

CRYO ELECTRON MICROSCOPY: SCIENCE & TECHNOLOGY

NEWS:

WHAT'S IN THE NEWS?

U.S. researchers have developed the MagIC method to enhance cryo-electron microscopy, enabling imaging of rare biomolecules at concentrations 100 times lower than before.

It uses magnetic beads for sample clustering and the DuSTER algorithm for noise reduction, improving accuracy and speed in structural biology studies.

Context

- U.S. researchers have developed a novel technique called MagIC (Magnetic Isolation and Concentration), a breakthrough in cryo-electron microscopy (cryo-EM), which allows the imaging of biomolecules at concentrations up to 100 times lower than previously required.

About Cryo-Electron Microscopy (cryo-EM)

- Cryo-EM is an advanced, high-resolution imaging technique used to visualize the structure of biological molecules like proteins, DNA, viruses, and enzymes.
- The method involves flash-freezing samples in vitreous ice, preserving their natural structure without chemical fixation or staining.
- Samples are then observed using an electron beam under cryogenic temperatures, minimizing radiation damage and maintaining integrity.
- It provides near-atomic level resolution, making it valuable in structural biology, virology, and drug discovery.
- A key limitation is the requirement of high sample concentration, making it challenging to study rare or low-abundance molecules.

Cryo-EM Infrastructure in India

- India has established national cryo-EM facilities to support structural biology research:
 - National Centre for Biological Sciences (NCBS), Bengaluru (first facility established in 2017)
 - Indian Institute of Science (IISc), Bengaluru
 - Regional Centre for Biotechnology (RCB), Faridabad
 - Indian Institute of Technology (IIT), Kanpur

About the MagIC (Magnetic Isolation and Concentration) Method

- Developed by researchers to overcome the concentration limitation of cryo-EM.
- Allows imaging of biological samples even at ultra-low concentrations (as low as 0.0005 mg/ml).

- Works by tagging target biomolecules with 50-nanometer magnetic beads.
- The beads are then magnetically concentrated in a small area, enabling denser sampling on the EM grid.
- This clustering improves visibility and allows more efficient targeting of molecules for imaging.

Innovative Computational Strategy – DuSTER

- DuSTER (Duplicated Selection To Exclude Rubbish) is an algorithm that enhances signal-to-noise ratio.
- It scans cryo-EM images full of noise, selecting particles in two rounds.
- Only particles that appear consistently in the same location in both rounds are retained.
- This dramatically reduces false positives and enhances the quality of particle datasets.

Key Advantages of MagIC

- **Scientific Advancement:** Enables imaging of molecules that were previously too rare or too diluted to study, opening new avenues in protein biology and virology.
- **Sample Efficiency:** Reduces required sample quantity to just 5 nanograms per grid, making it cost-effective and less invasive.
- **Faster Data Collection:** Magnetic clustering makes it easier to find particle-rich areas quickly under the microscope, reducing scanning time.
- **Higher Data Quality:** Combines physical magnetic concentration with digital filtering (DuSTER) for clearer, more accurate structural data.

Significance for Research and Healthcare

- Facilitates research on low-abundance proteins involved in diseases.
- Helps accelerate drug development by enabling study of potential drug targets with minimal sample.
- Useful in pandemic preparedness, allowing quick structural analysis of novel viruses at low viral loads.

Source: <https://www.thehindu.com/sci-tech/science/magical-new-technique-brings-very-dilute-samples-into-focus/article69681972.ece>