SPECTROSCOPY

Surviving the gas phase

Researchers demonstrate a method for observing intact membrane protein complexes by mass spectrometry.

Most scientists are probably familiar with the application of mass spectrometry to proteomics or for analyzing small molecules, but mass spectrometry can also be used to answer questions about protein topology, subunit stoichiometry and ligand binding. Carol Robinson and her group at the University of Cambridge have been at the forefront in developing this unique technology.

Although Robinson's group and others have had some remarkable successes in using mass spectrometry to study the structures of intact soluble protein complexes, they hit a stumbling block when it came to membrane protein complexes. "It's always been a frustration: … it was one of those things that seemed as though it should be simple but never was," says Robinson.

Membrane protein complexes need detergents for stabilization, but detergents can suppress ionization in the mass spectrometer. The researchers had tried to tackle the problem by removing the detergent before mass spectrometry analysis, but then they just saw the complex fall apart in the gas phase.

So recently, they tried a new approach with $BtuC_2D_2$, a vitamin B_{12} importer with two transmembrane and two cytoplasmic subunits. Using a mass spectrometry–compatible detergent at very high concentrations in combination with maximum electrospray ionization acceleration voltages, they observed transfer of detergent micelles containing $BtuC_2D_2$ into the gas phase.

"It seemed counterintuitive that we were really upping the instrumental conditions but yet the complexes were surviving," says Robinson. They attributed this to the presence of the micelle, which protects the complex during the harsh ionization conditions. "For years, people have always said (me included) that hydrophobic interactions were not favorable in the gas phase because there was no water around to stabilize them," explains Robinson. "So the fact that they survived in the gas phase was a surprise." By increasing the pressure inside the collision cell, they could liberate the naked yet still intact $BtuC_2D_2$ complex. They also observed ATP binding to the $BtuC_2D_2$ complex.

Robinson's group has also successfully tested four other membrane protein complexes and are working on others. "We want to see how general the method is and how widespread we can make it," says Robinson.

Allison Doerr

RESEARCH PAPERS

Barrera, N.P. *et al.* Micelles protect membrane complexes from solution to vacuum. *Science* **321**, 243–246 (2008).