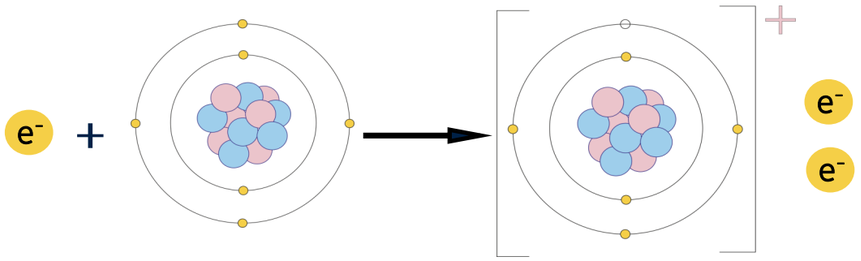
Mass Spectrometry: An Analytical Heavyweight

Time of Flight Mass Spectrometry

1 Molecules are first vaporised (to make them gaseous) and ionised. One method is to collide the molecules with high-energy electrons, 'knocking out' an electron from the molecule, and giving it a positive charge.



2 Ions are accelerated by an electrode, giving them all the same kinetic energy. q is the charge of the ion and V is the voltage of the electrode.

$$KE = qV$$

3 The ions then enter a field-free region and travel towards a detector. They all have the same kinetic energy, so lighter ions have a higher velocity (v), and will hit the detector earlier than heavier ions. This leads to 'peaks' in the signal at different times.

$$KE = 1/2\ mv^2$$

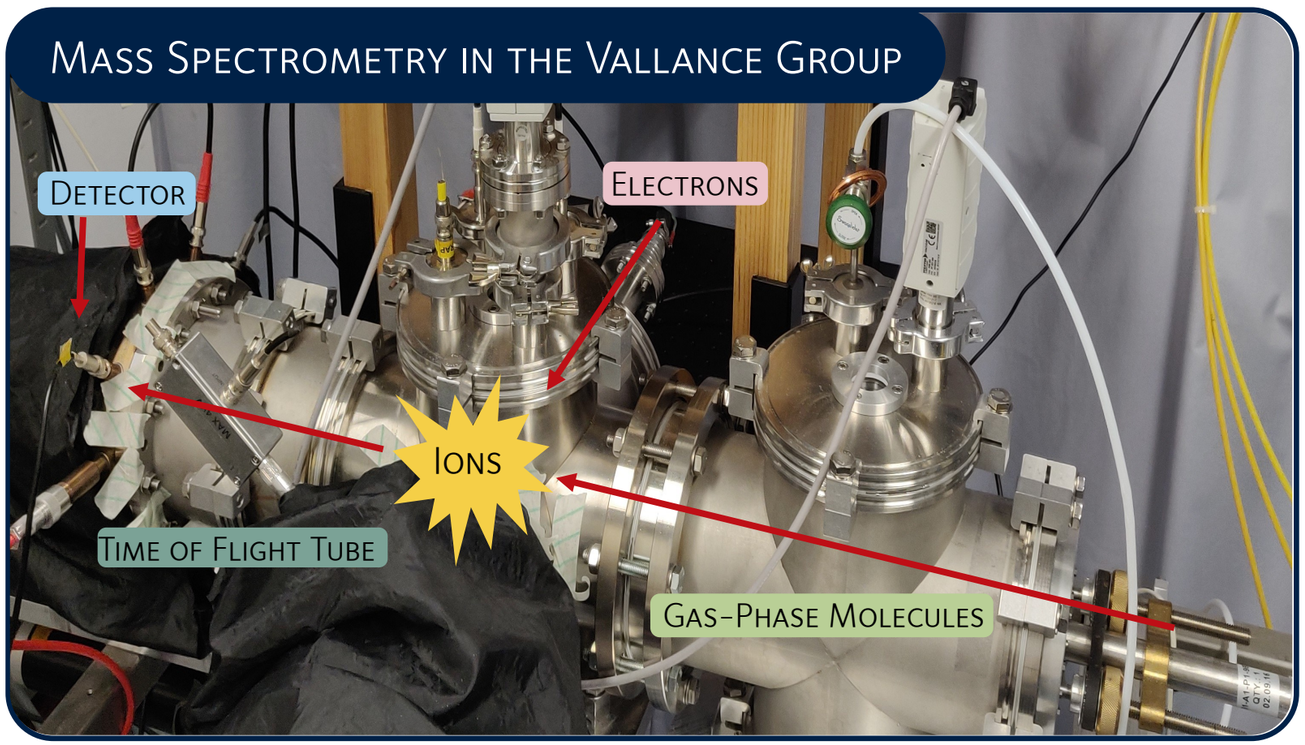
4 Time of flight can be converted into a mass-to-charge ratio, helping the ions to be identified.

