

## Microsymposium

MS100.O05

### *Structure Refinement at Low-resolution: Strategies and Validation*

G. Schröder<sup>1</sup>, M. Levitt<sup>2</sup>, A. Brunger<sup>2</sup>

<sup>1</sup>Forschungszentrum Juelich, Institute of Complex Systems (ICS-6), Juelich, Germany, <sup>2</sup>Stanford University, Department of Structural Biology, Stanford, CA, USA

In the refinement of macromolecular structures at low resolution (worse than 3.5 Å) over-fitting becomes a serious problem since the number of degrees of freedom (i.e. atomic coordinates) is often much larger than the number of experimental observables (number of unique reflections). Applying additional restraints help to reduce the effective number of degrees of freedom but will necessarily limit the conformational freedom of the structure during the refinement. These restraints could therefore prevent finding the optimum solution, which means the choice of restraints is important. Strategies will be presented to choose such restraints. For example the Deformable Elastic Network (DEN) approach adapts restraints automatically, on the one hand to allow for relevant conformational changes to occur and on the other hand to keep those degrees of freedom well restrained for which no experimental data are available [1]. Some recent examples [2] of low-resolution structures will be presented including the refinement of the chaperonin TRiC in a closed (3.8 Å) and open (5.5 Å) conformation [3]. This example also shows that new validation tools might be important at low resolution in addition to traditional cross-validation. For example exhaustive sampling of alternative models can provide additional information on the reliability and statistical significance of the optimum structure solution.

[1] G.F.Schröder, M.Levitt, A.T.Brunger, *Nature*, 2010, 464, 1218-1222, [2] A.T.Brunger, P.D.Adams, P.Fromme, R.Fromme, M.Levitt, G.F.Schröder, *Structure*, 2012, 20, 957-966, [3] N.Kalisman, G.F.Schröder, M.Levitt, *Structure*, 2013, 21, 540-549

**Keywords:** Refinement, Low-resolution, Validation