

Oral Contributions

[MS4] Advances in refinement, phasing and autobuilding

Co-Chairs: Michael Kokkinidis (GR), Isabel Uson (ES)

[MS4-01] Using Phaser for Phasing in Conjunction with Wide-Convergence Refinement and Model Building Techniques

Airlie J. McCoy, Gabor Bunkoczi, Rob D. Oeffner, Thomas C. Terwilliger, Massimo Sammito, Claudia Millan, Isobel Uson & Randy J. Read

Molecular replacement with Phaser is an immensely powerful method for phasing macromolecular crystal structures. For template models with a sequence identity of greater than 30% to the target and suitable model editing methods [1], Phaser will usually succeed in generating a clear solution with a translation function Z-score (TFZ) greater than 8, a value that invariably indicates a correct placement [2]. Nevertheless, pushing the boundaries of phasing by molecular replacement with poor template structures will always result in a class of problems for which there isn't a clear solution from Phaser. The question of what to do in such cases is being addressed by incorporating Phaser into extended pipelines that use high convergence radius refinement and model building methods such as Rosetta [3] or Morphing [4] to distinguish correct from incorrect solutions from a list of potential solutions from Phaser. Fragment based approaches to molecular replacement, for which the signal to noise in the translation function is extremely low, pose particular problems for refinement and model building due to the very poor phases from the incomplete and/or inaccurate initial (sub)structure. For these cases, techniques traditionally associated with experimental phasing such as density modification and direct methods can be used to dramatically improve map quality and pull solutions from seemingly hopeless initial Phaser results [5,6].

[1] **Improvement of molecular-replacement models with Sculptor.** G. Bunkoczi and R. J. Read *Acta Cryst.* D67, 303-312 (2011)

[2] **Improved estimates of coordinate error for molecular replacement** R. D. Oeffner, G. Bunkoczi A.J. McCoy and R. J. Read (In press)

[3] **Increasing the Radius of Convergence of Molecular Replacement by Density and Energy Guided Protein Structure Optimization** Frank DiMaio, Thomas C. Terwilliger, Randy J. Read, Alexander Wlodawer, Gustav Oberdorfer, Eugene Valkov, Assaf Alon, Deborah Fass, Herbert L. Axelrod, Debanu Das, Sergey M. Vorobiev, Hideo Iwai, P. Raj Pokkuluri & David Baker (2011) *Nature*, 473, 540-543.

[4] Thomas C. Terwilliger, *per. Comm.*

[5] **Molecular replacement using ab initio polyalanine models generated with ROSETTA** D. J. Rigden, R. M. Keegan and M. D. Winn (2008) *Acta Cryst.* **D64**, 1288-1291

[6] **Crystallographic Ab Initio protein solution far below atomic resolution.** Dayte D. Rodríguez Martínez, Christian Grosse, Sebastian Himmel, César González, Iñaki M. de Ilarduya, Stefan Becker, George M. Sheldrick and Isabel Uson. *Nature Methods* 6(9): 651-653 (2009)