$$KE = \frac{1}{2}mv^2 = \frac{1}{2}m\left(\frac{d}{t}\right)^2 \qquad qV = \frac{1}{2}m\left(\frac{d}{t}\right)^2 \qquad t = \sqrt{\frac{md^2}{2qV}} = \sqrt{\frac{m}{q}}\sqrt{\frac{d^2}{2V}}$$

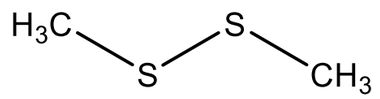
This will be a known value for an experiment, so m/q can be calculated.

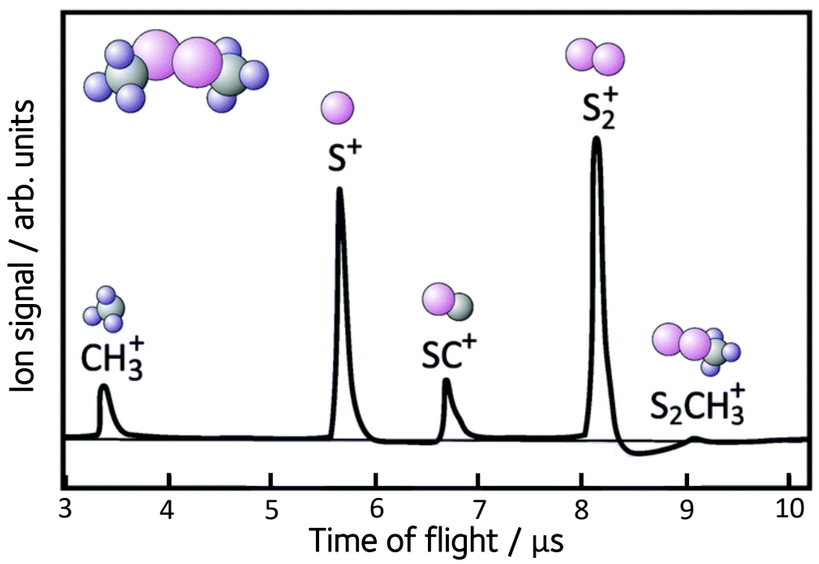
5 The ions are often unstable and will break apart. This can help identify the structure of the starting molecule, different chemicals will form different fragments, or different amounts of each fragment.

Mass Spectrometry in the Vallance Group



Time of Flight Spectrum





Time of flight spectrum for photodissociation of dimethyl disulfide.

