

# Cryogenic electron microscopy (cryo-EM)

Amazing views of life's machinery



slac.stanford.edu  
cryoem.slac.stanford.edu

## Facts

- World-leading facilities
- 9 advanced instruments on SLAC and Stanford campuses
- 2 NIH centers for research and training

Taking pictures of tiny, flash-frozen things with electrons is revolutionizing biology and technology. SLAC and Stanford host one of the world's leading facilities for doing cryo-EM research, improving the technology and making it available to researchers across the country.

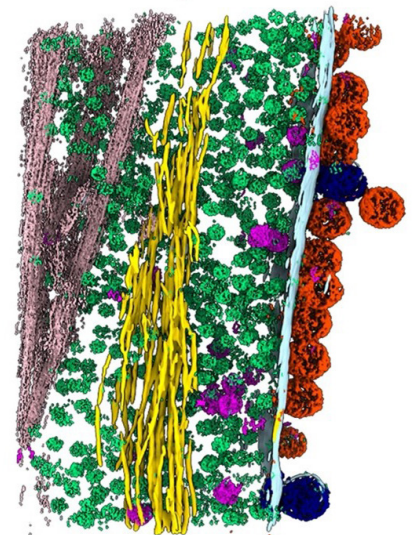
Invented 40 years ago as an offshoot of electron microscopy, cryo-EM technology has improved so much and so fast in the past 10 years that it can now make clear images of individual atoms. Those rapid advances earned three of its key developers a 2017 Nobel Prize.

## Biology in action

Cryo-EM allows scientists to make detailed 3D images of DNA, RNA, proteins, viruses, cells and the tiny molecular machines within the cell, revealing how they change shape and interact in complex ways while carrying out life's functions.

By stringing hundreds of thousands of these snapshots together into a 3D model, we can watch biology in action.

One recent study revealed how chikungunya virus particles form inside an infected cell and emerge from the cell (red blobs, right) to spread the infection. It also showed how antibodies keep new particles from forming, suggesting a way to treat illnesses caused by chikungunya and similar viruses.



These super-detailed images and movies have given SLAC and Stanford researchers important new information about chicken pox, tuberculosis and coronavirus infections, how cancer spreads through the body and how organisms out in nature assemble antibiotics, among many other things.

**A new frontier: batteries and materials**

SLAC and Stanford pioneered the use of cryo-EM to look at battery materials, and they're exploring other ways to use it to investigate things like solar panel materials, semiconductor films and catalysts used in electrochemistry.

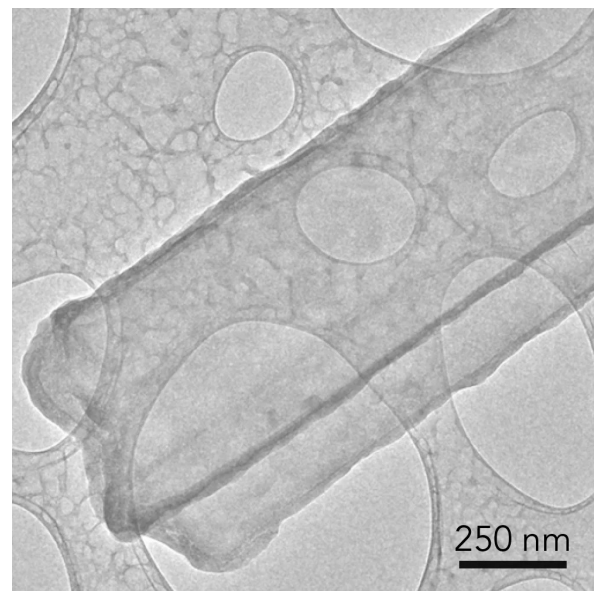
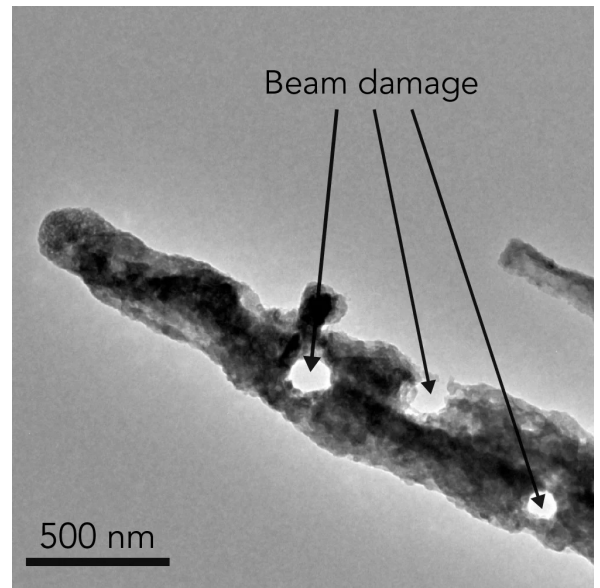
One of those studies made the first atomic-level images of finger-like growths called dendrites that can pierce the barrier between battery compartments and trigger short circuits or fires. Another revealed how lithium-ion battery electrodes deteriorate as they age.

**Expanding our reach**

The Stanford-SLAC Cryo-EM Center (S<sup>2</sup>C<sup>2</sup>) at SLAC operates four advanced cryo-EM instruments that serve researchers from all over the country. It includes two large-scale National Institutes of Health centers that operate independently but in synergy with S<sup>2</sup>C<sup>2</sup>. The NIH centers make cryo-EM available to researchers nationwide and train them in how to use it.

The Stanford Cryo-EM Center (cEMc) at the Stanford School of Medicine operates an additional five instruments.

Another Stanford-SLAC program called Stanford Electron Microscopy-X holds virtual seminars where hundreds of scientists from around the world share information about electron microscopy methods and discoveries.



Top right: In this room-temperature transmission electron microscope image, exposure to air has corroded a lithium metal dendrite and the electron beam has melted holes in it. Bottom right: In contrast, a cryo-EM image of a dendrite shows that freezing has preserved its original state, revealing that it's a crystalline nanowire with well-defined facets.

**How cryo-EM works**

Cryo-EM is a version of electron microscopy that freezes many copies of a delicate sample into a glassy state and hits them with an electron beam. Electrons pass through the copies to create images in a detector. Then a computer sorts and recombines the images into a high-res 3D model of the sample.

