

Measuring the Relative Abundance of Low-Level Isotopes With Laser Desorption Time-of-Flight Mass Spectrometry

P. Jane Gale, Kevin Hayden, and Marvin L. Vestal

Virgin Instruments, Sudbury, MA

Introduction

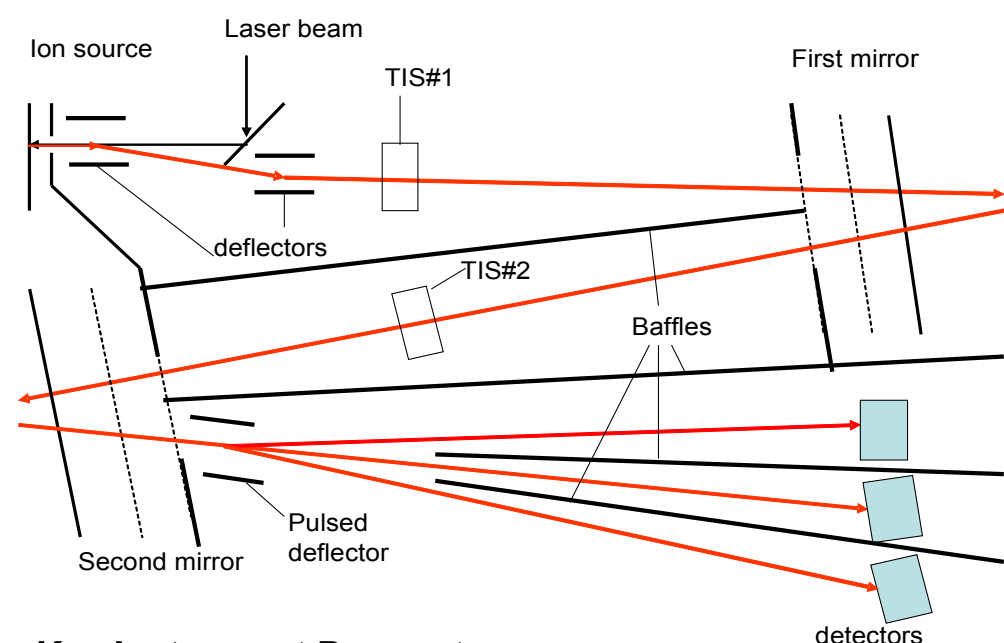
We are developing¹ a multi-stage time-of-flight mass spectrometer (TOFMS) that uses laser desorption from solids to obtain accurate relative isotopic abundances at very low levels. A potential analytical target is ¹⁴C in radiocarbon dating and biological tracer studies. Another important possible target is the ⁴¹Ca isotope in studies of human bone production and loss. Given its very long half-life (>10⁵ yr), radioactive ⁴¹Ca is safe to administer to humans and can serve as a sensitive tracer if measurements of 10⁻¹⁰ to 10⁻¹⁵ relative abundance can be achieved.

Although accelerator mass spectrometry (AMS) has demonstrated the utility of such measurements for both ¹⁴C and ⁴¹Ca, proliferation of applications has been limited by the relatively high cost and inaccessibility of the complex AMS instruments. We report here preliminary studies demonstrating feasibility for use of laser desorption TOFMS instruments for such applications. The much lower cost of these instruments compared to ASM makes them an attractive alternative for use in clinical settings.

Performance Challenge

Very high abundance sensitivity required. Must detect an ion in the presence of a huge excess of another.

Instrument Design: Three-Stage TOF for determination of isotope ratios



Key Instrument Parameters

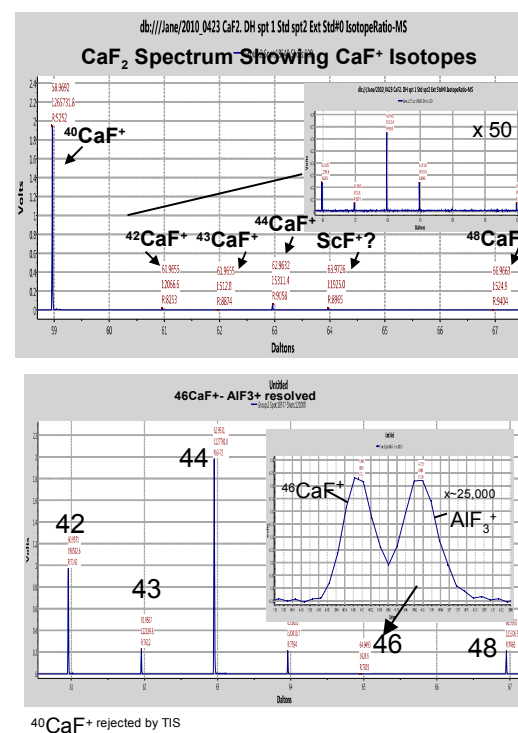
2-field source 3 mm each; flight path ~3.5 m
 Deflection angle: 1.5°; Detectors 1&3 off-center by ±2.25°
 Acc Volt: 8kV
 Laser: Explorer 5kHz, ~100 μJ/pulse;
 Pulse width 5 nsec; spot size ~30 μm

The instrument design includes a two-field source with a set of ion deflectors allowing on-axis laser irradiation and trajectory compensation required for the large final deflection angle. It also includes two Bradbury Nielson mass gates, the 1st located at the source focus and the 2nd located at the focal point of the first of two 2-field ion mirrors. The 1st gate rejects all but the narrow range of ions of interest for the isotope measurement, while the 2nd gate selects individual ions that are then focused to one of three ion detectors with the second ion mirror. A pair of pulsed ion deflectors located at the exit of the second ion mirror gates selected ions to one of the three detectors.

