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## **Development of Direct Injection/Ionization Mass Spectrometry Methods for Whole Molecule Characterization**

Determining uranium isotopic and concentration information from environmental samples typically involves extensive chemical and physical processing prior to analysis. Harsh sample preparation results in the loss of the original uranium chemical speciation (i.e. what the uranium was bonded to/with when found in the environment) as well as the mixing of anthropogenic uranium with background material contained within the collection media (e.g. a swipe or soil). The objective of this work is to adapt a bioanalytical mass spectrometry technology called paper spray ionization mass spectrometry for the rapid analysis of intact uranium complexes. Soft ionization facilitates detection of whole molecule uranyl complexes including uranyl acetate, uranyl nitrate, and uranyl-tributylphosphate complex. Cotton swipe samples doped with a multi-element standard containing  $\mu\text{g}$  levels of U, Bi, Pb, Cd, Fe, and Zn were directly analyzed without purification, representing a major improvement over existing methods. Uranium quantitation is demonstrated using internal standards to obtain linear calibration curves. Limits of detection were determined to be approximately 100 ng for  $\text{UO}_2$  and uranyl acetate through measurement of ppb level solutions. The development and qualification of PSI-MS techniques could lead to significant safeguards-related cost reduction and timeliness by facilitating the triage and queueing of swipe samples for more sensitive and time-consuming analyses.

## **Awards and Recognition**

Technical aspects of the project have been accepted for presentation at the Southeastern Region American Chemical Society (SERMACS) meeting in Augusta, GA in October 2018.

## **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**

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Signature

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Date

## Development of Direct Injection/Ionization Mass Spectrometry Methods for Whole Molecule Characterization

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**Collaborators:** C. Cody (JEOL USA Inc.)

**Thrust Area:** National Security

**Project Start Date:** October 1, 2017

**Project End Date:** September 30, 2019

*Paper spray ionization mass spectrometry (PSI-MS) was utilized for rapid chemical and isotopic characterization of trace uranium samples. Soft ionization facilitates the detection of whole molecule uranyl complexes including uranyl acetate, uranyl nitrate, and uranyl-tributylphosphate complex. Cotton swipe samples doped with a multi-element standard containing  $\mu\text{g}$  levels of U, Bi, Pb, Cd, Fe, and Zn were directly analyzed without purification or concentration. All elements doped on the cotton substrate were detected and*

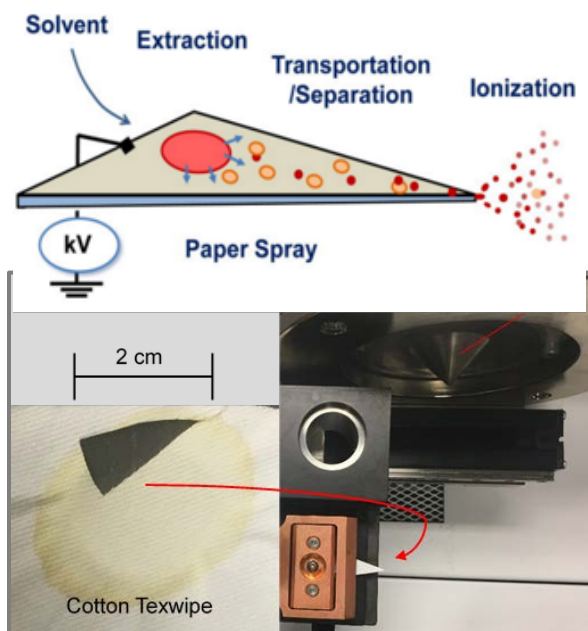
*demonstrated strong signal to noise from collection periods of approximately 1 min. Uranium quantitation is demonstrated through the use of internal standards to obtain linear calibration curves. Limits of detection were determined to be approximately 100 ng for  $\text{UO}_2$  and uranyl acetate through measurement of ppb level solutions. The development and qualification of PSI-MS techniques could lead to significant safeguards-related cost reduction and timeliness by facilitating the triage and queueing of swipe samples for more sensitive and time-consuming analyses.*

### FY2018 Objectives

- Perform scoping trials at vendor facility to develop a proof-of-concept data set
- Procure and install the instrument at SRNL
- Disseminate SRNL developments in the form of manuscripts and seminar presentations

### Introduction

Determining uranium isotopic and concentration information from environmental samples typically involves extensive chemical and physical processing prior to analysis. Harsh sample preparation results in the loss of the original uranium chemical speciation (i.e. what the uranium was bonded to/with when found in the environment) as well as the mixing of anthropogenic uranium with background material contained within the collection media (e.g. a swipe or soil). The objective of this work is to adapt a bioanalytical mass spectrometry technology called paper spray ionization mass spectrometry (PSI-MS) for the rapid analysis of intact uranium complexes. PSI-MS is a recently developed atmospheric pressure mass spectrometry technique which allows for rapid



**Figure 1.** (top) Diagram of paper Spray analysis from Ren et al.[1] (bottom) cotton Texwipe with uranyl doping that has been sectioned and loaded into a paper spray ionization source by SRNL.

