MS01-1-1 Analytic representation of inhomogeneous-resolution density maps and real-space refinement

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Abstract
Real-space refinement of atomic models improves such models by their fit to experimental density maps in crystallography or to scattering electrostatic potential maps in cryo electron microscopy. This procedure has a number of advantages in comparison with reciprocal-space refinement, is complementary to it in crystallographic studies and is the principal technique in cryo EM. An accurate real-space refinement of atomic models can be done by comparison of the model maps with the experimental ones, when the former mimic imperfections of the latter, mainly a limited resolution and an atomic disorder. Model maps can be calculated as a sum of atomic contributions, i.e., atomic images at given conditions. In three-dimensional space, such image is represented by a peak surrounded by spherically symmetric Fourier ripples. To describe a solitary spherical wave, a function Ω(x;μ,v) with required properties has been especially designed (Urzhumtsev & Lunin, 2022). A three-dimensional interference function G(x), which is an image of an immobile point atom, can be highly accurately decomposed into a sum of 'shell' terms, each being a function Ω(x;μ,v) with appropriate parameters. This decomposition leads to a series of conclusions (Urzhumtsev & Lunin, 2022):
- An image of an atom of any chemical type at any resolution and with any displacement factor can be presented analytically as a sum of Ω(x;μ,v) terms.- Atomic displacement parameter and resolution are arguments of these analytic functions; function parameters are coefficients of a multi-Gaussian approximation to the atomic scattering factors and those of the G(x) shell-decomposition, both sets are known.- Model density map, even when its resolution varies from one its region to another, can be calculated in a single run, with no Fourier transform used.- In each its point, a model density map becomes an analytic function of atomic parameters, i.e., their coordinates, displacement parameter and the local resolution associated now with atom.- As a consequence, for a score function describing the model-to-experimental maps fit, its partial derivatives with respect to all atomic parameters become also analytic functions; all these parameters, including the local resolution, can be really 'real-space' refined using gradient methods, with no need in structure factors and Fourier transform.- Being associated with atoms, the local resolution can be reported in the PDB files together with the coordinates and displacement factors; this value is a measure of confidence of the atomic parameters charactering the map region in which the atom has been identified.- When the variation of the local resolution can be neglected, one can use a simplified form of a decomposition of images at a given resolution into a sum of Ω(x;μ,v); this reduces the number of terms, in turn reducing CPU time and improving convergence; this is an option at earlier and intermediate stages of refinement.
To decompose oscillating spatial curves, such as atomic images of a limited resolution, programs in fortran77, their equivalents in python3, as well as a GUI version, have been developed. Implementation of these algorithms into phenix.refine (Afonine et al., 2012) is in progress.

References
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