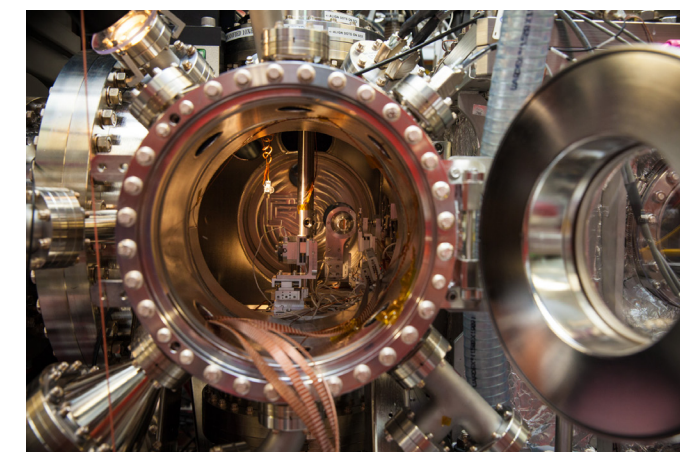
The unique combination of powerful X-ray tools at SLAC, which includes a mile-long ultrabright X-ray laser and a third-generation synchrotron ring, allows researchers to engage in a broad range of complementary studies that are uncovering nature's long-held secrets.

X-rays have revolutionized research in many fields, giving scientists atomic-scale views of molecules such as proteins, the building blocks of life. Researchers have used X-rays to determine the structures of more than 100,000 proteins, which helps them understand how the proteins function and interact with other molecules. These discoveries also guide the design of new drugs that numb our reaction to pain, activate an immune response or lower our blood pressure.

SLAC's Stanford Synchrotron Radiation Lightsource (SSRL) was one of the first facilities to make bright X-ray beams available to the global biological and biomedical scientific community, and is now one of dozens operating worldwide.

SSRL research has addressed many critical questions in biology and biomedical research. Protein structures mapped at SSRL provided insight into how information stored in DNA is transcribed into a form readable by the cell's internal machinery, a scientific breakthrough celebrated by the Nobel Prize in Chemistry in 2006. Researchers have also used SSRL to study the structure of viruses – such as Ebola and the flu – and a potent antibody in humans that can neutralize a range of viruses, from the Spanish flu to the H5N1 bird flu. X-ray studies at SSRL have also contributed to the development of cancer medications and other drugs, including Osteltamivir, an antiviral marketed as Tamiflu; Avastin, which blocks the growth of blood vessels in tumors; and anti-HIV therapies.

In 2009, SLAC launched a new era of exploration with the Linac Coherent Light Source (LCLS), the world's first high-energy or "hard" X-ray free-electron laser. LCLS X-ray pulses, a billion times brighter than synchrotron X-rays, have enabled new forays into biomedical research, probing samples that are



In this experimental chamber at SLAC's LCLS, jets of liquids containing crystallized proteins are hit by intense, ultrafast X-ray pulses. The pulses produce patterns as they strike the crystals. Detectors capture these patterns, which are used to determine the atomic-scale structure of the proteins.

too small or delicate for study at synchrotrons. LCLS can also study the natural motion of biomolecules in real time, moving well beyond the structural studies conducted in more conventional facilities. This opens up new avenues of research into living systems and phenomena such as photosynthesis.

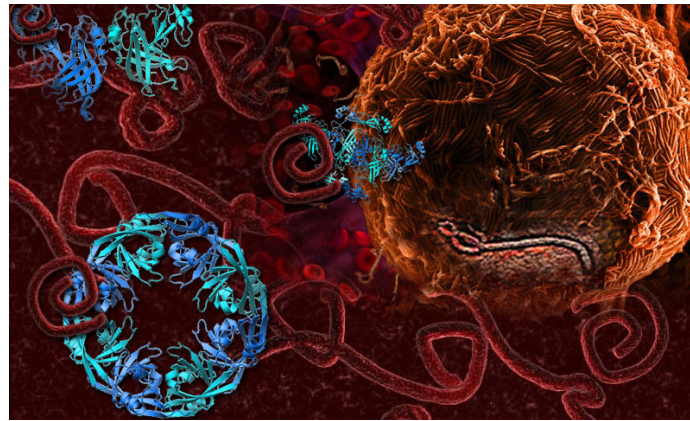
LCLS can reveal new details in proteins and other biomolecules that were previously out of reach or proved difficult to study at the atomic scale using conventional tools. For instance, scientists can use LCLS to map proteins that are embedded in cell membranes to learn more about how they bind to medications for pain, migraines and other disorders. Scientists have also used LCLS to study carboxysomes, structures in some bacterial cells that play a major role in Earth's life-sustaining carbon cycle. They can also study intact viruses, nature's photosynthetic machinery, and living cells and their components under more natural conditions.

