Poster

Direct real-space determination of atomic parameters from inhomogeneous cryoEM and crystallographic maps

A.G. Urzhumtsev[1,2], N.L. Lunina[3], V.Y. Lunin[3]

[1]Centre for Integrative Biology, Institut de Génétique et de Biologie Moléculaire et Cellulaire, CNRS–INSERM-UdS, 1 rue Laurent Fries, BP 10142, 67404 Illkirch, France, [2]Université de Lorraine, Faculté des Sciences et Technologies, BP 239, 54506 Vandoeuvre- les-Nancy, France, [3]Institute of Mathematical Problems of Biology RAS, Keldysh Institute of Applied Mathematics of Russian Academy of Sciences; 1, Professor Vitkevich St., Pushchino, 142290, Russia

sacha@igbmc.fr

Proposed new type of modelling, based on a specially designed function, allows new, fully real-space refinement procedures for cryoEM and crystallography, as well as a new representation of information about maps and atomic models obtained using these maps.

A numerical comparison of crystallographic and cryoEM model maps with the experimental ones is crucial for atomic model building and refinement. For such comparison, the former need to mimick imperfections of the latter. At the late stages of structural studies, when dealing with an atomic model, the principal residual imperfections are due to a structural disorder and to a limited map resolution, both may vary from one map region to another. Respective model maps can be calculated as a sum of atomic images given an atomic type, position, values of the displacement parameter (B), occupancy and a local resolution (D) which can be associated with atoms contributing to a chosen map region. The inverse problem is, given a map of a variable resolution, to find the values of all atomic parameters, including the local resolution.

While both structural disorder and a limited map resolution blur an atomic image, a resolution cut-off results additionally in Fourier ripples surrounded the central peak. Shape of both the central peak and the ripples depends on both disorder parameters B and D. In the frame of our new model, atomic images are expressed analytically using a spherically-symmetric function $(\mathbf{x};\square,\square)$ [1]. This function has been designed in such a way that its convolution with a Gaussian does not change the function itself but only its parameter $\square$. Changing the resolution is also reduced to a trivial modification of the two function parameters. A model density map, of a variable local resolution, can be now calculated in a single run, with no Fourier transform used [2,3] . Inversely, analytic expressions for both the target function comparing two maps and all its partial derivatives allows estimating and refining the values of B and D, assuming that atomic positions are known [4]. In particular, several examples of B and D values incorrectly assigned by conventional software have been found. The parameter values found by our model significantly improve the correspondence between the calculated and experimental maps [5] (Fig.1).

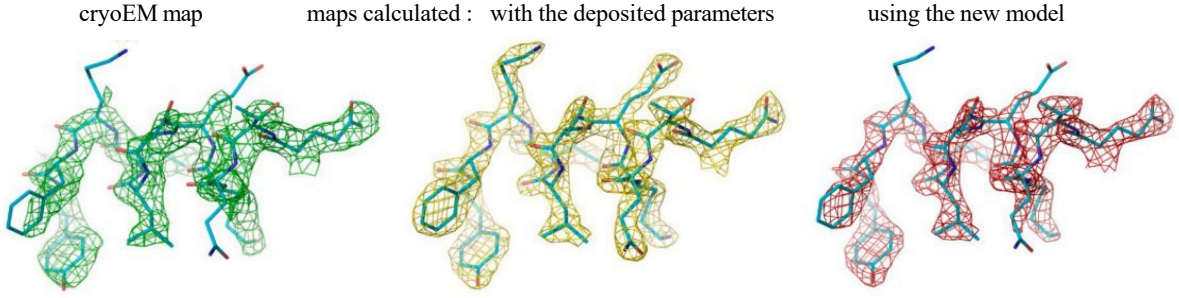

Figure 1. Experimental and calculated maps for a ribosome fragment [4].

[1] Urzhumtsev, A.G. & Lunin, V.Y. (2022). *IUCr Journal.* **9**, 728. doi: 10.1107/S2052252522008260

[2] Urzhumtsev, A.G., Urzhumtseva, L.M. & Lunin, V.Y. (2022). *Acta Cryst.* D**78**, 1451. doi: 10.1107/S2059798322010907

[3] Urzhumtsev, A.G. & Lunin, V.Y. (2022). *Int.J. of Molec. Sciences* **23**, 12101. doi: 10.3390/ijms232012101

[4] Lunin, V.Y., Lunina, N.L. & Urzhumtsev, A.G. (2023). *Current Res. Struct. Biol.* **6**, 100102. doi: 10.1101/2023.04.11.536420

[5] Frechin, L., Holvec, S., von Loeffelholz, O., Hazemann, I. & Klaholz, B.P. (2023). *J. Struct. Biol.* **215**, 107905. doi: 10.1016/j.jsb.2022.107905

AU acknowledges the French Infrastructure for Integrated Structural Biology FRISBI (ANR-10-INBS-05) and the support and the use of resources of Instruct-ERIC through the R&D pilot scheme APPID 2683.