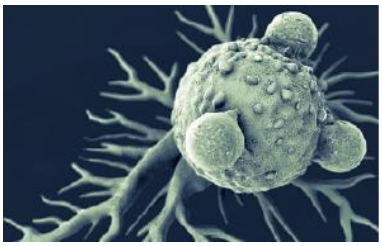
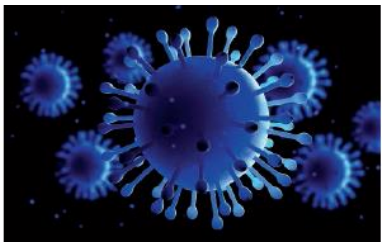
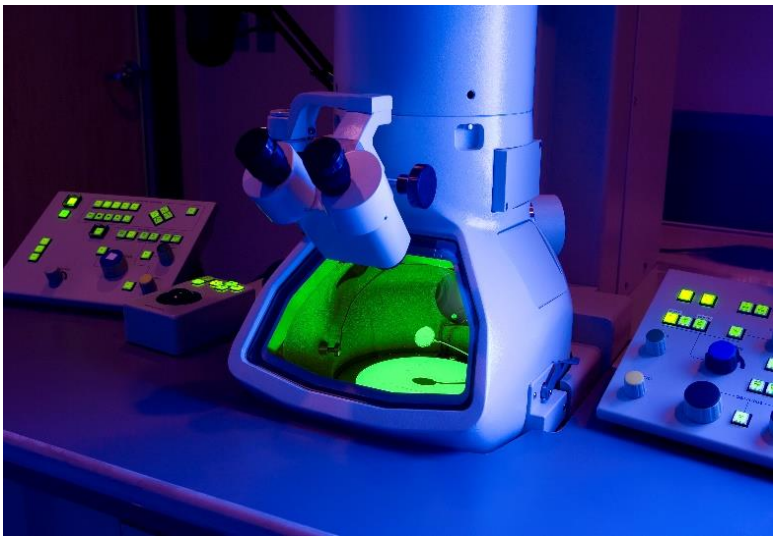
Precision Drives for Electron Microscopy

Precision Drives for Positioning and Moving of Specimen in TEM, Scanning TEM, Cryo-TEM, SEM and for the Vitrification of Samples for Cryo-TEM Onto Metal Grids







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Electron Microscopy

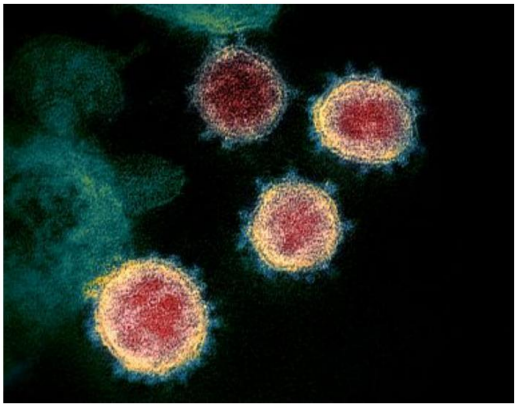
Applications for electron microscopy cover a broad spectrum from semiconductor inspection, through materials research to molecular biology research. In conventional TEM as well as in the newer Cryo-TEM, which was awarded the Nobel Prize in 2017, the samples have to be precisely nanopositioned with precision in an XYZ coordinate and then tilted around one axes to produce a certain number of transmission images for image reconstruction. Especially in the Cryo-TEM, which uses very thin, vitrified slices of samples of typically 50nm thickness, the contrast is low. Therefore, typically thousands of images from several tilt angles are needed for reconstruction.

However, when scanning samples with TEM or SEM (Scanning Electron Microscopy) not only is the precise initial positioning of the specimen a main aspect of the method but also a very precise scanning of the specimen in the nanometer and sub-nanometer range.

This means, all electron microscopy methods need precision drives for several dimensions of freedom, typically between three and six dimensions, including XYZ, rotations, and tilt movements depending on the specific hardware setup. Besides sample holder for the sample movements sometimes also slit assays have to be actuated by a precision motion drive.

To achieve highest dynamics, smallest outer dimensions of the microscope and highest convenience for the user, these drives have to be placed preferably inside the vacuum chamber with pressure requirements typically between 10^{-4} mbar to 10^{-6} mbar. Further requirements for the drives are the use of non-magnetic materials and for Cryo-TEM additionally the working temperature of liquid ethane (-160° C) or even liquid nitrogen (-196° C).