Scientists are pursuing methods to assemble ultrafast X-ray snapshots of active biology into movies that show life in motion at its smallest scales. And, in cooperation with the international scientific community, SLAC is working toward atomic-scale imaging of many types of intact biological samples.

Research Highlights

New Insights to Fight Ebola Virus

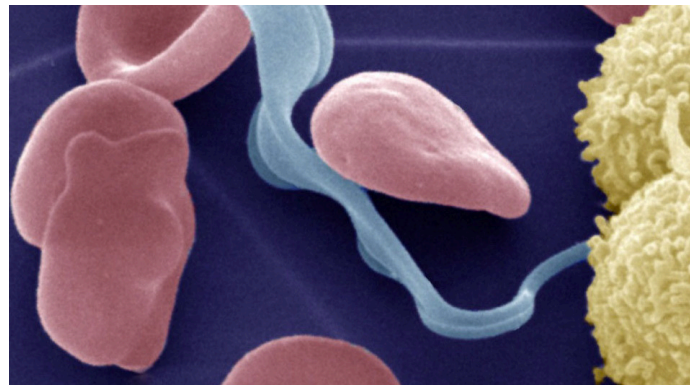
A study based in part on X-ray research at SSRL shows how a protein of the deadly Ebola virus can arrange itself into three shapes with distinct functions. The study found that the shapes correspond to different stages in the virus cycle, and their structures provide clues for the development of antiviral drugs.



VP40, a protein of the Ebola virus, can arrange itself into three very different shapes (blue), each with a distinct function. (SLAC National Accelerator Laboratory and Zachary Bornholdt/The Scripps Research Institute)

Drug Target for African Sleeping Sickness

An experiment at LCLS revealed the detailed structure of an enzyme associated with transmission of African sleeping sickness, which is responsible for tens of thousands of deaths each year. The disease is caused by a parasite carried by tsetse flies, and this parasite uses the enzyme to break down the tissues of its victims. Researchers grew crystals of the enzyme within living cells and used LCLS to determine its molecular structure – a step toward developing a new drug.

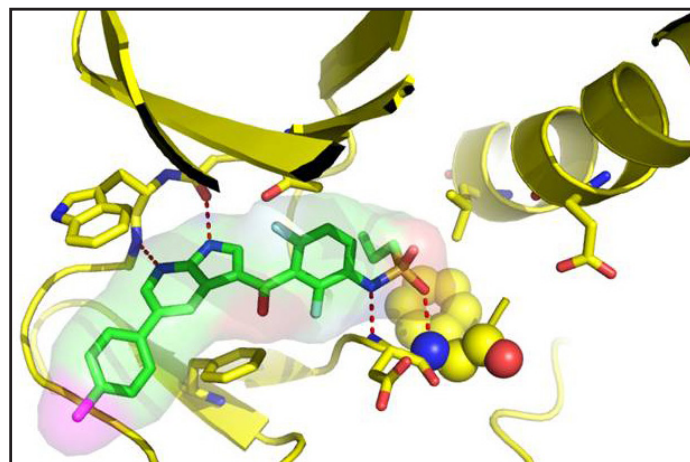


Colored electron micrograph of the bloodstream form of the *Trypanosoma brucei* parasite (light blue) that causes African sleeping sickness. Upon infection of the mammalian host by bite of the tsetse fly, the parasite lives within the bloodstream and later invades the central nervous system and the brain. (Michael Duszenko/University of Tübingen)

