Cryo-EM at Jefferson: Driving a New Era of Scientific Discovery

Scientific discovery is often the product of a delicate dance between intellectual insight and technological capabilities. It is a synergistic cycle of advancement where the desire to test a research hypothesis may motivate the creation of a new technology, and the new technical capacity yields unanticipated opportunities for wider discovery. And one of the most important drivers of new knowledge is the development of technologies for viewing biology's fundamental building blocks: the atoms and molecules that comprise living cells.

Since late 2020, Jefferson researchers have been using one of the most powerful devices for "seeing" molecular structures at the atomic level: Cryo-Electron Microscopy (Cryo-EM). The development of Cryo-EM reflects the convergence of technological skill and biomedical purpose. And at Jefferson the device will create opportunities across a broad spectrum—from basic biology discovery research to applications in materials science and textile engineering.

"For many years, X-ray crystallography has been the predominant technique for studying the three-dimensional structure of biological macromolecules in detail," says **Gino Cingolani, PhD**, professor and vice chair of biochemistry and molecular biology and director of Jefferson's X-ray crystallography facility. "But it has limitations: crystallizing macromolecules is arduous and time-consuming; many proteins won't crystallize and the process can alter the structure, misrepresenting the molecule's folding."

Being able to move beyond those limitations is one of the reasons why Dr. Cingolani is so pleased to be guiding the University's newly established Cryo-EM facility. Cryo-EM has become the state-of-the-art technology for describing biological complexes and their mechanisms at their most basic level," he explains. "It enables researchers to generate three-dimensional images of biomolecules, see how they function and how they interact with each other."

In awarding the 2017 Nobel Prize in Chemistry to the developers of Cryo-EM, the Nobel Committee said, "This technology has taken biochemistry into a new era." In fact, we are benefiting from that "new era" right now. "The mRNA-based COVID-19 vaccines created by the Pfizer-BioNTec, Moderna and others are premised on an understanding of the novel coronavirus's chemical structure," Dr. Cingolani points out. "It was Cryo-EM that enabled scientists to define that structure in just weeks, rather than the years it would have taken using X-ray crystallography."

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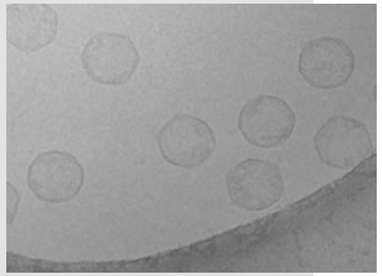
Jefferson is one of fewer than a dozen research centers in the eastern United States with a dedicated Cryo-EM facility. "This groundbreaking technology is opening exciting new research opportunities across the University," Dr. Cingolani says. "It will vastly expand our ability to understand the mechanisms driving disease at the cellular, molecular, and atomic levels. And it will be a catalyst for development of targeted, highly effective new treatments for a wide range of diseases." ■



The Cryo-EM device captures thousands of two-dimensional images, such as the image ABOVE. It uses computer algorithms to integrate them into three-dimensional visual models of individual and complex molecules, like the image on the RIGHT.