Atom Probe Tomography of Single Proteins

Andersson, M.[1], Hulander, M.[1], Sundell, G.[1] and Pihl, A.[1]

[1] Chalmers University of Technology, Sweden

Proteins are the building blocks of life and participate in virtually all processes within living organisms. Protein receptors in the cell membrane govern transport in and out of the cell, and are therefore the target for over 50% of all modern medicinal drugs[1]. A critical aspect of the field of structural biology is to characterize the structure of proteins in three dimensions. Knowledge of the shape of a e.g. a transmembrane protein can allow for design of new pharmaceutical substances that inhibit virus infections[2].

Traditionally, the functional structure of proteins has been determined using X-ray crystallography or nuclear magnetic resonance (NMR). However, X-ray crystallography can only be applied to proteins in a crystallized state, which restricts its applicability. NMR often relies on excessively complex computer calculations, which limits the technique to the study of small molecules. More recently, development of direct electron detectors has sparked a revolution in cryo electron microscopy for structural biology applications.

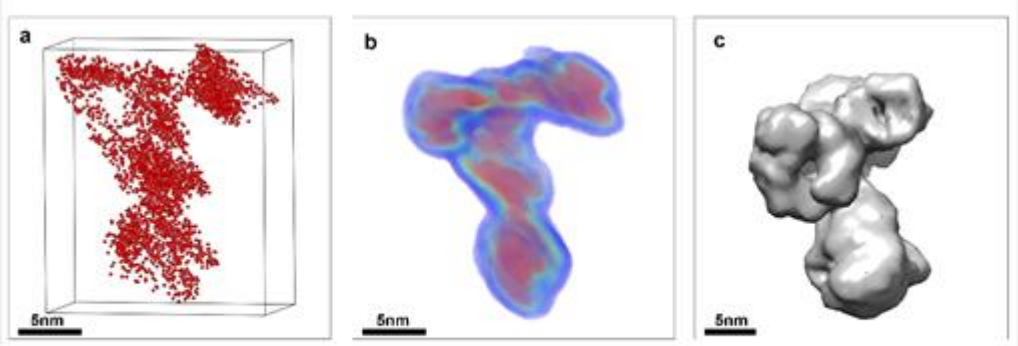

Figure 1: (a) and (b) atom probe reconstructions of IgG, (d) reference pdb structure of IgG as retrieved from the protein databank.

Here, we show for the first time that atom probe tomography may constitute a complementary method in proteomics, providing both chemical information as well as high-resolution 3D structural information. We have encapsulated the human antibody Immunoglobulin G (IgG) in a solid silica glass matrix to provide the requisite mechanical stability to allow for atom probe analysis.

We present atom probe reconstructions of the antibodies, both in an aggregated and monomer state. We compare the results with known structures retrieved from the protein databank[3]. The challenges and opportunities that are associated with this approach are discussed.

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3. Berman, H. M. *et al.* The protein data bank. *Nucleic Acids Res.* **28,** 235 - 242 (2000).