

Innovations and Enhancements in the Upcoming CCP4 Release 10

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The forthcoming CCP4 [1] version 10 delivers key infrastructural and functional upgrades to support macromolecular structure determination. The suite now runs on Python 3.11 and continues to evolve its two main front ends: ccp4i2, the graphical desktop interface, and CCP4 Cloud, the web-based platform that integrates with Moorhen - a browser-based interactive graphical model builder like Coot [2].

Among the new tools, NucleoFind [3] stands out as a deep-learning-based solution for segmenting nucleic acid electron density maps. It identifies phosphate, sugar, and base atoms, significantly enhancing model-building speed and quality. NucleoFind integrates with tools like ModelCraft [4] and outperforms traditional methods, even in challenging, noisy datasets.

PanDDA 2, a rewrite of PanDDA [5], is also included in this release. It introduces two major methodological advances: dynamic selection of dataset subsets to optimize statistical contrast for each test dataset, enabling better handling of subtle heterogeneity, and automated event model building with ranking based on fragment model quality. These improvements enhance the detection and prioritization of ligand-binding events.

CCP4 continues to support a comprehensive pipeline for macromolecular structure solution, including tools for data processing, molecular replacement, experimental phasing, model building, and validation. Ongoing development focuses on leveraging predicted models in phasing (MRParse, SliceNDice). MrParse and MrBUMP have been updated to search the entire AlphaFold database for search models in molecular replacement when used through CCP4 Cloud. Monthly updates ensure the suite remains at the forefront of crystallographic software innovation.

[1] Agirre L. *et al.* (2023). *Acta. Cryst.* **D79**, 449-461.

[2] Emsley P., Sanchez F., McNicholas S., Noble M. <https://moorhen.org>

[3] Dialpuri J. S., Agirre J., Cowtan K. D., Bond P. S. (2024). *Nucleic Acids Research* **52**, e84.

[4] Bond P. S., Cowtan K. D. (2022). *Acta Cryst. D* **78**, 1090.

[5] Pearce N. Krojer, T., Bradley, A. *et al.* (2017). *Nat Commun* **8**, 15123.