Ezine

Weighing up Viral Differences

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Mass spectrometry is generally applied to molecules. But, what about using it to study much larger entities such as viruses? US researchers have now reported the mass spectrometric examination of intact viruses based on a new technique of charge-detection mass spectrometry. This allows them to simultaneously determine both the charge and the mass-to-charge ratio of individual viral particles.

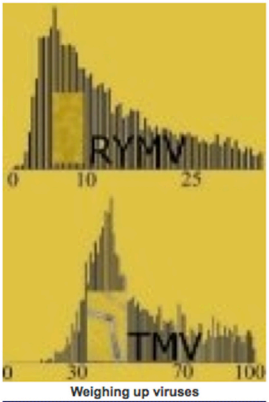
The study of the subtle differences in the outer surface proteins of viruses is at the heart of why it is difficult for the body to become immune to the likes of the viruses that cause colds - they never look the same to the immune system from one infection to the next. While a cure for the common cold might remain a nice idea, more serious diseases, such as AIDS, also rely on their ability to remain essentially invisible to the immune system by changing their protein coat from one viral generation to the next. A relatively quick and easy way to characterise such viruses might provide researchers with important clues as to how to design effective vaccines or drugs for treating the disease.

Mass spectrometry has previously been used in viral research and in 1996 Gary Siuzdak of The Scripps Research Institute Center for Mass Spectrometry in La Jolla California and colleagues used electrospray ionisation MS to demonstrate that whole viruses could be vaporized and ionised as well as pass through the vacuum of the mass spectrometer without being destroyed. However, they could not make mass measurements.

Siuzdak scaling the mass peaks

Now, Siuzdak together with Henry Benner of the Lawrence Berkeley Laboratory and Stephen Fuerstenau of the Jet Propulsion Laboratory at Caltech have found a way to analyse an intact virus, which has allowed them to take a mass spec snapshot.

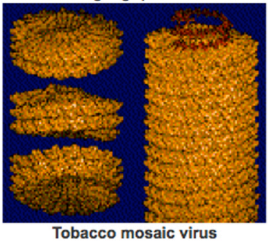
In a mass spectrometric analysis, molecules are ionised, separated and detected depending on their mass but if one wishes to explore a virus with the same approach, its megadalton mass stretches standard instrumentation too far. Indeed, individual large biomolecules, with their inherent fragility pose something of a challenge to mass spectrometers. Benner and Siuzdak have applied charge-detection mass spectrometry instead of carrying out a straightforward MS analysis. This technique, neatly sidesteps the problem of measuring very high mass to charge values. For a virus, these are simply too high to analyse in an ESI quadrupole mass spectrometer and even if the instrument had a sufficiently high mass range, the resolution would be so low as to make assignment of peaks impossible.



Weighing up viruses

Siuzdak and colleagues believed the direct detection of charge number would circumvent this obstacle to viral analysis by measuring charge and the mass-to-charge ratio simultaneously. The detection technique permits the mass analysis of electrospray ions with virtually unlimited mass, explains Siuzdak, because in traditional instruments detection was dependent on the ion?s velocity where slow, high mass ions, could not be detected, charge detection allows for detection of these slow moving ions.

The team has subjected two viruses to this analysis - the ubiquitous and well-studied tobacco mosaic virus (TMV) and the rice yellow mottle virus (RYMV). TMV is a rod-shaped virus formed from 2140 identical, wedge-shaped proteins that self-assemble to form a cylinder around the viral RNA. RYMV is an icosahedral virus and wider than TMV at 29 nanometres diameter compared to TMV?s 19 nm. The team measured thousands of ions over a collection period of some thirty minutes and found that TMV has a molecular weight of 40.5 megadaltons while RYMV weighs in at 6.5 megadaltons. While this demonstrates proof of principle, the researchers plan to further improve the accuracy of the technique by increasing the length of the instrument?s flight tube.



Tobacco mosaic virus

The researchers point out that the viruses they subjected to mass spec survive the mild ionisation conditions and, remarkably, remain infectious even though a virus? component parts are generally held together by non-covalent interactions rather than covalent bonds. These measurements could allow us to study virus-antibody interactions or even attachment to the receptors from their host cells, Siuzdak explained. At the same time, the mass of the viruses could provide valuable information about different viral subpopulations. Over the past decade, mass spectrometry has undergone tremendous technological improvements allowing it to be used in studying DNA, drugs, and a host of other biomolecules. It is because of the new technology, adds Siuzdak, that mass spectrometry is becoming an irreplaceable tool in the biological sciences, technology that now is allowing us to measure whole viruses!