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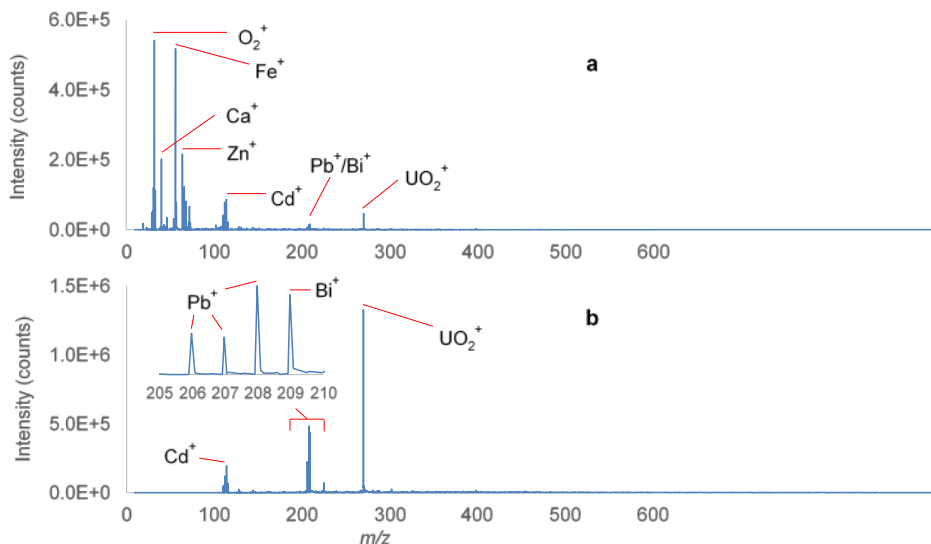
(<5 min) sample analysis with no sample preparation (Figure 1). PSI-MS has been utilized for the direct analysis of blood,[2-4] urine,[5, 6] and environmentally collected chemical warfare agent simulants.[7] Paper spray ionization sources consist of a small triangle of paper (or other fibrous material such as cotton swipes) containing chemicals of interest to which a drop of solvent is added. High voltage is applied to this wedge which induces transport and “electrospray-like” ionization of chemicals present on the fibrous material (Figure 1). In the case of swipe samples, particulate on the swipe is extracted or solvated by the solvent, ionized via electrospray ionization mechanisms, and guided into the mass spectrometer by electric fields, resulting in a mass spectrum representative of species present on the swipe. Despite the promising nature of PSI-MS, no studies have previously been reported regarding U analysis by PSI-MS.

