Contract No:

This document was prepared in conjunction with work accomplished under Contract No. 89303321CEM000080 with the U.S. Department of Energy (DOE) Office of Environmental Management (EM).

Disclaimer:

Summary Statement

Matrix-Assisted Ionization is a new and highly promising mass spectrometry technique for rapid analysis of uranium; however, the chemistry and physics underlying this ionization mechanism are largely unknown. This effort seeks to understand the fundamental ionization phenomena by characterizing both ionization matrix materials themselves and analyte chemistry ionization trends.

Introduction

Ambient mass spectrometry is a collection of methods for the rapid detection and characterization of trace inorganic analytes with minimal sample preparation. Matrix-Assisted Ionization (MAI) is one of the most recently discovered ambient mass spectrometry techniques, wherein ions are produces without the application of heat, photons, electrons, or high voltage as required for conventional mass spectrometry (***Figure 1***).[1, 2] Although SRNL was the first to demonstrate that this technique could be used to ionize inorganic compounds in aqueous solutions,[3] the underlying ionization phenomena remains uncharacterized.[1, 4-10] This effort seeks to examine fundamental aspects of MAI via a combination of mass spectrometry experiments, x-ray diffraction of MAI matrix chemicals, and modeling/simulation. This research will shed light on this fascinating ionization phenomena and could lead to sensitivity and accuracy gains to inform future development of fieldable mass spectrometry methods.

The first year of the project encompassed 1) instrument familiarization and parameter optimization for inorganic analytes, 2) mass spectrometry studies to investigate the origin of previously identified matrix derived ions, and 3) procurement and light microscopy of various MAI matrix compounds. The second year of the project focused on understanding the effect of periodic table trends on ionization through mass spectrometry comparison studies of the lanthanides. MAI matrix chemicals were screened for their ability to ionize cerium to determine matrix impact on ion production. The impact of matrix crystal size on ion abundance was also investigated. Lastly, the crystal structure of one MAI matrix was solved and modeling/simulation was undertaken to identify intermolecular interactions.

Approach

The objective of this project was to investigate the MAI inorganic ionization mechanism through systematic experimentation and to develop a testable theory for the inorganic ionization process. A key part of developing an ionization theory is to develop and understand the factors of an MAI formalization equation as shown in ***Equation 1***. The main investigative avenues of this project are to characterize the influence of matrix and analyte properties on MAI ionization. Initial instrument optimization was performed to determine the parameters and sample introduction methods that resulted in high reproducibility and ion sensitivity. Additionally, an RStudio data processing suite was developed to standardize and expedite data analysis.

To investigate the matrix factor, the chemical matrix 3-nitrobenzonitrile (3-NBN) was studied as a model matrix. This chemical was examined via mass spectrometry analysis using three ionization methods (***Figure 2***) and collision induced dissociation (CID) to determine the origin of matrix-derived ions. Single-crystal X-ray diffraction (SC-XRD) was performed to determine crystal structure (***Figure 3***) and subsequent modeling/simulation was done to determine intermolecular contacts. Mass spectrometry experiments were also conducted to 1) investigate the impact of matrix crystal size on ion production and 2) examine other MAI matrix chemicals for cerium ionization (***Table 1***). To investigate the analyte factor, the lanthanide series of elements were selected for spectrometric analysis due to their well characterized physical and chemical trends. Comparative MAI and electrospray ionization (ESI) analysis was performed on solutions of single element lanthanide nitrates to determine if similarities exist between the two ionization methods.

Accomplishments

- Demonstrated that 3-NBN matrix-derived ions are formed within the first few centimeters of the instrument and are created from the MAI process.
- Resolved the crystal structure of 3-NBN using SC-XRD, a previously unknown structure.
- Discovered that two matrix-derived ions are detected in ion complexes with lanthanides using MAI. There is no evidence that these complexes form in solution.
- Demonstrated that various MAI matrix chemicals ionize cerium in both positive and negative ion modes.
- Analyzed and detected a selection of transition metals using MAI in negative ion mode (copper, cobalt, nickel, palladium, scandium, yttrium, zinc, and zirconium).
- Determined that MAI ion abundance of the lanthanides correlates with various chemical properties in a similar manner to complimentary ESI studies. (***Table 2***).
- Produced convincing evidence that inorganic ion formation using MAI is driven by a different mechanism than in ESI ion formation.
- Demonstrated that inorganic ion abundance appears inversely related to matrix crystal size suggesting a matrix crystal surface area impact (***Figure 4***).

