Improving molecular replacement with morphing

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Abstract

Molecular replacement is an immensely powerful method for determining macromolecular crystal structures. The method nevertheless remains limited by the requirement for a template structure that is similar to the structure to be determined. Normally a template with an rmsd of core main-chain atoms of about 1.5-2 Å is required. The applicability of molecular replacement would be greatly expanded if templates differing from the target structure by 2 to 3 Å rmsd could routinely be used. Here we take advantage of the observation that many pairs of proteins have local structures that can be superimposed much more closely than can their complete structures. For example, a β-sheet in one protein may be locally similar to a sheet in another, but when the two structures are superimposed using all atoms, the sheets may be translated relative to each other. We have developed a method for applying local distortions to a structure (morphing it) using an electron density map to guide the distortions. This procedure allows local similarity to be maintained while global structure is changed. We show that morphing molecular replacement templates after placing them in their approximate locations in the crystallographic unit cell can greatly improve subsequent model-building.

Morphing can be carried out with the PHENIX tool phenix.morph_model. PHENIX software is available at http://www.phenix-online.org.