

### MS11-O3 Analysis of flexible multidomain glycoproteins with SAXS, analytical ultracentrifugation, and torsion-angle molecular dynamics

Jordi Bella<sup>1</sup>, Thomas A. Jowitt<sup>1</sup>, Clair Baldock<sup>1</sup>, David Garrod<sup>1</sup>, Lydia Tabernero<sup>1</sup>

1. Faculty of Life Sciences, University of Manchester, Manchester M13 9PT

email: jordi.bella@manchester.ac.uk

The extracellular regions of many cell-surface receptors and extracellular proteins are built from tandems of domains (immunoglobulin-like, cadherin, EGF-like, fibronectin type-III, etc) that are connected by inter-domain linkers of variable flexibility. This conformational flexibility, often combined with glycosylation, makes structural analysis of these multi-domain proteins particularly challenging. When high-resolution methods fail, biological small-angle X-ray scattering (SAXS) can provide at least some structural information about these molecules, mainly in terms of overall shape and dimensions. Drawbacks are the low resolution and limited amount of data, which can easily lead to overfitting or non-meaningful solutions that fit the data equally well. SAXS analysis of multi-domain proteins (or glycoproteins) often involves exploring their conformational space by generating a library of thousands of conformers, built from atomic models typically based on high-resolution crystal structures of homologous proteins. These conformers are then tested in turn against the SAXS data, and ensembles of best-fitting conformers are generated to describe the flexible states of these multi-domain proteins in solution (Tria *et al.*, 2015, *IUCrJ*, 2: 207-17). Torsion-angle molecular dynamics, as implemented in the popular crystallographic package CNS (Brunger *et al.*, 1998, *Acta Cryst. D54*: 905-21) offers an attractive route for exploring the conformational space of multi-domain proteins with much smaller libraries of conformers, thus requiring a smaller computational effort. In addition, it provides a more precise control of the flexibility between domains, allows for simultaneous sampling of the protein and sugar components of glycoproteins, and overcomes topological limitations for the definition of the flexible and rigid elements of the multidomain protein or glycoprotein being explored. Hydrodynamic data obtained from analytical ultracentrifugation can be combined with this conformational sampling to filter out conformers with unrealistic shapes and dimensions prior to their fitting to the SAXS data. This powerful combination increases the confidence in the SAXS analysis and produces more realistic models. Applications of this methodology will be illustrated with successful examples from our laboratory (Tariq *et al.*, 2015, *PNAS* in press).

**Keywords:** SAXS, molecular dynamics, analytical ultracentrifugation, hydrodynamic modeling

### MS11-O4 Solving complex zeolite structures by combining electron crystallography, solid state NMR and powder X-ray diffraction

Xiaodong Zou<sup>1</sup>, Tom Willhammar<sup>1</sup>, Allen W. Burton<sup>2</sup>, Yifeng Yun<sup>1</sup>, Junliang Sun<sup>1</sup>, Mobae Afeworki<sup>2</sup>, Karl G. Strohmaier<sup>2</sup>, Hilda Vroman<sup>2</sup>

1. Berzelii Centre EXSELENT on Porous Materials and Inorganic and Structural Chemistry, Department of Materials and Environmental Chemistry, Stockholm University, SE-106 91 Stockholm, Sweden

2. Corporate Strategic Research, ExxonMobil Research & Engineering Co. Inc, 1545 Route 22 East, Annandale, New Jersey 08801, USA

email: xzou@mmk.su.se

Zeolites are crystalline, microporous aluminosilicates that are used as catalysts or adsorbents in a wide array of industrial processes. Stable, multidimensional and extra-large pore zeolites are desirable by industry for catalysis and separation of bulky molecules. Here we report EMM-23, the first stable, three-dimensional extra-large pore aluminosilicate zeolite[1]. The structure of EMM-23 was determined from sub-micron sized crystals by combining electron crystallography, solid state NMR and powder X-ray diffraction.

The polycrystalline nature, the large unit cell and especially the presence of Q<sup>2</sup> and Q<sup>3</sup> Si species make the structure determination of EMM-23 challenging. Electron crystallography has unique advantages for structure solution of nano- or micron-sized crystals[2]. We applied the recently developed the rotation electron diffraction (RED) method[3] and collected 252 ED frames covering a tilt range of 63.74° (Fig. 1). The crystallographic phase information from high resolution transmission electron microscopy (HRTEM) images has been used to facilitate the space group determination. The structure was solved from the RED data using direct methods, and refined by powder X-ray diffraction. Solid state NMR indicated that the zeolite possesses a high density of Q<sup>2</sup> and Q<sup>3</sup> silicon species, which was not observed before in zeolites. The solid state NMR data provided important information about the possible disorders in the structure, which were used for the structure refinement. The framework contains highly unusual tri-lobe shaped pores that are bound by 21-24 Si/Al atoms. These extra-large pores are intersected perpendicularly by a 2D 10-ring channel system. EMM-23 is stable after calcination at 540°C.

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