

# Bio-molecular Structure Solution and Modeling with the Phenix Project: Cutting-Edge Advances and Exciting Horizons

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Structural biology is the discipline that reveals the atomic-level architecture of biomacromolecules such as proteins and nucleic acids (RNA/DNA), transforming this knowledge into actionable insights across a wide range of applications. These include drug discovery and design, vaccine development, understanding diseases at the molecular level, and advances in biomaterials and biofuels.

Over the past decade, structural biology has experienced two groundbreaking revolutions. The first is the so-called "resolution revolution" in electron cryo-microscopy (cryo-EM), which has elevated cryo-EM to a formidable alternative to the long-standing cornerstone of the field—X-ray crystallography. The second is the integration of artificial intelligence, most notably through tools like AlphaFold, which have enabled highly accurate predictions of atomic structures. Both advancements have been recognized with Nobel Prizes, underscoring their transformative impact on the field.

This talk will provide an overview of the current state of structural biology and examine how molecular structures are determined today. Special emphasis will be placed on the computational tools that power and drive these discoveries, particularly the Phenix software suite—one of the most widely used platforms in the field—for which the speaker is a key developer.

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[2] Terwilliger, T. C., Adams, P. D., Afonine, P. V., Sobolev, O. V. "A fully automatic method yielding initial models from high-resolution cryo-electron microscopy maps", *Nature Methods*. 15, 905-908, (2018).

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