

TEACHING & LEARNING

From Atomic Structures to Molecular Medicine: Nobel Laureate Joachim Frank Introduces the Technology Transforming Modern Drug Discovery

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After receiving his doctorate from the Technical University of Munich, Prof. Joachim Frank moved to the United States for postdoctoral research, where his work at NASA's Jet Propulsion Laboratory (JPL) inspired the development of SPIDER, a landmark image-processing system for cryo-electron microscopy.

When the COVID-19 pandemic swept across the globe, scientists redoubled their efforts, racing not only against the virus, but against time itself.

One of the most decisive tools in that race, Nobel laureate Joachim Frank informed his audience at National Taiwan University on May 6, was cryo-electron microscopy — a technology capable of revealing the architecture of life at near-atomic resolution.

In his lecture titled “*CCryo-electron Microscopy, A New Foundation for Molecular Medicine and Drug Design.*” Frank traced how a once highly specialized imaging



NTU President Wen-Chang Chen (right) presenting the Raymond Soong Chair Professorship trophy to Prof. Joachim Frank (left).

method has evolved into one of the definitive scientific instruments of modern medicine. During the pandemic, he explained, cryo-EM enabled researchers to rapidly visualize the structure of the coronavirus spike protein at a speed unattainable using traditional X-ray crystallography, accelerating both vaccine development and the identification of neutralizing antibodies.

Frank, a professor at Columbia University and a member of both the U.S. National Academy of Sciences and the American Academy of Arts and Sciences, shared the 2017 Nobel Prize in Chemistry with Jacques Dubochet and Richard Henderson for pioneering advances in cryo-electron microscopy.

Capturing Life in Motion

At the heart of Frank's lecture was a larger shift in modern biology: the transition from static structural analysis to what he described as a truly dynamic understanding of life.

Traditional structural biology often depended on isolating molecules in vitro and crystallizing them before study. But living systems, Frank noted, are never motionless. Proteins, ribosomes and cellular complexes operate like microscopic machines, constantly changing shape as they carry out biological functions.

To understand those processes, scientists have needed a tool capable not only of imaging molecules, but of capturing them in motion. Cryo-electron microscopy has answered precisely that call.

The Algorithm That Changed Structural Biology

A major breakthrough came through Frank's development of "SPIDER," a pioneering image-processing system that has transformed the field.

The software reconstructs thousands of noisy two-dimensional electron microscope images into highly accurate three-dimensional molecular models. The achievement overcame one of the central obstacles in electron microscopy: biological samples are easily damaged by electron beams.

Unlike X-ray crystallography — which often requires years of effort to grow high-quality crystals — cryo-EM allows scientists to observe biomolecules in conditions that closely resemble their natural physiological state. For researchers studying ribosomes, viral infection pathways or drug-binding mechanisms, the technology has opened an entirely new visual frontier.

Frank explained that the arrival of high-voltage 300 kV electron microscopes has advanced the technology even further, enabling structural analysis at near-atomic resolution and fundamentally reshaping experimental biology.

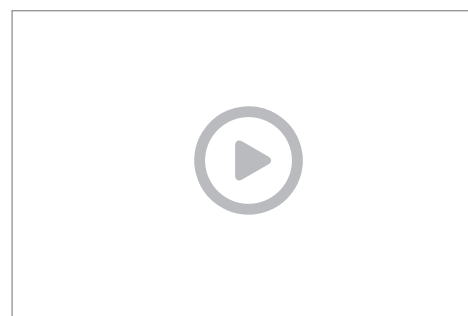
Today, scientists can observe the dynamic behavior of ribosomes and protein complexes in real time, extending research into realms of molecular motion hitherto unimaginable using classical crystallography.



Prof. Frank noted that cryo-electron microscopy has become an indispensable tool in modern drug discovery and life science research, playing a critical role in the fight against cancer, cardiovascular disease and global pandemics.



Group photo following the lecture.



Highlights of Prof. Joachim Frank's public lecture, "Cryo-electron Microscopy, A New Foundation for Molecular Medicine and Drug Design."

A New Compass for Precision Medicine

The implications for medicine are profound. Cryo-EM now allows researchers to visualize how small-molecule drugs bind to cancer-related proteins, analyze the dynamic conformations of ion channels inside heart muscle cells, as well as design therapeutics with unprecedented precision.

In concluding, Frank described cryo-electron microscopy not simply as an imaging technology, but as one of the foundational instruments of precision medicine — a tool that is rapidly reshaping research on cancer, cardiovascular disease and emergent infectious threats.

During the question-and-answer session, Frank expressed hearty admiration for the depth of the questions raised by NTU students and encouraged the young researchers to study widely and cultivate their interdisciplinary thinking. “The future breakthroughs,” he insisted, “will come from people who can move seamlessly between physics, computational science and biology.”

For Frank, the next frontier of life science will belong not to a single discipline, but to those capable of connecting multiple disciplines.

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