FA3-MS03-O1

Structure of Microsomal Prostaglandin E Synthase 1 as Determined by Electron Crystallography.

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We have determined the structure of human microsomal prostaglandin E synthase 1 (MPGES1) in complex with the tripeptide γ-L-glutamyl-L-cysteinyl-glycine, glutathione (GSH) at 3.5 Å in-plane resolution using electron crystallography [1]. Pair wise acquisitions of electron diffraction patterns at a camera length of 200 cm were made. A tilted recording was followed by a 0º pattern which was used entirely for classification and quality assessment. The trimeric model of microsomal glutathione transferase 1 (MGST1) [2] was used for a molecular replacement search since the sequence identity between these proteins is high. A final structure of the MPGES1 trimer was obtained following numerous rounds of refinement using tight geometry restraints and medium non-crystallographic symmetry in REFMAC5 in combination with geometry idealisation and manual rebuilding in O. The subunits of MPGES1 form a homotrimer (here related by non crystallographic symmetry) in a similar way as for MGST1 [2], FLAP [3] and LTC4S [4,5], i.e. other structurally characterized members of the same superfamily. An omit map calculated between the observed electron diffraction amplitudes and amplitudes calculated from the protein model showed three distinct U-haped densities corresponding to GSH. The thiol group of GSH is stabilized by an arginine residue directed towards the membrane between helices one and four from neighbouring subunits. In MPGES1 theses helices are closer together than in LTC4S and do not allow access to GSH suggesting that our MPGES1 structure represents a closed conformation of the enzyme.

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Keywords: prostaglandin; membrane protein; electron microscopy

FA3-MS03-O2

Oxide Surfaces.

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While it is probably fair to say that we understand relatively well the structure of metal surfaces as well as those of semiconductors, in many other cases particularly for oxides the situation is much less clear.. As a consequence it is still hard to guess a plausible structure for an oxide surface with much confidence.

One invaluable method that avoids the need to guess a plausible method is direct methods. Developed originally for bulk materials, with some attention to how they are done we were able a few years ago to apply them first for two-dimensional transmission electron diffraction data [1, 2], relatively quickly for two-dimensional surface x-ray diffraction data [3-5] and then extend them to three-dimensional surface x-ray diffraction data [6] basing the approach on a feasible set methodology [7]. The method has proved useful in determining some unexpected oxide structures which one would not have guessed [8-10], as well as a number of perhaps not so unexpected defect structures at surfaces [11, 12].

This presentation give an overview of some recent results on the structure of oxide surfaces, particularly combining direct methods and transmission electron microscopy with DFT analyses taking care with the choice of functional, as well as using auxiliary tools such as XPS to check the surface chemistry.

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Keywords: electron diffraction; direct methods; surfaces