FIG. **8**A is FIG. **3** of the Ognibene et al Manuscript showing the results of 10-second measurements of a graphitic sample of ANU sucrose while varying the stripper pressure FIG. **8**B shows a section of the graph of FIG. **8**A in greater detail.

FIG. **9** is FIG. **4** of the Ognibene et al Manuscript showing plotted results.

FIGS. **10**A, **10**B, **10**C, **10**D and **10**E correspond to.

FIGS. **11**A and **11**B are FIGS. **2***a* and **2***b* of the Salazar Manuscript showing calculated CO2 concentration profiles.

FIGS. **12**A and **12**B are FIGS. **3***a* and **3***b* of the Salazar et al. Manuscript showing a representative example of the beam current of $_{12}C_-$ ionized from CO_2 pulses.

FIGS. **13**A, **13**B, **13**C, and **13**D are Figures from FIG. **4** of the Salazar et al. Manuscript) showing the ionization efficiency.

DETAILED DESCRIPTION OF SPECIFIC EMBODIMENTS

Referring to the drawings, to the following detailed description, and to incorporated materials, detailed information about the invention is provided including the description of specific embodiments. The detailed description serves to explain the principles of the invention. The invention is susceptible to modifications and alternative forms. The invention is not limited to the particular forms disclosed. The invention covers all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the claims.

AMS is a type of isotope-ratio mass spectrometer (IRMS). The accuracy and precision of an AMS ratio determination is well documented, since AMS is routinely used in the much more stringent application of isotope chronometry (i.e., ^{14}C–dating). Isotope ratio MS quantitation requires that all related processes be free of isotope effects, that is, minimal or constant isotopic fractionation. Analytical separation processes fractionate, both isotopically and (by definition) chemically. Isotope fractionation in chemical definition of the sample is negligible for most "bulk" processes, but must be assessed as AMS is mated to micro-bore and other velocity-dependent separation techniques. Applicants define AMS process fractionation as that occurring after a particular point of chemical speciation and homogenization. Historically, this point has been the total oxidation or combustion of a carbon sample to CO_2. This process guarantees full equivalence and equilibrium between sample, tracer compound, and any added carrier compounds. Accurate analyses with AMS also depend on careful sample "accounting": homogenization, control of any volatile components, and quantitation of amounts of carrier compounds. All three of these time consuming efforts will be eliminated by more sophisticated sample definition and improved sample spectrometer interface development. Quantitative conversion of the separated analyte to this gas is the heart of our approach.

Current cesium-sputter ion sources used for AMS are relatively efficient (1-10%) but create negative elemental ions in a low-energy environment in which the acquisition of an electron is a velocity dependent function. This type of ion source does fractionate, but the effect is controlled if all samples and standards are introduced into the ion source as a common physical/chemical form. This fractionation problem has been solved for ^{14}CAMS through quantitative conversion of carbon in a sample to CO_2 by total combustion and subsequent reduction of the CO_2 to graphite.

In Applicants Center for Accelerator Mass Spectrometry's (CAMS) ion source, graphite samples produce intense negative ion beams (>150 pA of C). Graphite has no "vapor pressure" which makes sample handling easier, and controls contamination in the case of "hot" samples (>10 fmol ^{14}C/mg C). One of the main features of the Cs-sputter ion source is the low memory effect between samples. Because of its high ionization efficiency and large ion currents, counting times can be minimized, while maintaining high precision and accuracy. Finally, graphite allows for remote sample production with the measurement conducted at a regional spectrometer.

The conversion of carbonaceous samples to graphite has been extremely successful for the vast majority of AMS applications. However, significant human handling is required and the whole process suffers from low sample throughput (–150 samples processed/day), long turnaround times (–2 days minimum), and sample size limitations (>250 ugs carbon are needed). The addition of carrier carbon can also limit sensitivity to –2 amol ^{4}C/mg C. Another consideration is the total cost of analysis, especially for quantitation of biochemicals separated by High performance Liquid chromatography (HPLC) or other types of liquid chromatography (LC) such as size exclusion or ion exchange. Applicants typically collect 30 second-wide LC fractions and treat each as an individual sample for analysis. These fractions represent a tradeoff between the cost of the analysis (based on the total number of samples) and the chromatographic resolution. At –$150/sample, one 30 minute LC trace costs $9000; which increases if higher resolution is required. In some instances, the number of samples from an LC trace can be reduced by collecting only fractions containing the peaks of interest. However, this is not always a viable option, especially in studies, where entire metabolite profiles are required.

The online conversion of a sample to CO_2 gas fed directly into an ion source for trace isotope analysis overcomes this bottleneck. Applicants have developed an online combustion interface can be used for the analysis of discrete small samples. This will improve throughput, reduce costs by decreasing human involvement in sample preparation, as well as by reducing accelerator analysis time, while potentially increasing the sensitivity of ^{14}C. An integrated liquid sample-AMS system will allow many studies to be addressed more rapidly and with smaller samples. CO_2 gas ion sources offer several advantages over solid sample ion sources. They make more efficient use of the sample; hence much smaller sized samples may be analyzed. Less sample handling is required, increasing throughput, while reducing turn-around leading to reduced background contamination. Finally, they are amenable to the measurement of the continuous output of a gas stream, giving higher time resolution for flow separations. In addition, the direct coupling of a gas-accepting source to separatory instrumentation (e.g., HPLC) can, in principle, be achieved using an online combustion interface producing a direct CO_2 feed into the ion source.

Despite these advantages, the direct analysis of $^{14}CO_2$ has not gained widespread acceptance in the AMS research community. Mainly because gas sources generally have lower ion output than solid sources leading to a decrease in sample measurement throughput for certain samples. Also, the background level increases with time if high isotope concentrations are introduced without efforts to reduce this contamination of the ion source. Thus, few gas-ion sources find routine use on spectrometers that require the highest precision and accuracy. With the advent of smaller, less expensive spectrometers, some operating on potentials as low as 200 kV, the role of a gas-fed ion source can be revisited to obtain more efficient use of sample material. A Modern (10^{-12} ^{14}C/C) sample containing 500 pg of carbon, our preferred sample