Mass spectrometry: From plasma proteins to mitochondrial membranes

Beginning with the preservation of the first soluble complexes from plasma in the gas phase of a mass spectrometer, I will describe our early experiments that capitalise on the heterogeneity of subunit composition during assembly and exchange reactions. To assess the overall topology of these complexes we adapted ion mobility and soft-landing methodologies to show how ring-shaped complexes could survive the phase transition. The next logical progression from soluble complexes was to membrane protein assemblies but this was not straightforward. We encountered many pitfalls along the way, largely due to the use of detergent micelles to protect and stabilise these complexes. Further obstacles presented when we attempted to distinguish lipids that co-purify from those that are important for function. By developing new experimental protocols, we have subsequently defined lipids that change protein conformation, mediate oligomeric states, and facilitate downstream coupling of G protein-coupled receptors. Recently, using a new method — ejecting protein complexes directly from native membranes into mass spectrometers — we provided insights into associations within membranes and mitochondria. I will trace the history of these developments in my presentation and also look towards future innovations and discoveries.