Melanoma Treatment Blocks Mutant Enzyme

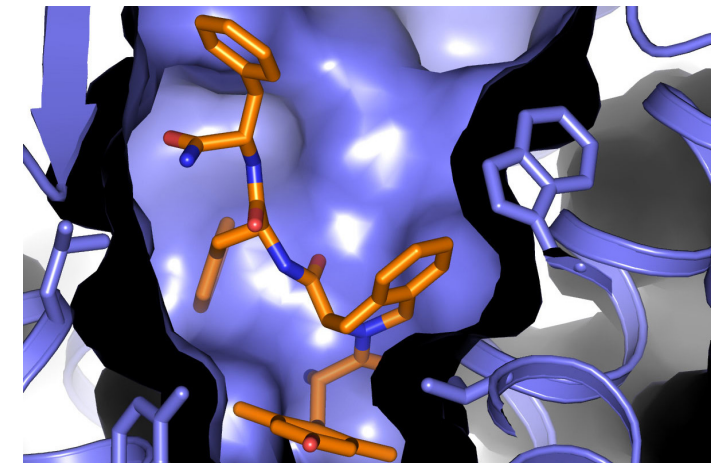
Researchers at Plexikon, a drug-discovery company, determined the structure of a mutated protein involved in malignant melanoma, the deadliest form of skin cancer, with experiments at SSRL and other facilities. The research led to a new drug, vemurafenib. In a clinical trial, patients receiving the drug lived six months longer than those who did not receive it. However, the drug is not yet a cure for melanoma, underscoring the need for more research.

This image shows how an anti-cancer drug prevents a mutated enzyme from promoting the growth of tumors. In its normal form, this enzyme helps regulate cell growth in our bodies.



View of a Promising New Painkiller

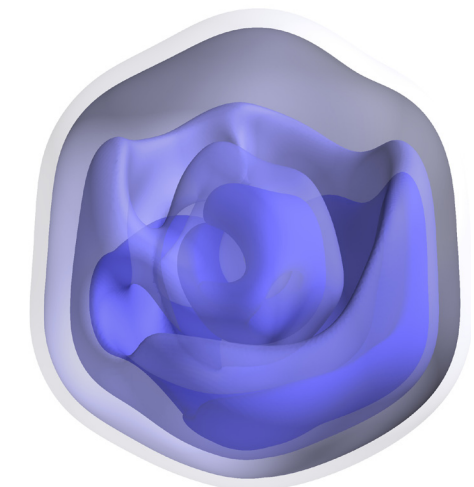
Morphine, a powerful and popular painkiller derived from opium poppies, also carries the risk of abuse and dependency. An LCLS study showed how an alternative, and potentially less risky, drug compound docks with a receptor in cell membranes that regulates the body's pain response. About 40 percent of prescription drugs interact with this class of cell membrane receptors, known as G protein-coupled receptors or GPCRs; but only a couple dozen of the hundreds of GPCRs have been mapped in atomic detail. LCLS has the potential to make it much easier to map GPCRs, which will help scientists develop and refine medications that target these receptors.



This rendering shows a type of cellular membrane protein known as a delta opioid receptor (purple) with a compound derived from a naturally occurring peptide (orange, blue, red) bound inside its "pocket." The peptide compound shows promise as an alternative to painkillers like morphine because it both activates a powerful pain-relief response and suppresses unwanted side effects. (University of Southern California)

Portraits of Living Bacteria, Infectious Viruses

LCLS has provided the first-ever X-ray images of living cyanobacteria, also known as blue-green algae, and intact, infectious viruses including the giant Mimivirus. Researchers spray the bacteria or viruses in a thin stream of humid gas into the path of the X-ray laser and combine many images into a 3-D reconstruction that shows some general internal features. They hope to improve their techniques to shed light on viral infection, cell division, photosynthesis and other processes that are important to biology, human health and the environment.



Cyanobacteria (illustration at left), an abundant form of bacteria, play a key role in the planet's oxygen, carbon and nitrogen cycles. Mimivirus (3-D reconstruction above), an example from a class of giant viruses discovered just a decade ago, may hold clues to the family tree of cell-based life. (SLAC National Accelerator Laboratory and Uppsala University)