Peer-reviewed Publications

There are three draft publications in preparation that encompass this effort:

1. Understanding Matrix-Assisted Ionization Through an Investigation of the Lanthanides. Submitting to *Journal of the Analytical Chemical Society,* 2022*.*
2. Uranium Isotopic Analysis with Matrix-Assisted Ionization. Submitting to *Analytical Chemistry,* 2022.
3. Characterization of 3-Nitrobenzonitrile as a Model Matrix-Assisted Ionization Matrix. Submitting to *Chemistry of Materials*, 2022.

Conference Presentations

- Matrix-Assisted Ionization Mass Spectrometry for the Detection and Characterization of Uranium Species. The Great Scientific Exchange (SciX) 2021 Conference, Providence, RI September 26-October 1, 2021. Invited Oral Presentation.
- Matrix-Assisted Ionization and Quantitative Analysis of Uranium Isotopic Composition and Assay by AccuTOF Time-of-Flight Mass Spectrometry. 69th American Society for Mass Spectrometry (ASMS) Conference on Mass Spectrometry and Allied Topics, Philadelphia, PA October 31-November 4, 2021. Oral Presentation.
- Matrix-Assisted Ionization Mass Spectrometry for Uranium Measurement in Field Environments. 12th International Conference on Methods and Applications of Radioanalytical Chemistry (MARC), Khona, HI April 3-8, 2022. Oral Presentation.
- Matrix-Assisted Ionization Time-of-Flight Mass Spectrometry of Lanthanides. 70th American Society for Mass Spectrometry (ASMS) Conference on Mass Spectrometry and Allied Topics, Minneapolis, MN June 5-9, 2022. Poster Presentation.

Funding Agency Presentations

- Matrix-Assisted Ionization Mass Spectrometry for the Detection and Characterization of Uranium Species. NA-22 Brown Bag Seminar, Virtual Presentation, November 16, 2021. Invited Oral Presentation.
- Matrix-Assisted Ionization Mass Spectrometry for the Detection and Characterization of Uranium in Austere Environments. NA-24 Research Seminar, Virtual Presentation, June 22, 2022. Invited Oral Presentation.

Intellectual Property
There is no intellectual property to report for this effort.

Total Number of Post-Doctoral Researchers
Abigail (Abby) Waldron, SRNL (FY22)
Elizabeth (Betsey) Pettit, SRNL (FY21)

Total Number of Student Researchers
None in FY22.

Figures

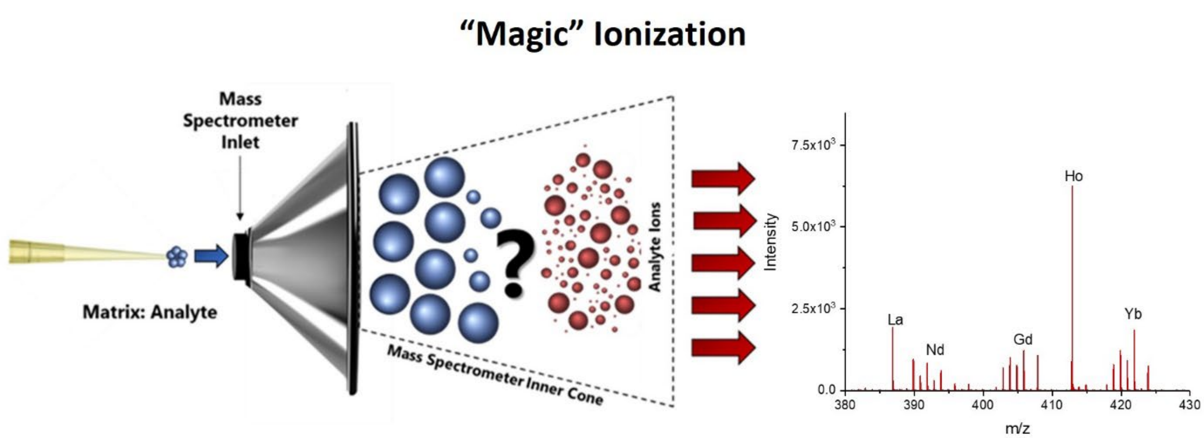


Figure 1. Schematic of matrix-assisted ionization (i.e., magic ionization) showing how introducing a matrix-analyte mixture into the mass spectrometer orifice results in analyte ion production.