## Approach

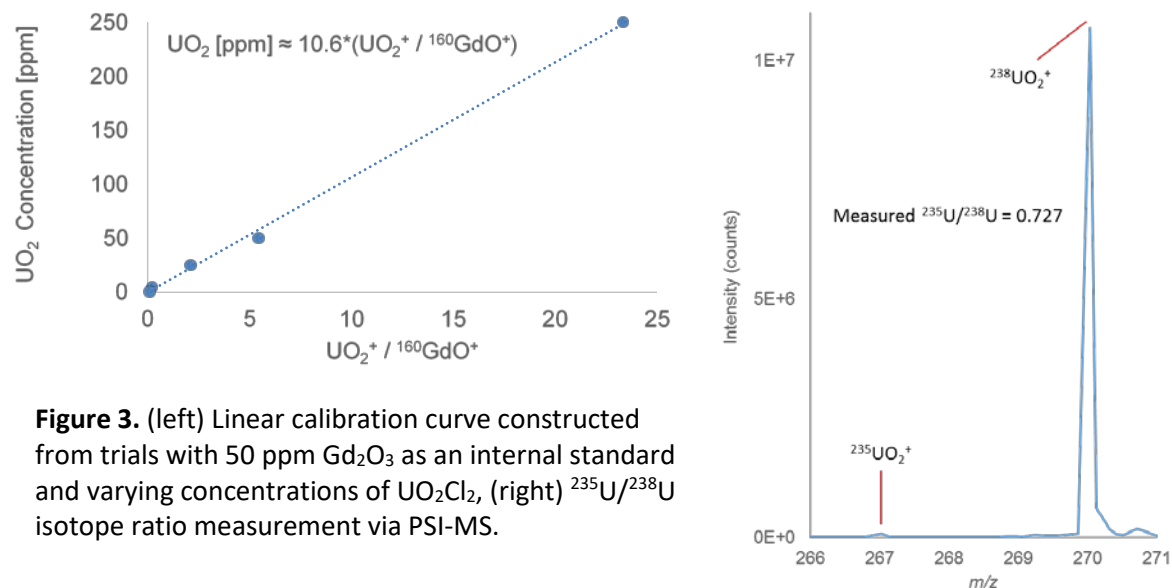
The overall project goal is to develop SRNL technical expertise in the arena of PSI-MS for uranium detection and characterization. This will be accomplished via a logical series of tasks which begin with training, reproduction of vendor scoping measurements, method development for various uranium species detection, and preliminary exploration of advanced PSI-MS techniques. These efforts are planned for FY18/19 with technical efforts beginning in FY18, post instrument installation, and continuing in-depth within the subsequent FY19. Work products from the effort will include peer-review publications on uranium analytical developments and exploration of advanced customer-relevant analytical concepts.

## Results/Discussion

Proof-of-concept research was conducted under the guidance of experts at the JEOL facility in Peabody, MA. Figure 2 shows mass spectra collected from the direct analysis of swipe samples containing U in a heavy metal matrix with no sample preparation. All species deposited on the swipe were detected (U, Bi, Pb, Cd, Fe, and Zn) with strong signal-to-noise ratios ( $\mu\text{g}$  levels of mass loading) when extracted via solvent (80/20 MeOH and  $\text{H}_2\text{O}$ ). The measured isotope abundances were in good agreement with natural abundances for most of the major isotopes characterized. Minor background constituents were observed from the cotton swipes and the cotton swipes were found to produce stronger and more stable ion beams than the classic filter paper substrates. No major interfering species for U analysis was detected, and  $\text{UO}_2^+$  was observed rather than atomic  $\text{U}^+$ .



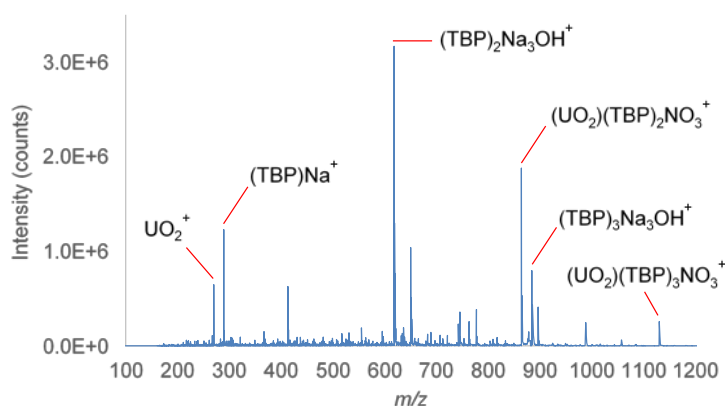
**Figure 2.** Positive ion mass spectra of a directly analyzed cotton Texwipe with mixed element doping in a) low mass and b) high mass operation modes and extracted via MeOH/ $\text{H}_2\text{O}$ . High mass mode can be used to increase sensitivity for species with mass-to-charge ratios >100 through modulation of the ion guide voltage; sensitivity for  $\text{UO}_2^+$  increased by approximately one order of magnitude in high mass mode.



**Figure 3.** (left) Linear calibration curve constructed from trials with 50 ppm  $\text{Gd}_2\text{O}_3$  as an internal standard and varying concentrations of  $\text{UO}_2\text{Cl}_2$ , (right)  $^{235}\text{U}/^{238}\text{U}$  isotope ratio measurement via PSI-MS.

