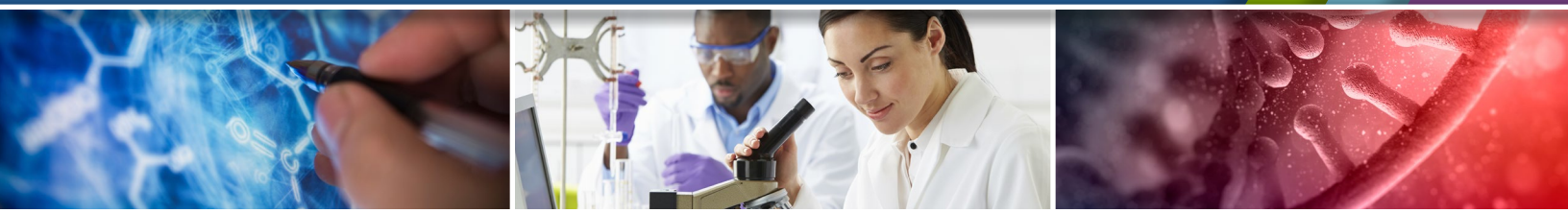
TRANSFORMATIVE HIGH-RESOLUTION CRYOELECTRON MICROSCOPY (CryoEM)

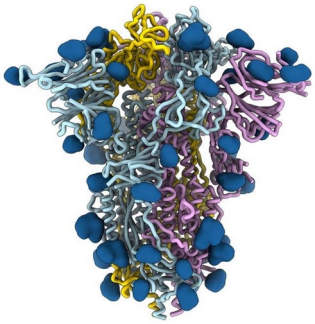


What Is CryoEM?

Cryoelectron microscopy (cryoEM) and tomography (cryoET) are methods used to obtain detailed images of biological molecules in their native state. Such images can provide fundamental insights into mechanisms of action and guide scientists in identifying potential new therapeutic targets for vaccines and drugs to combat diseases. Recent advances in cryoEM/ET technology enable users to determine structures with unprecedented detail. However, many laboratories have limited expertise and lack access to the necessary high-end microscopes, slowing both adoption of these powerful technologies and progress in a range of biomedical fields.

Why the NIH Common Fund CryoEM Program?

To address this issue, the NIH Common Fund, which supports trans-NIH programs that focus on major biomedical challenges and emerging opportunities, is seeking to improve the availability and utility of cryoEM/ET by establishing the National Centers for Cryoelectron Microscopy, the National Network for Cryoelectron Tomography, and curriculum development efforts through the Transformative High-Resolution Cryoelectron Microscopy program. The program's mission is to broaden the use of cryoEM/ET by offering access to instrumentation, education materials, and training. The CryoEM Centers and CryoET Network (see below) provide access to facilities with state-of-the-art microscopes. The curriculum development efforts (see other side) are focusing on online approaches to maximize outreach and broaden impact.



SARS-CoV-2 spike protein trimer rendering from cryoEM data, courtesy of Dr. David Veesler

The Centers have developed a shared site for NIH Common Fund Transformative High-Resolution Cryoelectron Microscopy Program Centers at https://www.cryoemcenters.org. A universal certification system, the Merit Badge Program, currently is underway to allow users to apply their training across Centers in the network. Updates are posted on this site.

National Centers for CryoEM

S²C² Stanford-SLAC Cryo-EM Center

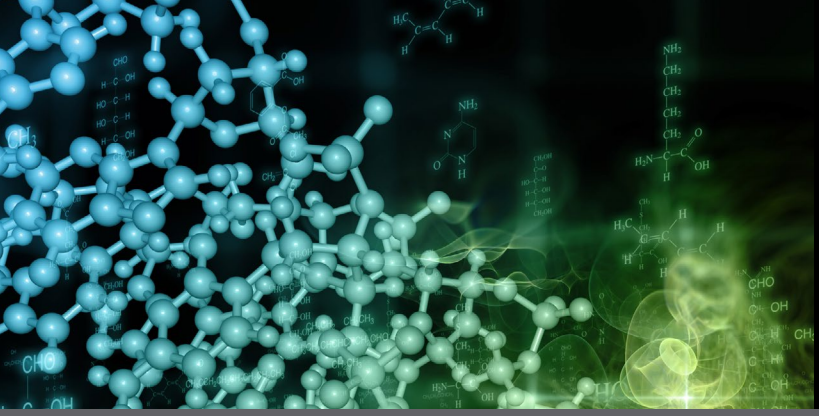
- Located at the SLAC National Accelerator Laboratory, Menlo Park, CA.
- User proposals are being accepted for both in-person and remote data collection; in-residence and short-form training also are provided.
- Five instruments (four 300kV EM Titan Krios; one 200kV Talos-Arctica) are available.
- Website: https://cryoem.slac.stanford.edu/s2c2