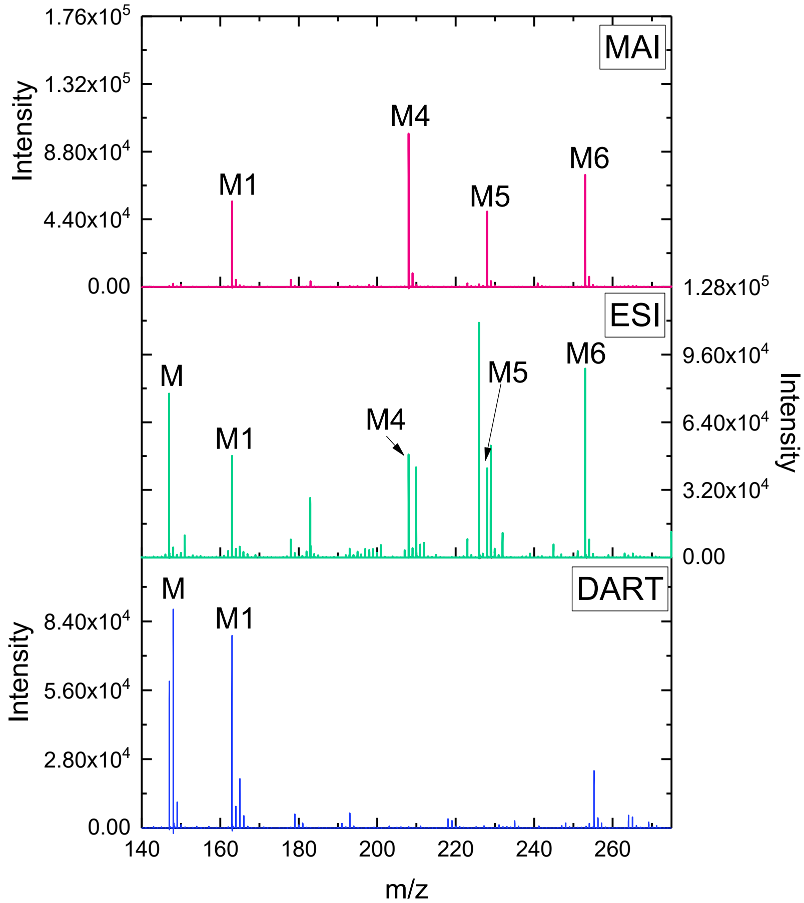


Figure 2. Mass spectra generated from 3-NBN using three mass spectrometry methods: (top) matrix-assisted ionization, (middle) electrospray ionization, and (bottom) direct analysis in real time.

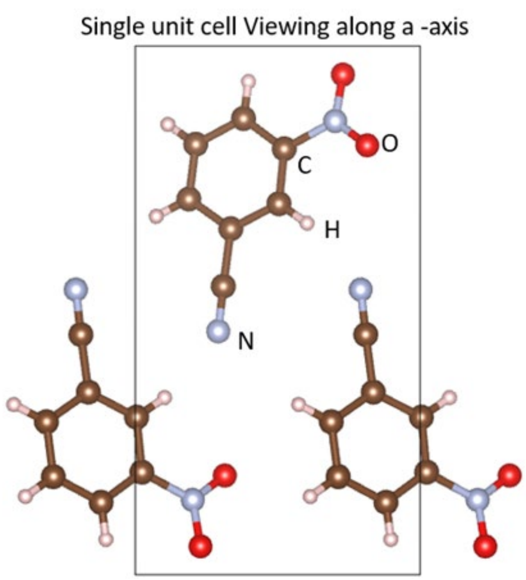
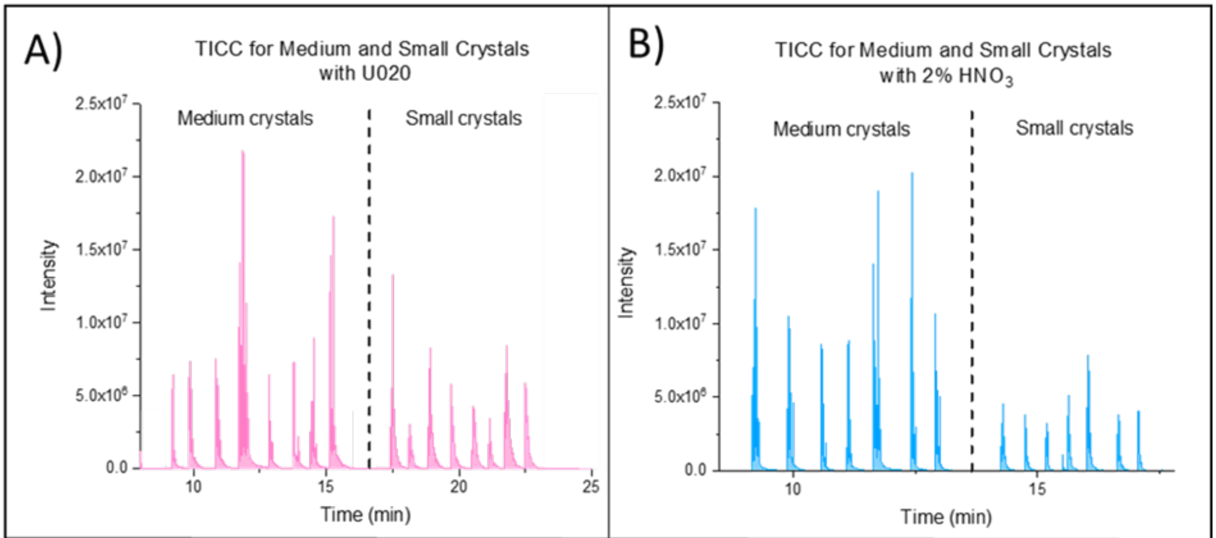
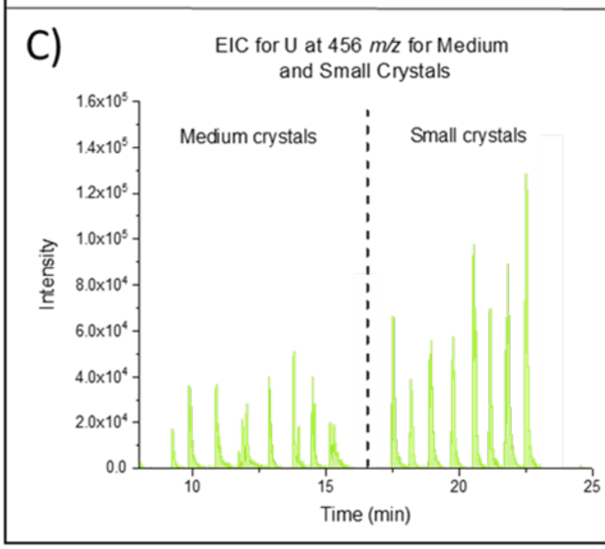


