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Ctrl-D, a versatile tool for analyzing processed diffraction data

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Good native data are an asset for phasing, because they allow you to obtain and improve solutions to the phase problem even in the absence of a suitable homologous template. The question often explored in Molecular Replacement (MR) is: Is the model good enough to solve the structure? Here we explore the reverse: Are the data good enough for the distant homolog model to succeed? ARCIMBOLDO_SHREDDER (1) derives compact model fragments starting from a distant homolog template, evaluating their performance in a process driven by the experimental data, provided that a resolution of at least 2.5 Å is available. This method uses partial fragments that need to be very accurate. The following stages can be distinguished:

- *Partition and annotation of the template:* The template model is dissected into fragments that will be disassembled to give the model additional degrees of freedom.
- *Generation of the models:* The size of the fragments is derived from a target eLLG, set to be large enough to find correct solutions, but small enough to generate potentially accurate fragments.
- *Evaluation against the likelihood rotation-function target*
- *Gyre refinement* (2)*:* The orientation and relative translation of the rigid groups identified in the first step are refined against the rotation-function target.
- *Translation search*
- *Packing test*
- Refinement: Depending on the data and the expected deviation of the models, a set of different strategies can be trialed at this stage: refinement of the r.m.s. error attributed to the model, superposition of the original template on each placed fragment with trimming and refinement, *gimble* refinement against the likelihood translation-function target subdividing the model into the same rigid groups as in *gyre*, or *phaser*'s likelihood-based pruning.
- *Phase combination*: Consistent phase sets can be combined with *ALIXE* in order to complete partial solutions and increase their information content.
- *Density modification and autotracing for expansion of the substructure to a full solution*: The single or combined phase sets are used to calculate starting maps for iterative density modification and autotracing with *SHELXE*.

The method described has been successful in solving previously unknown structures, including Slt (3), a lytic transglycosylase from the pathogen *Pseudomonas aeruginosa*. Moreover, it has helped to increase our knowledge about how to best exploit the available data and models in the context of fragment-based MR. In this presentation, both the method and its application to different cases will be discussed.

References:

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