U quantitation via the use of an internal standard was investigated. The ratio of the measured  $^{238}\text{U}^{16}\text{O}_2$  to  $^{160}\text{Gd}^{16}\text{O}$  intensity can be plotted against the deposited uranyl concentration to construct a calibration curve (Figure 3). The linear relationship between the  $^{238}\text{U}^{16}\text{O}_2 / ^{160}\text{Gd}^{16}\text{O}$  intensity ratio and the deposited uranyl concentration demonstrates that uranyl quantitation with PSI-MS is possible using an internal standard. Nanogram-level limits of detection were determined for uranyl through evaluation of serial dilutions of ppm ( $\sim 7 \mu\text{L}$  deposition volumes) level solutions. In practice, internal standard would be contained in the solvent and metered solvent flow would be used to determine the mass quantities of internal applied to the swipe sample.  $^{235}/^{238}\text{U}$  isotope ratio measurements were also investigated (Figure 3). Initial results from scoping work indicates that low isotope ratio errors ( $<1\%$  error) can be achieved with PSI-MS through adequate count rates (similarly to other mass spectrometry based analytical methods). Additionally, swipe limit of blank (LOB) for U is suspected to be lower for PSI-MS than other analytical methods as the swipe material is not digested for analysis by PSI-MS, preventing U within the natural fibers from contributing to the background and distorting measured isotope ratio values.

Uranyl tributylphosphate (TBP) complexes were prepared with a mixture of ligand and uranyl nitrate, briefly stirred, and then small volumes were directly injected on the paper substrate. The 1:2 and 1:3 uranyl-TBP complexes were detected in positive ion mode alongside TBP-Na adducts and the uranyl cation (Figure 4). These findings are similar to those reported by PNNL for ESI-MS characterization of aqueous uranyl-TBP mixtures, however, several differences



**Figure 1.** Positive ion mass spectrum of  $0.2 \mu\text{M}$  uranyl nitrate and  $0.5 \mu\text{M}$  TBP deposited on ( $7 \mu\text{L}$ ) on cellulosic filter paper. Complete identification of the observed species was tabulated separately.

were observed which warrant further investigation.[8] Soft-ionization, resulting from electrospray-like mechanisms, allows for the ionization of uranyl complexes while preventing ion fragmentation. In addition to uranyl-TBP complexes, uranyl acetate was also successfully analyzed via PSI-MS.

## FY2018 Accomplishments

FY18 accomplishments were primarily focused on method development for the JEOL AccuTOF mass spectrometer and the logistics associated with the instrument procurement, delivery, and installation. Early in FY18 SRNL staff visited the JEOL USA demonstration facility in Peabody MA for a two-day demonstration visit where JEOL experts ran numerous experiments at SRNL direction. In addition to general instrument operation the team demonstrated several key capabilities including:

- Direct analysis (i.e. no sample preparation) of uranyl containing swipes.
- Quantification of uranyl via an internal standard demonstrated.
- Direct analysis of inorganic multi-element containing swipes.
- Successful analysis of intact organo-uranyl complexes.



**Figure 5.** Team members being trained on the JEOL AccuTOF at SRNL after successful vendor installation; the JEOL AccuTOF can be seen in the back left of the image.

The generated data has been utilized to develop a data analysis pipeline written in R language and has also been incorporated into a draft manuscript to be submitted to *Envi. Sci. & Tech. Lett.* The project successfully coordinated a JEOL/SRNL nondisclosure agreement to enable better technical communication and data sharing between the two organizations. An instrument purchase order was placed in early February and was delivered May 15th, 2018 (meeting the primary FY18 project deliverable); installation was completed in early September 2018. The project has employed both a SRNL postdoctoral research associate and a DOE SULI intern with statistics/data analysis experience.

## Future Directions

- Rigorous determination of limits of detection (LOD) and limits of quantitation (LOQ) from direct analysis of reference materials.
- Rigorous characterization of isotope ratio measurement accuracy.
- Analysis of biota (e.g. leaves) contaminated with U and other species of interest from SRS.
- Development of method protocols for various uranyl complexes of national security interest.
- Proof-of-concept experiments for nanoparticle characterization for industrial hygiene related applications.
- Engineering stabilization modifications for the analyte injection apparatus.
- Proof-of-concept experiments for other organic species relevant to national security interest.

## FY 2017 Publications/Presentations

1. *Paper spray mass spectrometry applications for uranium ion and molecular detection.* Expected: Communication in *Envi. Sci. & Tech. Lett.* in fall 2018.

2. *Paper spray ionization mass spectrometry for rapid chemical and isotopic characterization of trace uranium samples.* Upcoming presentation at SERMACS.

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## Acronyms

(PSI-MS) paper spray ionization mass spectrometry

(TBP) Tributylphosphate

## Intellectual Property

There is no intellectual property to report for this effort.

## Total Number of Post-Doctoral Researchers

- (1) Joseph Mannion