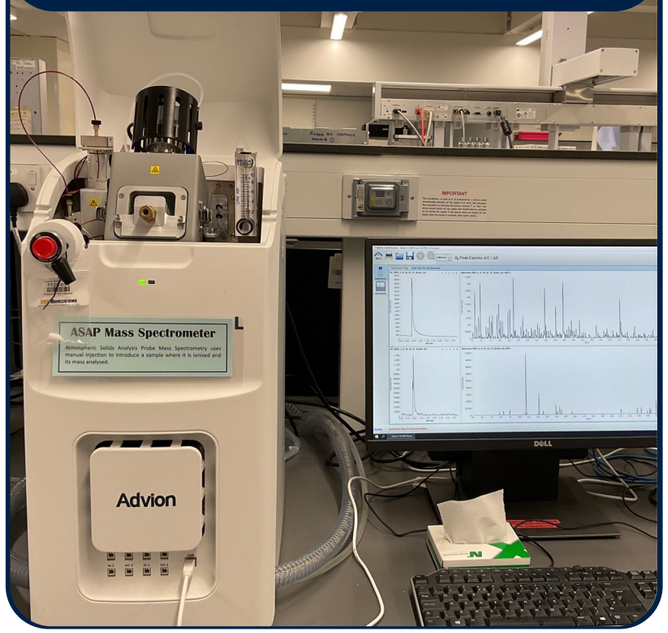
Taken from Vallance C. *Chem. Commun.*, 2019, **55**, 6336-6352

Department of Chemistry

Mass Spectrometry: An Analytical Heavyweight

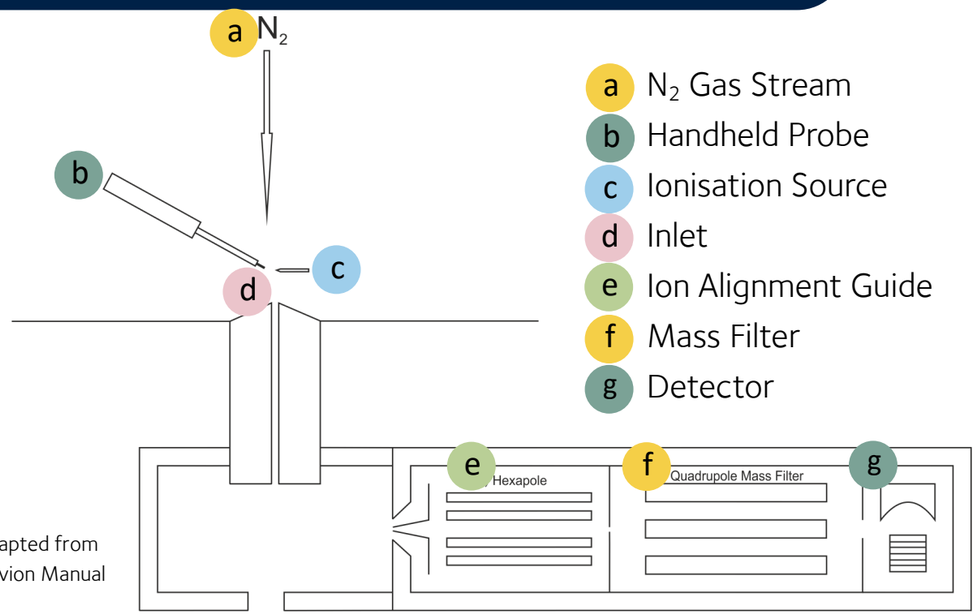
University of Oxford

ASAP Mass Spectrometry



Inside

ASAP—Atmospheric Pressure Solid Analysis Probe



a N_2 Gas Stream
b Handheld Probe
c Ionisation Source
d Inlet
e Ion Alignment Guide
f Mass Filter
g Detector

