

Graphical interfaces for structure model refinement: Integration of *Servalcat* and *MetalCoord* in *CCP4i2* and *CCP-EM Doppio*

M. Malý¹, K. Yamashita², K. H. Babai³, F. Long¹, M. Wojdyr⁴, S. McNicholas⁵, P. Bond⁵, T. Burnley⁶, C. M. Palmer⁶, A. P. Joseph⁶, G. N. Murshudov^{1,3}

¹MRC Laboratory of Molecular Biology, Francis Crick Avenue, Cambridge CB2 0QH, United Kingdom; ²Structural Biology Division, Research Center for Advanced Science and Technology, The University of Tokyo, 4-6-1 Komaba, Meguro-ku, Tokyo 153-8904, Japan; ³Institute of Molecular Biology and Biotechnology, Ministry of Science and Education, 11 Izzat Nabiyeu, Baku, Azerbaijan; ⁴Global Phasing Ltd, Cambridge, United Kingdom; ⁵York Structural Biology Laboratory, Department of Chemistry, University of York, York YO10 5DD, United Kingdom; ⁶Scientific Computing Department, STFC, Rutherford Appleton Laboratory, Fermi Ave, Harwell, Didcot OX11 0QX, United Kingdom
martin.maly@mrc-lmb.cam.ac.uk

The *CCP4* [1] and *CCP-EM* [2] suites distribute widely used software for macromolecular crystallography and cryo-electron microscopy (cryoEM). Here, we present recent developments that enhance atomic structure model refinement workflows. *Servalcat* [3], a modern refinement program extending the methodologies established in *Refmac5/Refmacat* [4], has been implemented in *CCP4i2* and *CCP-EM Doppio*. These new graphical interfaces provide detailed reports including refinement progress, validation metrics, geometry outliers and B-value histograms to guide users to optimise their refinement strategy and subsequent atomic structure. To improve model geometry and stabilise refinement, *Servalcat* is integrated in a pipeline with restraint-generating programs such as *ProSMART* and *MetalCoord* [5]. Specifically for crystal structures (*refine_xtal_norefmac* mode), *Servalcat* supports direct refinement against reflection intensities. This approach improves the quality of density maps as it avoids the French-Wilson calculation of structure factor amplitudes which can introduce additional errors. The twin refinement algorithm was significantly revised. For cryoEM single particle analysis (*refine_spa_norefmac* mode), *Servalcat* supports advanced features including a weighted and sharpened $F_o - F_c$ difference map to inspect the agreement between model and data, and cross-validation using two half-maps for checking potential overfitting. Where applicable, a structure can be refined under symmetry constraints (helical or point group), reducing computational time and also simplifying manual model building. A mask can be automatically generated from the model. The *MetalCoord* program [5] addresses the longstanding challenge of modelling and refinement of metal coordination environments in macromolecular structures. Comprehensive analysis of coordination geometries is carried out using the data from the Crystallography Open Database (COD) [6] as a reference. The program generates interatomic distance and angle restraints, describing ideal stereochemistry, which can then be used in the common model building and refinement programs such as *Servalcat* [3], *Refmac5/Refmacat* [4], *phenix.refine* and *Coot*. Moreover, *MetalCoord* has been implemented into the *AceDRG* program [7] to enhance generation of stereochemical dictionaries. The monomer library with updated dictionaries for all the metal-containing ligands is available in the most recent release of the *CCP4* suite and via GitHub (<https://github.com/MonomerLibrary/monomers>).

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

[2] Burnley, T., Palmer, C. M., Winn, M. (2017). *Acta Cryst. D73*, 469-477.

[3] Yamashita, K., Palmer, C. M., Burnley, T., Murshudov, G. N. (2021). *Acta Cryst. D77*, 1282-1291.

[4] Yamashita, K., Wojdyr, M., Long, F., Nicholls, R. A., Murshudov, G. N. (2023). *Acta Cryst. D79*, 368-373. [5] Babai, K. H., Long, F., Malý, M., Yamashita, K., Murshudov, G. N. (2024). *Acta Cryst. D80*, 821-833.

[6] Gražulis, S., Chateigner, D., Downs, R. T., Yokochi, A. F. T., Quirós, M., Lutterotti, L., Manakova, E., Butkus, J., Moeck, P., Le Bail, A. (2009). *J. Appl. Cryst.* **42**, 726-729.

[7] Long, F., Nicholls, R. A., Emsley, P., Gražulis, S., Merkys, A., Vaitkus, A., Murshudov, G. N. (2017). *Acta Cryst. D73*, 112-122.

This work was supported by the BBSRC (grant No. BB/Y008839/1; MM, GNM), the STFC (grant No. 8521412, MM) and the Medical Research Council Partnership (grant No. MR/V000403/1; TB, CMP, APJ).