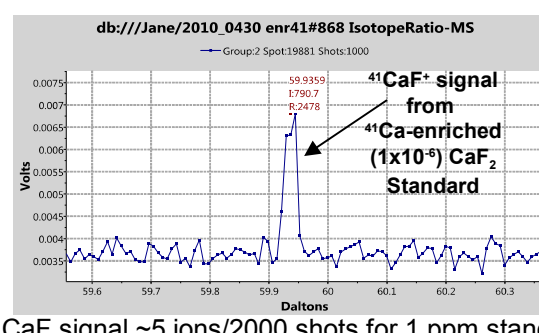
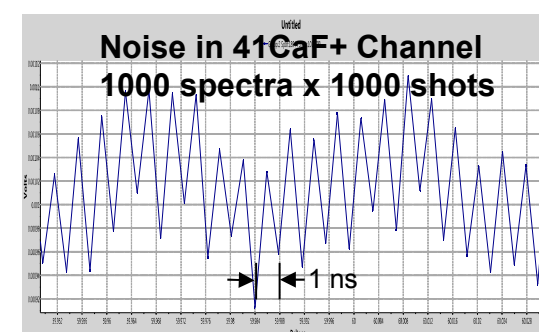
The ion detector system consists of one faraday cup and 2 ETP MagneTOF electron multipliers all connected to an Acqiris AP240 2channel 2 GHz averager. ETP detectors are rotated relative to the final gated deflection angle for trajectory error compensation. The instrument is designed for bipolar operation. Timing of ion source mass gates and pulsed detectors and averager are synchronized to the 5 kHz laser and controlled by a computer –controlled multichannel generator with 1 nsec precision and accuracy.

Results of Preliminary Studies

CaF⁺ or CaF₃⁻ ions are produced by laser bombardment of CaF₂ standards (~10 mg) deposited in wells on gold-coated plates and covered with a thin layer of paraffin. Detector gains are set for the ion intensity anticipated, based on relative abundances.



Mass	Mass	% Rel Abun
40CaF ⁺	58.960	96.9
41CaF ⁺	59.959	
42CaF ⁺	60.956	0.647
43CaF ⁺	61.954	0.135
44CaF ⁺	62.953	2.086
46CaF ⁺	64.951	0.004
48CaF ⁺	66.950	0.187



Potential Interferences with ⁴¹ CaF ⁺ & ⁴⁶ CaF ⁺		
Ion	Mass (da)	RP Req'd
⁴¹ CaF ⁺	59.96013	ref
⁴¹ KF ⁺	59.95968	133,000*
⁶⁰ Ni ⁺	59.93023	2,005
C ₂ O ₂ H ₄ ⁺	60.02058	992
⁵⁹ CoH ⁺	59.94047	3,050
Na ³⁷ Cl ⁺	59.95512	11,973*
⁵⁸ FeH ₂ ⁺	59.94838	5,100
³² SC ₂ H ₄ ⁺	60.00282	1,405
³¹ PC ₂ H ₅ ⁺	60.01234	1,148
²⁸ SiO ₂ ⁺	59.96621	9,865
⁴⁶ CaF ⁺	64.95210	ref
AIF ₄ ⁺	64.97834	2475

Resolving power of ~5000 is sufficient to eliminate most anticipated interferences

Potential Interferences with ⁴¹ CaF ₃ ⁻ & ⁴⁶ CaF ₃ ⁻		
Ion	Mass (da)	RP Req'd
⁴¹ CaF ₃ ⁻	98.967	ref
C ₂ H ₄ NO ₂ ⁻	98.025	1470
⁹⁸ Ru ⁻	97.906	1876
⁹⁸ Mo ⁻	97.906	1880
⁴⁶ CaF ₃ ⁻	102.949	ref
¹⁰³ Rh ⁻	102.906	2370
AIF ₄ ⁻	102.975	4030

*not expected to be stable under laser desorption conditions

Overall efficiency and speed of analysis – key factors are ions per sample molecule desorbed and ions produced per laser pulse
Precision and accuracy of the ratio measurements – ion statistics dictate that for an average signal/shot of 100 summed over 10,000 yields ~0.1% precision. This has been demonstrated for ⁴⁶Ca at the natural abundance (40 ppm). Precision of 3.2% for ⁴¹Ca at part per trillion abundance requires detection of 1000 ions from ⁴¹Ca; this corresponds to production of 10¹⁵ ions from ⁴⁰Ca in 10⁶ laser shots.

Present Status:

Resolving power sufficient to remove potential interferences; 10¹² abundance sensitivity appears feasible; **But** we need to increase ionization rate by ca. 10³ for practical applications.

Next Steps

- Explore alternative ion production techniques to enhance sensitivity
- Investigate sample preparation procedures appropriate to the clinical settings in which the instrument will operate
- Add TDC for measuring low level signal by ion counting

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