Adapted from Advion Manual

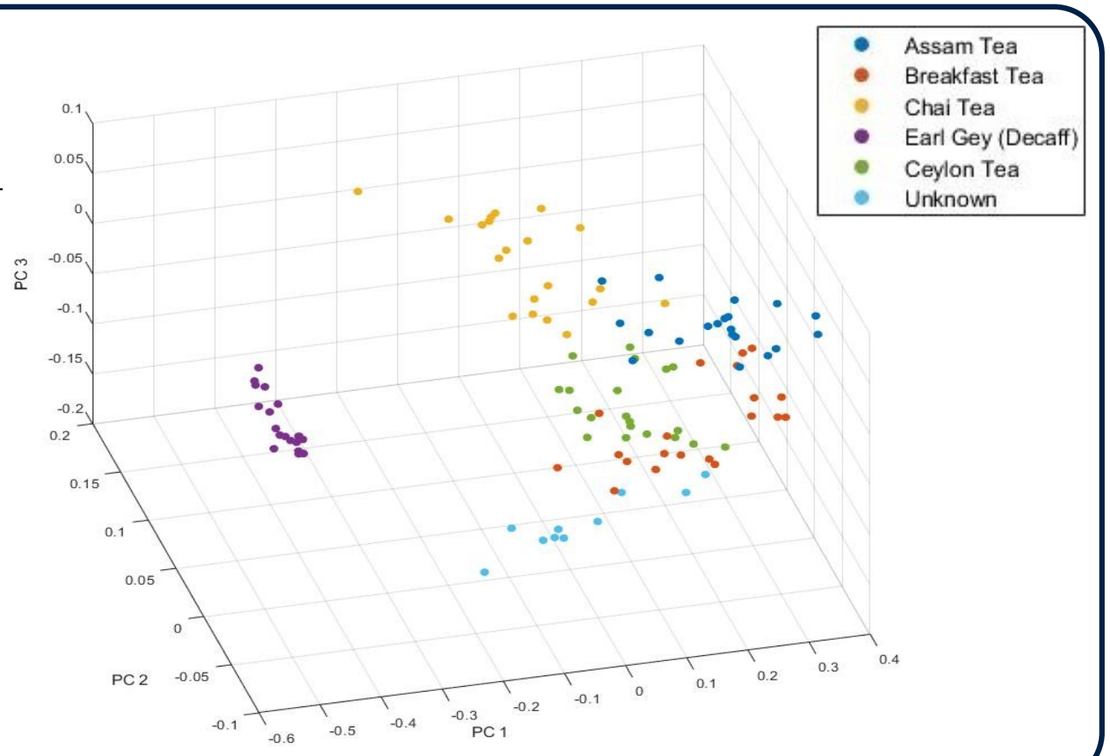
Unlike Time of Flight Mass Spectrometry, the ASAP uses a different method to identify the mass to charge ratio (m/z) of ions. ASAP uses a mass filter to only allows ions of a specific m/z to hit the detector at a given time. The spectrometer is able to scan through all m/z ratios in a 0.5 second time period. This gives us a spectra of number of ions recorded against m/z.

Machine Learning

Combining Machine Learning with Mass Spectrometry allows for the identification of unknown compounds. Once optimised on training data, an algorithm can correctly categorise the spectra of an unknown sample. The Vallance group have demonstrated this by correctly predicting the identity of an unknown tea leaf sample using a number of different machine learning algorithms.

In the graph on the right, we can see how an unsupervised machine learning algorithm (Principal Component Analysis) separates different tea samples into clusters according to their type. This leads to the algorithm identifying the unknown sample as Breakfast Tea.

The group aims to apply this concept to medical applications. For example, to correlate spectra of STEMI (a type of heart attack) patients' blood plasma to various clinical parameters.



Department of Chemistry

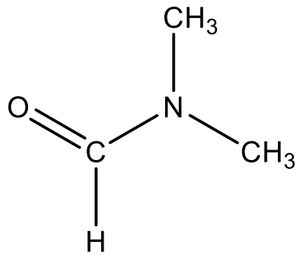
Mass Spectrometry: An Analytical Heavyweight

University of Oxford

Universal Applications

In the Vallance group, research is focused on what happens to molecules when they collide with electrons or with photons from a laser. This mimics the radiation molecules are exposed to in space and the Earth's upper atmosphere, to help develop more accurate models.

Other research in the Vallance group focuses on small biological molecules. When you are exposed to harmful radiation, molecules on the surface of your skin absorb incoming radiation, and these molecules often release low-energy electrons. By studying the interaction between low-energy electrons and small biological molecules such as DNA building blocks or simple peptide bonds, we can better understand radiation damage to the body in order to track, treat and prevent it.



