Biomolecular mass spectrometry and structural proteomics

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Introduction
Our research is focussed on the development and application of mass spectrometry (MS) to investigate the structure and function of biomolecules. We use non-covalent electrospray ionisation (ESI)-MS, tandem mass spectrometry (MS/MS) and ion mobility spectrometry (IMS)-MS to determine the mass, conformational properties, stoichiometry, stability, and binding characteristics of biomolecules and their complexes. Specifically we study protein folding, function and self-aggregation, protein-ligand interactions and biomolecular complex assembly [1-11]. We also use chemical labelling methods in conjunction with ESI-MS and ESI-MS/MS to map protein folding and aggregation pathways [2, 4] and to characterise non-covalently bound biomolecular complexes (Figure 1).

Results
Our major projects are aimed at characterising amyloid protein aggregation and inhibition, for which we have developed a high-throughput screening method to evaluate potential small molecule amyloid inhibitors [1, 3, 5, 8, 11], investigating ribosome function [6, 7], mapping virus capsid assembly pathways [9], determining membrane protein structure and function [10], and developing new biomolecular MS methodologies [2, 4] (Figure 2).

Figure 1: Chemical labelling methods used with MS for structural proteomics to study protein structure and locate protein:protein and protein:ligand interactions include: hydrogen-deuterium exchange (HDX) [2], hydroxyl radical footprinting (FPOP) [4] and chemical crosslinking.

Figure 2: (a) Immunoglobulin protein; (b) (i) oxidation of solvent-exposed sites using OH• radicals gives rise to (ii) oxidised protein. Location of the oxidised amino acid residues is achieved by (iii) proteolysis followed by (iv) LC-MS. Comparing the oxidation sites of the native protein (c) with those of the partially folded (DM) and unfolded (TM) variants indicates conformational differences.
Publications


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