

the shape of its Automated Transfer Vehicles. Three of these crewless disposable freighters have already carried supplies to ISS, and another two are in the works. Some ESA members want to develop the technology further by transforming it into the “service module” for NASA’s planned Orion capsule. The detachable service module provides propulsion and control to Orion while it’s in space but would be jettisoned before the capsule descends to

Earth. Orion may carry four-person crews as far as the moon or an asteroid after 2020.

Developing and supplying the service module could form an in-kind contribution to NASA toward ESA’s ISS subscription for 2017 to 2020. But negotiations on how to fund the development fell short of the required amount until the United Kingdom stepped up as an unlikely savior. For decades, the United Kingdom has eschewed any involve-

ment in human spaceflight, but for this council Willetts came armed with more funding than usual (*Science*, 16 November, p. 868), of which he pledged €20 million for the service module. “British technology will now have an important role [in Orion],” Willetts says. “This is the first time ESA has contributed to a crew transport vehicle,” Dordain said. “For me that is a breakthrough.” An interesting 48 hours indeed. —DANIEL CLERY

## STRUCTURAL BIOLOGY

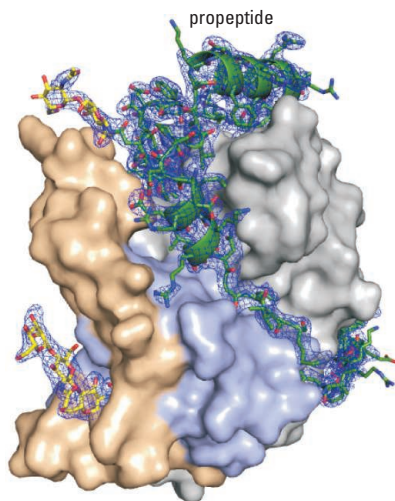
## News Flash: X-ray Laser Produces First Protein Structure

For the first time, an ultraintense x-ray laser has revealed the previously unknown atomic-scale structure of a protein, researchers report online today in *Science* ([scim.ag/Redecke](http://scim.ag/Redecke)). The advance ushers in a new type of protein crystallography. However, it’s too early to tell whether so-called x-ray free-electron lasers (XFELs) will supplant conventional x-ray sources known as synchrotrons, which have cranked out tens of thousands of protein structures, or merely serve niche applications, structural biologists say.

Researchers have determined the structure of an enzyme key to the survival of the single-celled parasite *Trypanosoma brucei*, which causes African sleeping sickness, a disease that kills 30,000 people each year. Scientists already knew the structure of the active form of the enzyme, known as a cysteine protease cathepsin. The new data reveal the enzyme’s “precursor” form, in which its active region is covered by a molecular safety cap called a propeptide, report Henry Chapman, a physicist at the German Electron Synchrotron laboratory (DESY) in Hamburg; Christian Betzel, a structural biologist at the University of Hamburg; and 47 colleagues. That information could help researchers find molecules that mimic the propeptide and tie up the enzyme, killing the parasite, Betzel says.

The way the structure was determined is as important as the result itself. To grow crystals of the enzyme, biologists over-expressed it in cells, where it formed elon-

gated crystals a fraction of a micrometer wide and several micrometers long. These crystals were too small to be studied with the relatively weak x-ray beams produced by circular particle accelerators known as synchrotrons. So the team dropped them through the beam of the world’s first XFEL, the Linac Coherent Light Source (LCLS) at SLAC National Accelerator Laboratory in Menlo Park, California, which is powered by a straight-shot linear accelerator.



**Stopped.** An x-ray laser revealed how this enzyme is bound up and deactivated.

Shining a billion times brighter than a synchrotron source, the LCLS delivers x-ray pulses lasting only a few millionths of a nanosecond. As in any x-ray crystallography setup, the x-rays scatter, or “diffract,” off the myriad planes of atoms in the complicated crystals, and the angles and intensities of the scattered x-rays reveal the crystal’s structure, including that of the protein. But unlike the pulses at synchrotrons, those at the LCLS are so intense that they can probe submicrometer-size crystals even as they blow them apart—an approach known as diffraction before destruction. Adding up 178,875 individual diffraction patterns, the researchers deciphered the structure.

Chapman and colleagues had previously shown that the LCLS, which powered up in 2009, could reproduce a known protein structure. Researchers at a laboratory called RIKEN SPring-8 Center in Hyogo, Japan, fired up their own XFEL earlier this year. Researchers at DESY plan to turn on the larger European XFEL facility in 2015.

Just how big the advance is remains unclear. The team did not determine the structure from the x-ray data alone but used as a starting point the structure of the enzyme’s active form. So the result marks a step toward such from-scratch, or de novo, structure determination, says Keith Moffat, a biophysicist at the University of Chicago in Illinois. “The real utility of the x-ray free-electron lasers is if they can determine structures that we simply can’t begin to determine with a synchrotron,” Moffat says.

However, the new work shows another advantage of an x-ray laser, says William Weis, a structural biologist at Stanford University in Palo Alto, California. The smallest crystals that can be studied at a synchrotron are damaged by the x-rays even as the data accumulate. Ironically, diffraction before destruction lets researchers glimpse a pristine crystal before it’s obliterated, Weis says. “If the XFEL is going to have broad impact, I think it’s going to be in doing damage-free data collection,” he says.

Then there’s the matter of beam time. A synchrotron serves dozens of users simultaneously. The LCLS serves one user at a time, and even the European XFEL will likely serve at most 10 at once. So even researchers on the same team disagree on whether the XFEL will vie with the synchrotron for business. “I see it as an add-on that allows you to look at specific cases such as membrane proteins that won’t crystallize very well,” Betzel says. But Chapman says the lasers may be able to do things that synchrotrons cannot, such as study rapid changes in molecules. “Why wouldn’t they [draw away synchrotron users] if everything is so much better?” he says.

For researchers working on XFELs, the dream is to determine protein structures by zapping individual molecules. Weis and Moffat say it’s not yet clear that can be achieved. —ADRIAN CHO