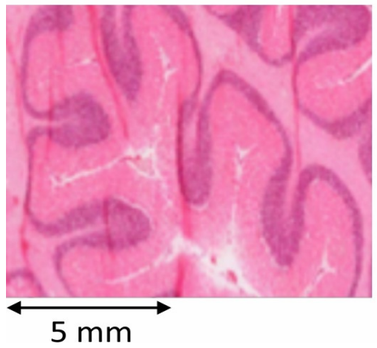
N,N-dimethylformamide, a simple peptide-bond-containing molecule used to model proteins.

Medical Marvels

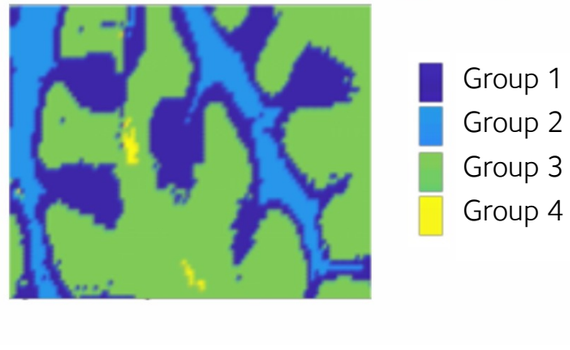
Mass spectrometry isn't only useful for very small molecules. Medium sized biological molecules like metabolites and blood plasma samples often have a signature fragmentation pattern. In the Vallance group, work is being done to use mass spectrometry to differentiate healthy tissue from tumour tissue, eventually allowing doctors to identify where to operate in real-time during surgery.

Comparison of tissue samples categorised by visual inspection and mass spectrometry.

Taken from vallance.chem.ox.ac.uk



Stained sample of human brain tissue microscope slide)

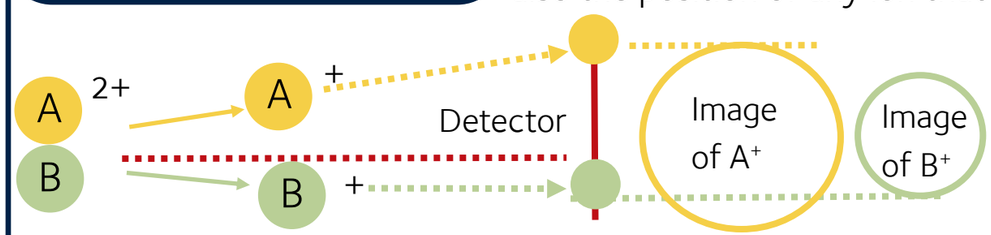


Pixels grouped by similar mass spectra from a hierarchical clustering analysis

Although the human eye is unable to spot differences, machine learning algorithms can be trained to differentiate increasingly complex spectra. Combining mass spectrometry with machine learning can result in a powerful tool we can use to improve patient outcomes in a wide range medical conditions.

Velocity-Map Imaging

The circular detector used in the Vallance group records the time of flight and also the position of any ion that hits it. When ion AB^{2+} fragments, there is an additional momentum 'kick' from kinetic energy released in the dissociation. If the experiment is run with certain voltages on the electrodes that accelerate the ions, the position the ion hits the detector relates to any velocity gained from a fragmentation. This is called velocity-map imaging (VMI). If A^+ is lighter than B^+, it receives a larger velocity 'kick' (due to conservation of momentum). Therefore, it hits the detector further away from the centre.



The image is a ring because AB^{2+} can fragment in any orientation. The kinetic energy release of the fragmentation is calculated from the velocity map image and can be used to understand the mechanism of the fragmentation.

The Vallance Group Jan 2022

University of Oxford
UKRI Engineering and Physical Sciences Research Council
wellcome

References: "Home page - Claire Vallance" (ox.ac.uk)

Vallance C. ***Chem. Commun.***, 2019,**55**, 6336-6352