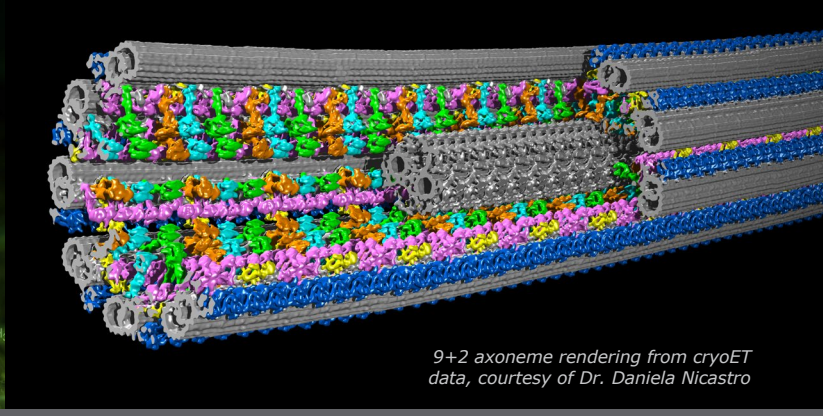
NCCAT National Center for CryoEM Access and Training

- Located at the New York Structural Biology Center, New York, NY.
- User proposals are being accepted for sample preparation, screening, and data collection; embedded cross-training and facility manager training programs also are provided.
- Six instruments (four 300kV EM Titan Krios; one 200kV Glacios; one 120kV Hitachi) are available.
- Website: https://nccat.nysbc.org

Pacific Northwest Cryo-EM Center

- Located in Portland, OR, through partnership between Oregon Health & Science University and Pacific Northwest National Laboratory.
- Open for user proposals for limited or general access; preparatory online training, hands-on training in the laboratory, and ongoing skill development training programs also are available.
- Five microscopes (four 300kV EM Titan Krios; one 200kV Talos-Arctica) are available.
- Website: https://pncc.labworks.org





9+2 axoneme rendering from cryoET data, courtesy of Dr. Daniela Nicastro

National Network for Cryoelectron Tomography

More information and applications for user access can be found on the Network's portal: https://www.cryoetportal.org.

Midwest Center for Cryo-Electron Tomography (MCCET): Located at the University of Wisconsin–Madison, MCCET serves as the network's hub. MCCET provides access and training in all aspects of the cryoET pipeline, including data collection. The hub is responsible for coordinating the National Network for CryoET activities between the NIH, Network Centers, and users. https://cryoem.wisc.edu/about-mccet.

CU Boulder Center for Cryo-ET (CCET): Located at the University of Colorado, CCET serves as one of the three network spokes. The Center focuses on cryo-specimen preparation for cryoET applied to cells, organelles, and large supramolecular assemblies. Resources and equipment are available for plunge freezing, high-pressure freezing, fluorescence imaging of vitrified specimens, and cryo-focused ion beam milling. http://dosequis.colorado.edu/CCET/index.html.

The National Center for *in situ* Tomographic Ultramicroscopy (NCITU): Located at the New York Structural Biology Center, NCITU is dedicated to developing and providing access to both standard and advanced methods for *in situ* cryoET specimen preparation and to disseminate this expertise through a cryoET cross-training program designed to serve a wide variety of skill levels and career goals. https://ncitu.nysbc.org.

Stanford-SLAC CryoET Specimen Preparation Center (SCSC): Located at Stanford University, SCSC enables users to prepare samples for cryoET by providing access to, and support for, advanced cryo-specimen preparation techniques for a wide range of samples with biomedical applications. The Center will offer a comprehensive program to train and cross-train scientists to become independent cryoET investigators. https://sites.slac.stanford.edu/scsc-cryoet.

CryoEM Online Educational Resources

Getting Started in CryoEM Video Lectures: A comprehensive online curriculum that covers the theory and practice of major cryoEM modalities. The curriculum serves both naïve and expert users, including principal investigators teaching cryoEM courses. The course provides additional resources, including exam questions, review slides, and more. https://cryo-em-course.caltech.edu.

CryoEM 101: An online media-rich curriculum to supplement users' own hands-on cryoEM training. The material contains videos, animation, and interactive simulations and, once fully developed, will cover the major components of cryoEM workflow, from sample purification to image processing. https://cryoem101.org.

Virtual Reality (VR) Augmented Hands-On CryoEM Training: CryoVR provides self-paced training tools to familiarize new users with cryoEM equipment through a free, safe, easily accessible, virtual environment. Interested users can overcome constraining barriers, such as high costs and limited access. A standalone version for personal computers, CryoVR Lite, is in development. https://va.tech.purdue.edu/cryoVR.

Principles of CryoEM Structure Determination: This curriculum includes videos, software, and an e-book that provide the foundation for understanding cryoEM image processing and reconstruction, including principles of single-particle reconstruction and cryoelectron tomography. http://cryoemprinciples.yale.edu.

CryoEDU: An online platform that offers self-paced training in cryoEM/ET data interpretation and analysis. A cloud-based desktop environment provides a simulated hands-on data processing experience using pre-calculated results to process a data set from start to finish. Users will learn approaches for independently processing a variety of cryoEM/ET data sets. https://cryoedu.org.

Connect With Us!

Common Fund program website: https://commonfund.nih.gov/cryoem

Listserv: https://list.nih.gov/cgi-bin/wa.exe?SUBED1=NIH-OSC-L&A=1

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QR Code for Common Fund General Information