Figure 3. Single unit cell of the 3-NBN crystal structure based on SC-XRD crystallographic data.





D)

Small vs. Medium Crystal Peak Area for Analysis	Single Factor ANOVA p-value
U020 456 *m/z* EIC	0.000971
U020 TICC	0.695116
2% HNO_3 TICC	0.004457

Figure 4. Experimental results of the impact of crystal size on inorganic analyte ionization: A) total ion current chromatogram (TICC) produced by two crystal sizes with a uranium spike, B) TICC produced by two crystals with a 2% nitric acid spike, C) extracted ion chromatogram (EIC) of the primary uranium peak produced from analysis A, and D) single-factor ANOVA results for peak areas generated from A, B, and C to determine if the difference between crystal size populations is significant.

Table 1. Results of MAI matrix screening test to assess for cerium ionization in positive and negative ionization modes.

MAI Matrix Name	Cerium Detected (+ mode)	Cerium Detected (- mode)
1,2-Dicyanobenzene	Yes	Yes
1,2-Dinitrobenzene	No	Yes
1,4-Dihydroxy-2,6-dimethoxybenzene	No	No
2-Bromo-2-nitro-1,3-propanediol	No	No
2-Bromo-3-nitroacetophenone	No	No

2-Hydroxy-5-nitroacetophenone	Yes	No
2-Methyl-2-nitro-1,3-propanediol	No	Yes
2-methyl-5-nitrobenzonitrile	No	Yes
2-Napthol	No	Yes
2-Nitrobenzontrile	No	Yes
3,6-Dibromocarbazole	No	Yes
3-Nitrobenzoyl chloride	No	No
4-Aminophthalonitrile	No	No
4-Hydroxy-3-nitrocoumarin	No	No
4-Methyl-3-nitroaniline	No	Yes
4-methylphthalonitrile	No	No
5-Bromo-3-nitropyridine-2-carbonitrile	No	No
5-Nitroindole	Yes	Yes
9-vinylcarbazole	No	No
Coumarin	No	Yes
Methyl-2-methyl-3-nitobenzoate	Yes	No
Phthalic anhydride	Yes	No

Table 2. Results of a linear correlation analysis to examine correlations between lanthanide ionization trends and periodic table trends. ESI data shows clear correlation between lanthanide ionization and periodic table trends, but no significant correlation is observed with MAI. Legend: The numerical value is r calculated with the Person method. All data exhibits a p-value < 0.001.

