

## MS25-05 | USING ARCIMBOLDO'S FRAGMENT-BASED MR FOR SOLVING MICROED DATA FROM MACROMOLECULAR STRUCTURES

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The proof of principle of protein structure determination using MicroED (micro electron diffraction) from sub-micron sized 2D protein crystals was established with lysozyme in 2013, for which molecular replacement (MR) was performed for phasing. Since that milestone, a number of different cases with resolution ranging from 3.2-1.0 Å have been solved. For atomic resolution, *ab-initio* methods, relying only on the measured intensities, were used for phasing. For lower resolutions, MR has been the phasing method of choice, but it requires a model.

ARCIMBOLDO performs fragment-based MR with PHASER, using as models either secondary structure elements, or libraries of small local folds or fragments from a distant homolog. Such small accurate fragments produce many solutions from which only a few are correct, but density modification and mainchain autotracing with SHELXE allows the completion and discrimination of correct substructures. For non-atomic resolutions but better than 3 Å, this method has been successful in many X-ray structure determinations.

Recently, we are adapting ARCIMBOLDO to work with electron scattering factors and using our model fragments, a number of MicroED datasets can be solved. In this work we will discuss the results of these cases and the current and future developments in our software for dealing with MicroED data.

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