M06.0B Structural Enzymology and Unusual Chemistry

Chair: W.H.E. Saenger
Co-Chair: G. Oliva

Attendance: 106

This microsymposium “Structural Enzymology and Unusual Chemistry” was organized by chair W. Saenger and cochair G. Oliva around enzymes utilizing unusual cofactors to perform their tasks. The cofactors were or included metal ions in different environments except for the last enzyme in this series.

The opening by J. Fontecilla-Camps was on hydrogenases containing Fe in their active site or a combination of Fe and Ni coordinating CO, CN and/or cysteine thiolate. The function of the metal ions was discussed with emphasis on the spin state of Fe. Since the active site is at the center of the hydrogenases, H_2 has to diffuse through long channels in the proteins which were beautifully illustrated by loading them with Xe.

A “movie” of snapshots by C. Wilmot showed convincingly the reaction pathway of amino oxidase from E.coli. The catalytic cycle of this enzyme utilizing Cu and 2,4,5-trihydroxyphenylalanine quinone as cofactors was studied by single crystal microspectrometry; individual steps of the reaction were flash-frozen and X-ray analyzed at high resolution. The quinone „jumps“ from one to the next step in the reaction cycle and, surprisingly, O_2 was seen to bind to Cu prior to oxidizing amine to the corresponding aldehyde.

U. Ermler described methyl-coenzyme M reductase, a 300 kDa heterohexamer catalyzing the last step of methane metabolism. This step involves the oxidation of coenzyms M and B to a heterodisulfide under cooperation of coenzyme F_{430} containing a Ni-porphinoid, with transient formation of radicals and a Ni-Methyl complex. The active site is closed after substrate binding, as shown by a sequence of crystal structures.

Another multistep reaction was presented by K. Brown with the Zn and NAD^+ containing 3-dehydroquinate synthase, an enzyme in the shikimate pathway. The enzyme is unusual as it catalyzes different reactions: alcohol oxidation, carbonyl reduction, ring opening, phosphate b-elimination, intramolecular aldol condensation. Knowledge of the architecture of the active site with bound Zn, NAD^+, substrate analogs will be of interest for drug design as several parasites use this pathway, but no mammals.

Hollywood entered the scene with a movie shown by A. Anderson. It featured thymidylate synthetase and showed clearly the reasons for anticooperativity of this homodimeric enzyme. In complex with substrate dUMP and cofactor analog CB3717 the homodimer is asymmetric, binding two molecules of the former but only one of the latter. The reason for anticooperativity is seen in covalent bound formation between the catalytic cysteine and dUMP in one subunit that induces a conformational change in the other and prevents such bond formation, associated with modification of other enzyme/cofactor/substrate interactions.

The original program was extended by A. Becker presenting the acetyl-CoA synthesizing enzyme pyruvate formate-lysase, a homodimer with 340 kDa. In the reaction, the C1-C2 bond of pyruvate is cleaved utilizing a free and stable radical located at Gly734. There is no metal ion involved in radical formation, contrasting other known enzymes that engage Fe (III).

The organizers and the audience were impressed by the well prepared lectures which were followed by expert discussions. This was a beautiful stone in the mosaic of the Glasgow IUCr meeting.

Wolfram Saenger and G. Oliva