MS12-04 | Molecular Replacement Using Structure Predictions from new Generation Databases

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Molecular Replacement (MR) is the predominant route to solution of the phase problem in macromolecular crystallography. Where the lack of a suitable homologue precludes conventional MR, one option is predicting the target structure with bioinformatics. Such modelling, in the absence of homologous templates, is called *ab initio* or *de novo* modelling. Recently the accuracy of such models has improved significantly as a result of the availability, in many cases, of residue contact predictions derived from evolutionary covariance analysis. Covariance-assisted *ab initio* models representing structurally uncharacterised Pfam families are now available on a large scale in databases, potentially representing a valuable and easily accessible supplement to the PDB as a source of search models.

Here we deploy the unconventional MR pipeline AMPLE to explore the value of structure predictions in the Gremlin and PconsFam databases. We test whether these deposited predictions, processed in various ways, can solve the structures of PDB entries subsequently deposited. The results were encouraging: nine of 26 Gremlin cases solved, covering target lengths of 112-355 residues and a resolution range of 1.35-2.85Å, and with target-model shared sequence identity as low as 37%. AMPLE's cluster-and-truncate approach proved essential for most successes. For the overall lower quality structure predictions in the PconsFam database, remodelling with Rosetta within the AMPLE pipeline proved to be the best approach, generating ensemble search models from single structure deposits. Overall the results help point the way towards the optimal use of expanding *ab initio* structure prediction databases.