

MASS SPECTROMETER

[0001] The present invention relates to an isotope ratio mass spectrometer and a method of isotope ratio mass spectrometry.

[0002] It is known to measure the relative abundances of specific isotopes of an element using a mass spectrometer. This field of measurement is commonly referred to as Isotope Ratio Mass Spectrometry ("IRMS").

[0003] The measurement of the isotopes of carbon which comprise an organic material may be carried out by initially combusting the organic material in a combustion chamber having an atmosphere of oxygen. This process yields carbon dioxide, water and oxides of any other elements in the organic substance. The combustion chamber may comprise a catalyst, for example copper oxide, which may be heated, for example, to approximately 900° C. The carbon dioxide is then separated from the other products of oxidation by, for example, a process of cryogenic trapping. The carbon dioxide is then passed to an isotope ratio mass spectrometer for measurement of the relative abundance of its isotopes.

[0004] A known isotope ratio mass spectrometer comprises an Electron Impact ion source, a magnetic sector mass analyser and three Faraday ion detectors. One of the ion detectors is arranged to detect ions having a mass to charge ratio of 44, another ion detector is arranged to detect ions having a mass to charge value of 45 and a further ion detector is arranged to detect ions having a mass to charge value of 46. Measurements of the relative ion signals for these three mass to charge values allows the carbon isotope ratio $^{13}\text{C}/^{14}\text{C}$ and the oxygen isotope ratio $^{18}\text{O}/^{16}\text{O}$ to be determined. Alternatively, if the sample is known to contain the radioactive isotope of carbon (^{14}C) and the oxygen isotope ratio is known, then the carbon isotope ratio $^{14}\text{C}/^{12}\text{C}$ may be determined.

[0005] It is also known to use a quadrupole mass filter instead of a magnetic sector mass analyser. The quadrupole mass filter may be arranged to be switched to transmit, in sequence, ions having mass to charge values of 44, 45 and 46 onto a single ion detector.

[0006] An alternative known arrangement which is suitable for measuring the isotopes of carbon comprises an Accelerator Mass Spectrometer ("AMS"). Accelerator Mass Spectrometers are, however, relatively large and expensive.

[0007] It is known to separate the components of a mixture by gas chromatography prior to combustion to carbon dioxide. However, many substances are not easily separated by gas chromatography. Substances that cannot be separated by gas chromatography include polar molecules and thermally labile molecules. These classes of substances include a large proportion of biological molecules which are potentially of interest. This class of substances also includes the metabolite products of endogenous and xenobiotic compounds.

[0008] It is known to attempt to measure the isotopes of carbon within organic materials or analytes which have been separated by reverse phase liquid chromatography. However, this is particularly problematic due to the fact that the solvent used in reverse phase liquid chromatography is usually a variable mixture of water and an organic solvent such as methanol or acetonitrile. Accordingly, the solvent will comprise varying amounts of organic materials containing the elements carbon and hydrogen (and possibly also oxygen, nitrogen and sulphur). These will be present at concentrations which are several orders of magnitude greater than the con-

centration of the analyte which is desired to be measured. As a result, any attempted measurement of the isotope ratios of carbon in the analyte will be severely distorted or masked by the significantly greater abundance of carbon from the solvent.

[0009] It is known to attempt to collect fractions from a High Pressure Liquid Chromatography ("HPLC") liquid eluent. The solvent present in the fractions is then allowed to evaporate. The remaining analyte material is then combusted with oxygen to yield carbon dioxide and other oxides. However, this approach requires a relatively large number of fractions to be collected and analysed since the exact elution time of any particular analyte of interest cannot be reliably predicted. If it is not known in advance what analytes may be present in a sample and which of these analytes may need to be analysed, then a very large number of fractions may potentially need to be obtained and subsequently analysed. This approach can therefore be significantly time consuming and expensive. Furthermore, an analyte eluting may end up being split between two or more fractions and/or a fraction may contain two or more analytes. If the analyte is split between two or more fractions then the precision of isotope ratio measurement may be reduced. If a fraction contains two or more analytes then the isotope ratio may be distorted due to the presence of another component with a different isotope ratio.

[0010] At present, a practical way of interfacing a High Pressure Liquid Chromatography ("HPLC") system to a combustion region arranged upstream of an isotopic ratio mass spectrometer such that all solvents (and in particular all organic solvents) are successfully removed prior to the combustion products being passed to the isotopic ratio mass spectrometer is not known. Furthermore, an interface which allows the measurement of isotope ratios in real time is also not known. Similarly, an interface which allows the isotope ratio for carbon and other elements to be measured for each component as it elutes from an HPLC column whilst retaining chromatography resolution is also not known.

[0011] Attempts have been made to directly interface an HPLC system to an isotope ratio mass spectrometer but these have historically been restricted to HPLC separations involving aqueous solutions only. This has, however, severely restricted the range of analyte materials, and their complexity, which can be analysed.

[0012] A mechanical arrangement which attempts to directly interface an HPLC system to an Isotope Ratio Mass Spectrometer is known. In this arrangement the liquid eluent from the HPLC system is deposited on to a continuously moving wire loop. The liquid droplets attach to the wire by surface tension. The wire is then heated by passing electrical current through it thereby promoting evaporation of the solvent. The wire with desolvated analyte material is then passed directly into the combustion region. The analyte is combusted in the combustion region in an atmosphere of oxygen thereby forming carbon dioxide and other oxides. The carbon dioxide isotope ratios can then be measured.

[0013] The known arrangement is, however, particularly problematic to regulate. Reverse phase liquid chromatography typically involves using two or more solvents in ratios that vary during the course of a liquid chromatography run. Accordingly, during the liquid chromatography run the solvent composition will change and as a result the solvent surface tension and volatility will also change. The optimum liquid flow rate will therefore also change. A yet further