SOLUTION BRIEF

Cryo-Electron Microscopy (Cryo-EM)
Intel® Scalable System Framework

Cryo-Electron Microscopy: Revolutionizing Drug Discovery Pipelines with 3D Proteins Imaged at Near-Atomic Resolutions

Accelerating Drug Discovery with Nobel Prize-Winning Cryo-Electron Microscopy

Jacques Dubochet (Switzerland), Joachim Frank (US), and Richard Henderson (UK) were awarded the Nobel Prize in Chemistry 2017 for their work in cryo-electron microscopy. Cryo-EM is "decisive for both the basic understanding of life's chemistry and the development of pharmaceuticals" said the Nobel Committee, "biochemistry is now facing an explosive development and is all set for an exciting future."3 Cryo-electron microscopy "fills an important gap and extends the range of molecules that can be determined at atomic resolution" according to Nobel recipient Frank.[4]

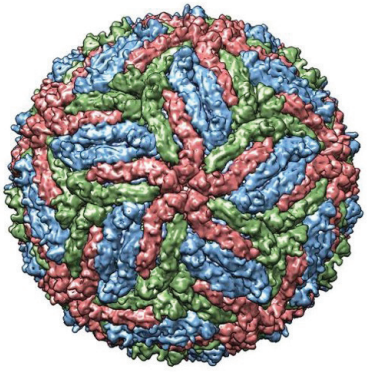

Image from the RCSB PDB (www.rcsb.org) of PDB ID 5IRE (Sirohi, D., Chen, Z., Sun, L., Klose, T., Pierson, T., Rossmann, M., Kuhn, R.) (2016) The 3.8 angstrom resolution cryo-EM structure of Zika virus. Science 352: 467-470

Cryo-Electron Microscopy (Cryo-EM) is a rapidly emerging technique used to construct three-dimensional models of proteins and molecules at near-atomic resolutions. The technique captures 2D images of protein molecules frozen in a thin layer of ice under cryogenic conditions using a transmission electron microscope (TEM). With the help of high-performance computing systems and optimized codes, thousands of these 2D images are then aligned and combined to form 3D models.

The structure of a protein determines how it interacts with drugs and other substances in the living system. Discovering and modeling a protein structure is therefore essential in streamlining the drug discovery process. Unlike in x-ray crystallography, cryo-EM doesn't require crystallization; a long, arduous process that, when possible, can take as long as several years and often locks the protein in an unnatural conformation. Single-particle cryo-EM enables the study of molecules in near-native environments, making it an essential tool for understanding how drugs and their target proteins may interact in the body. The technique can be applied to particles in a wide range of sizes, from hemoglobin (64 kDA) to particles of several megadaltons.[1]

While cryo-EM was invented in 1968, recent advances in technology have enabled it to regain traction, accurately modeling 3D proteins to a higher resolution than most x-ray crystallography procedures can achieve.[2] Technical advancements have increased scientific excitement for cryo-EM in the recent years, leading it to win Nature Journal's Method of the Year award in 2015[2] and the Nobel Prize for chemistry in 2017.[1,3]

Big Data in Cryo-EM

Recent advances in transmission electron microscopes and data analysis software have exponentially increased the data storage and computation requirements in cryo-EM. This presents some challenges:

- Burdens of Data Management: Petabytes of research and clinical data are being created which needs to be stored, managed, shared, and analyzed effectively and securely
- Converging Infrastructure: Local and cloud-based HPC big-data analytics workloads are converging, requiring high-level orchestration
- Compute limitations: The traditional compute cluster itself, working as the backbone of cryo-EM analysis, faces three common challenges: system bottlenecks, divergent workloads, and barriers to extending usage.

Cryo-EM has fundamentally changed research and development in structural biology, and thus demands new HPC infrastructure

...yet many institutions are uncertain how to size the HPC infrastructure required to support this innovative new field.

Reduce Time
Pre-validated Intel® SSF solutions reduce time to insight and remove constraints to life science research.

Optimal Performance
Intel® SSF solutions enable greater configurability and flexibility than contemporary supercomputers across storage, compute, fabric, and software. Intelligence at the hardware and software levels enables supercomputing sites to tune for optimal performance.

High Efficiency
With tight integration and high efficiency, Intel® SSF solutions deliver lower overall TCO by reducing server floorspace footprints, energy, and cooling costs.

Many workloads...One framework

Intel has been working on modernizing various 3D molecular reconstruction applications since 2013 as part of the Intel Parallel Computing Center Program (IPCC). The Intel® Scalable System Framework (Intel® SSF) is a holistic architectural approach that can help address key challenges faced by these improved cryo-EM applications. Intel® SSF is an HPC architecture that utilizes innovative Intel memory, fabric, storage, and system software technologies to increase performance and provide an overall system balance resulting in decreased time to complete the analysis. The balanced integration of system components and modernized code, developed collaboratively with scientists, makes Intel® SSF an ideal tool to help power innovative scientific research that is easy for enterprises to deploy. The framework is designed to improve cost models and scale efficiently as scientific workloads continue to grow. Intel® SSF for life sciences is designed to achieve optimized performance for a variety of workloads; from genomics to molecular imaging/dynamics to machine learning, deep learning, and AI. Intel® SSF also supports a heterogeneous compute environment and supports a scale-out model that enables the separate scaling of compute and storage.

"We are facing a revolution in biochemistry," said Nobel Committee Chairman Sara Snogerup Linse during the announcement. "Now we can see the intricate details of the biomolecules in every corner of our cells, in every drop of our body fluids. We can understand how they are built and how they act and how they work together in large communities." "Soon there are no more secrets," she said.[4]

Break Free From Current Compute Infrastructure Constraints Limiting Your Research

Intel® SSF solutions that include optimized software applications provide an effective cryo-EM platform that will help scientists achieve scalable results faster, maximize the use of available infrastructure, and enable them to achieve new breakthroughs in 3D protein modeling.

[1] Brzezinski, Peter. "Scientific Background on the Nobel Prize in Chemistry 2017: The Development of Cryo-Electron Microscopy." Nobel Prize, The Royal Swedish Academy of Sciences, 4 Oct. 2017, https://www.nobelprize.org/nobel_prizes/chemistry/laureates/2017/advanced-chemistryprize2017.pdf

[2] "Method of the Year 2015." Nature Journal, Springer Nature, 30 Dec. 2015, www.nature.com/nmeth/journal/v13/n1/full/nmeth.3730.html.

[3] "The 2017 Nobel Prize in Chemistry - Press Release". Nobelprize.org. Nobel Media AB 2014. Web. 9 Oct 2017. http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2017/press.html

[4] Vonberg, Judith. "Scientists Win Nobel for Work to Visualize Biomolecules." CNN, Cable News Network, 6 Oct. 2017, www.cnn.com/2017/10/04/world/nobel-prize-chemistry-2017-cryo-electron-microsopy/index.html.