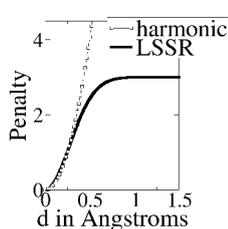


Refinement with Local Structure Similarity Restraints (LSSR) enables exploitation of information from related structures and facilitates use of NCS. O. S. Smart, M. Brandl, C. Flensburg, P. A. Keller, W. Paciorek, C. Vonrhein, T. O. Womack and G. Bricogne, Global Phasing Ltd., Sheraton House, Cambridge CB3 0AX, UK.

We have developed a novel restraint procedure that can be used in maximum-likelihood refinement to exploit information that the structure under consideration is similar to another. This similarity can be to an already solved structure, the “target”. For instance a high-resolution apo structure can be used as a target when refining a lower-resolution ligand-soak structure. Alternatively the similarity could be between two or more chains within the structure being refined and thus can enforce NCS. The restraint is defined by considering the distance r_{AB} between pairs of atoms A , B within the chain to be restrained. All pairs of atoms that are not bonded and have $r_{AB} < 5.5\text{\AA}$ are considered. Structural similarity implies that the distance r'_{AB} between the corresponding atoms in the other chain or target structure will in general be close to r_{AB} . LSSR imposes for each atom pair a penalty on the difference in distances $d = r_{AB} - r'_{AB}$. For targeting to an external structure, r'_{AB} remains constant in the refinement, whereas for NCS it will vary.



The LSSR functional form is not harmonic but instead plateaus as d gets large, thus automatically allowing differences to be accommodated if the X-ray data so demand. Because LSSR are local, there is no need to separate out domains. These features make it easy to use compared to conventional harmonic superposition-based NCS treatments which often require elaborate segmentations. BUSTER refinement with LSSR results in lower R_{free} and a narrower $R_{\text{free}}-R_{\text{work}}$ gap. The method is particularly applicable to the refinement of protein-ligand complexes and large oligomeric assemblies.