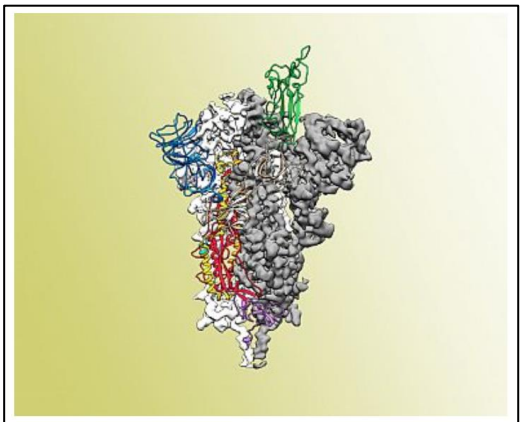
A topical example application case for Cryo-TEM is the fight against COVID-19. Here Cryo-TEM had already played and is continuously playing a crucial role in identifying the protein surface structure of the SARS-CoV-2 virus. Like other coronaviruses, SARS-CoV-2 particles are spherical and have proteins called spikes protruding from their surface. These spikes latch onto human cells, then undergo a structural change that allows the viral membrane to fuse with the cell membrane. The viral genes can then enter the host cell to be copied, producing more viruses. After the genome sequence of SARS-CoV2 by scientists in China in January 2020 a collaborative team including scientists from Dr. Jason McLellan's lab at the University of Texas at Austin and the NIAID Vaccine Research Center (VRC) isolated a piece of the genome predicted to encode for its spike protein based on sequences of related coronaviruses. The team then used cultured cells to produce large quantities of the protein for analysis.



Transmission electron microscope image shows SARS-CoV-2, the virus that causes COVID-19, isolated from a patient in the U.S. Virus particles are emerging from the surface of cells cultured in the lab. The spikes on the outer edge of the virus particles give coronaviruses their name, crown-like. *NIAID-RML*

Scientific Publication by: NIAID Vaccine Research Center, 2020

The researchers used Cryo-TEM to take detailed pictures of the structure of the spike protein. This involves vitrifying, means freezing virus particles and then taking tens of thousands of TEM images at different tilt angles. These images are then combined to yield a detailed 3D view of the virus. The researchers found that the SARS-CoV-2 spike was 10 to 20 times more likely to bind on human cells than the spike from the SARS virus from 2002. This may enable SARS-CoV-2 to spread more easily from person to person than the earlier virus.



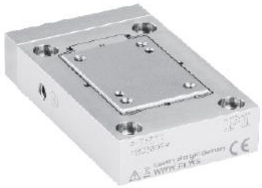
Atomic-level structure of the SARS-CoV-2 spike protein. The receptor binding domain, the part of the spike that binds to the host cell, is colored green. *UT Austin, McLellan Lab*

Scientific Publication by: UT Austin, McLellan Lab, 2020

Motion Solutions from PI

Typically the drive requirements for 3, 4, 5 or 6 - dimensions of freedom are solved by stacked drives. But also a fully parallel kinematic drive in form of a miniature hexapod is available. Some examples for potentially suitable drives, below. Cryo-versions only on specific request:

- P-752 High-Precision Nano-positioning Stage
  Piezo-flexure stage, capacitive sensors, repeatability: ±1nm, travel range to 35 µm, UHV compatible, non-magnetic



- N-310 NEXACT Miniature Linear Motor
  Travel range: 10 to 125 mm, Feed force: to 10 N / Holding force: to 12 N, Resolution: 0.03 nm (open loop) and 5 nm (closed loop), Velocity: to 10 mm/s, UHV compatible, non-magnetic

- P-911 UHV-Compatible Miniature Piezo Hexapod
  NEXLINE® piezo stepping, position resolution down to 0.1 µm in the linear axes, UHV-compatible to 10–9 hPa, Non-magnetic

Further recommended drives see PI brochure BRO037E.

Solutions for Cryo-TEM Sample Vitrification

With the Cryo-TEM sample vitrification, first a nanoliter droplet of the liquid specimen is placed onto a hydrophilic metal grid. For this purpose, a small applicator with a sharp tip is positioned at high velocities and with nanometer precision by XYZ drives. Afterwards, the grid with the droplet is placed into a vitrification chamber where it is vitrified at about minus 160°C by two ethane jets, which are offset to each other by 180 degrees.

Voice Coil Direct Drives

Piezo Actuators for Vibration Damping

- Sensitive instrumentation such as electron microscopes requires precise vibration isolation to exclude disturbing influences from the environment, so a proper performance is ensured. For this task, active vibration cancellation stages can be designed by the use of PICA Stack Actuators or PICMA® Piezo Linear Actuators. Due to the piezoelectric effect, these elements work both as sensors and actuators compensating ambient vibrations. The actuators exhibit high forces, short reaction times and superior durability, which makes them suitable for the use in complex systems made for performance over long periods of time.

PICA Piezoelectric Stack Actuators

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