Linear Correlation Analysis

Ionization Technique	Ratio of Interest	Atomic Number	(Ln–O) Dissociation Energy	Nitrate Solubility	Ionic Radius	Electro-negativity
ESI-MS	$[Ln(NO_3)_4]^-/[^{153}Eu(NO_3)_4]^-$	0.95	-0.82	-0.93	-0.94	0.94
MAI-MS	$[Ln(NO_3)_4]^-/[^{153}Eu(NO_3)_4]^-$	0.83	-0.81	-0.62	-0.84	0.80

Equation 1. Concept of the MAI formalization equation, with key investigative factors that are the focus of this work in brackets.

$$\frac{N_+}{N_0} \propto E_{MS}\ [M_F]\ DF\ [A_F]$$

E_{MS} is Mass Spectrometer Ion Transmission Efficiency
M_F is the Matrix Factor
DF is the Driving Force
A_F is the Analyte Factor

References

1. Trimpin, S.; Inutan, E. D., Matrix assisted ionization in vacuum, a sensitive and widely applicable ionization method for mass spectrometry. *Journal of The American Society for Mass Spectrometry* **2013,** *24* (5), 722-732.
2. Trimpin, S., " Magic" ionization mass spectrometry. *Journal of the American Society for Mass Spectrometry* **2016,** *27* (1), 4-21.
3. Mannion, D. R.; Mannion, J. M.; Kuhne, W. W.; Wellons, M. S., Matrix-Assisted Ionization of Molecular Uranium Species. *Journal of the American Society for Mass Spectrometry* **2020,** *32* (1), 8-13.
4. Inutan, E. D.; Trimpin, S., Matrix assisted ionization vacuum (MAIV), a new ionization method for biological materials analysis using mass spectrometry. *Molecular & Cellular Proteomics* **2013,** *12* (3), 792-796.
5. Lee, C.; Inutan, E. D.; Chen, J. L.; Mukeku, M. M.; Weidner, S. M.; Trimpin, S.; Ni, C. K., Toward understanding the ionization mechanism of matrix-assisted ionization using mass spectrometry experiment and theory. *Rapid Communications in Mass Spectrometry* **2019**.
6. Trimpin, S.; Lutomski, C. A.; El-Baba, T. J.; Woodall, D. W.; Foley, C. D.; Manly, C. D.; Wang, B.; Liu, C.-W.; Harless, B. M.; Kumar, R., Magic matrices for ionization in mass spectrometry. *International Journal of Mass Spectrometry* **2015,** *377*, 532-545.
7. Trimpin, S.; Lu, I.-C.; Rauschenbach, S.; Hoang, K.; Wang, B.; Chubatyi, N. D.; Zhang, W.-J.; Inutan, E. D.; Pophristic, M.; Sidorenko, A., Spontaneous charge separation and sublimation processes are ubiquitous in nature and in ionization processes in mass spectrometry. *Journal of The American Society for Mass Spectrometry* **2018,** *29* (2), 304-315.
8. Trimpin, S.; Lee, C.; Weidner, S. M.; El-Baba, T. J.; Lutomski, C. A.; Inutan, E. D.; Foley, C. D.; Ni, C. K.; McEwen, C. N., Unprecedented ionization processes in mass spectrometry provide missing link between ESI and MALDI. *ChemPhysChem* **2018,** *19* (5), 581-589.
9. Trimpin, S.; Inutan, E. D.; Karki, S.; Elia, E. A.; Zhang, W.-J.; Weidner, S. M.; Marshall, D. D.; Hoang, K.; Lee, C.; Davis, E. T., Fundamental studies of new ionization technologies and insights from IMS-MS. *Journal of The American Society for Mass Spectrometry* **2019,** *30* (6), 1133-1147.
10. McEwen, C. N.; Inutan, E. D.; Moreno-Pedraza, A.; Lu, I.-C.; Hoang, K.; Pophristic, M.; Trimpin, S., Sublimation driven ionization for use in mass spectrometry: mechanistic implications. *Journal of the American Society for Mass Spectrometry* **2020,** *32* (1), 114-123.

REVIEWS AND APPROVALS

1. Principal Investigator:

____

Name and Signature Date

2. Technical Review:

____

Name and Signature Date

3. PI's Manager Signature:

____

Name and Signature Date

4. PI's Division Director Signature:

____

Name and Signature Date

5. Intellectual Property Review:

This report has been reviewed by SRNL Legal Counsel for intellectual property considerations and is approved to be publicly published in its current form.

SRNL Legal Signature

____

Name and Signature Date