FINAL RESEARCH REPORT
(JANUARY 1, 2018 – DECEMBER 31, 2020)

Project Title: Coupling Gas Chromatography (GC) and Vacuum Ultraviolet (VUV) Spectroscopy for Forensic Applications (Award 2017-R2-CX-0018)

Award Amount: $390,473

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SUMMARY OF THE PROJECT

MAJOR GOALS AND OBJECTIVES

The primary aims of this project were to:

1. Assemble a GC system with a VUV detector.

2. Qualify and optimize performance of the GC/VUV system for the analysis of controlled substances.

3. Demonstrate the applicability of GC/VUV to realistic seized drug samples.

RESEARCH QUESTIONS

The three major research questions for this project were:

1. Is GC/VUV a viable technique for the forensic analysis of seized drugs?

2. What are the strengths and weaknesses of this technique?

3. Should GC/VUV be thought of as an alternative to GC/MS or simply as a complementary technique?

RESEARCH DESIGN, METHODS, ANALYTICAL AND DATA ANALYSIS TECHNIQUES

To achieve the project goals, the project was divided into six distinct phases:

Phase 1: Assemble the GC/VUV instrument and validate the performance of the VUV Detector

Phase 2: Establish the figures of merit of the VUV Detector and Compare to a MS Detector

Phase 3: Assess the Effects of Rydberg Transitions and Photoionization on VUV Spectra (this phase was truncated due to a lack of evidence of either Rydberg transitions or photionization)

Phase 4: Establish a Set of Optimized GC/VUV methods for Controlled Substances

Phase 5: Assess the specificity of VUV spectra for structural isomers using chemometric Methods (e.g., Principal Components Analysis (PCA) and Discriminant Analysis (DA))

Phase 6: Use GC/VUV to analyze a set of realistic seized drug samples

EXPECTED APPLICABILITY OF THE TECHNIQUE

This project has introduced, optimized, validated, and demonstrated the use of GC-VUV for seized drugs analysis. We expect that crime laboratories interested in adding GC/VUV to their capabilities now know the proper instrumentation to purchase as well as the parameters of methods useful for seized drugs of many types.

PARTICIPANTS AND OTHER COLLABORATING ORGANIZATIONS

This project formed most of the Ph.D. dissertation for Zackery Roberson, who received training in instrumental analysis, experimental design, and statistical methods via one-on-one work with Dr. Goodpaster.

The role, time worked, and contribution of Drs. Roberson and Goodpaster are summarized in this table:

Name	Project Role	Time Worked (person months)	Contribution	Funding
Roberson, Zack	research assistant	18	Assists with sample analysis and data interpretation	Graduate Student (IUPUI)
Goodpaster, John	principal investigator	3	Direct supervision of the graduate student, experiments, results, and interpretation.	This grant (10% summer salary)

None of the personnel listed above collaborated with an individual in a foreign country or traveled to a foreign country as a part of this project.

The Indiana State Police Drug Chemistry Unit graciously provided de-identified casework samples for Phase 6.

CHANGES IN APPROACH FROM ORIGINAL DESIGN AND REASON FOR CHANGE, IF APPLICABLE

We did not report photometric accuracy or repeatability in Phase 1 because it was not deemed feasible with the instrumental setup. In addition, phase 3 was changed from Rydberg

transitions and photoionization for fine peaks to considering rotational, vibrational, and thermal degradation for fine peaks.

OUTCOMES

ACTIVITIES/ACCOMPLISHMENTS

The major accomplishments of this project were:

1. Validation of a GC/VUV instrument, including establishing its figures of merit
2. Establishing a Set of Optimized GC/VUV methods for Controlled Substances
3. Assessing the specificity of VUV spectra for structural isomers using chemometric methods
4. Use GC/VUV to analyze a set of realistic seized drug samples

Additional details regarding these areas appears below.

RESULTS AND FINDINGS

FIGURES OF MERIT

The spectrophotometric properties of the detector were measured with the following results:

a) Wavelength Accuracy: Meets expected specifications of ±2 nm
b) Wavelength Repeatability: Exceeds expected specifications of ±1 nm, observed ±0.5 nm
c) Baseline Noise Level (Root Mean Square Noise): Exceeds expectations of 0.001 A.U., observed 0.0005 A.U.
d) Baseline Stability: Meets expected specification of < 0.003 A.U. h^{-1}

Using a model compound (cinnamaldehyde), the figures of merit for quantitation were found to be:

a) Linear Range: 3 – 1000 ppm
b) Slope = 0.0116 ppm^{-1}
c) LOD = 5 ng on column
d) Signal-to-noise is blank noise limited

OPTIMIZATION

We presented the first statistical optimization of parameters influencing analytes such as cocaine in the VUV flow-cell. Flow-cell temperature, make-up gas pressure, and carrier gas flow rate from the GC were examined. and optimized for the detection of controlled substances.

The optimization results for cocaine, heroin, methamphetamine and fentanyl are shown in the figure below.

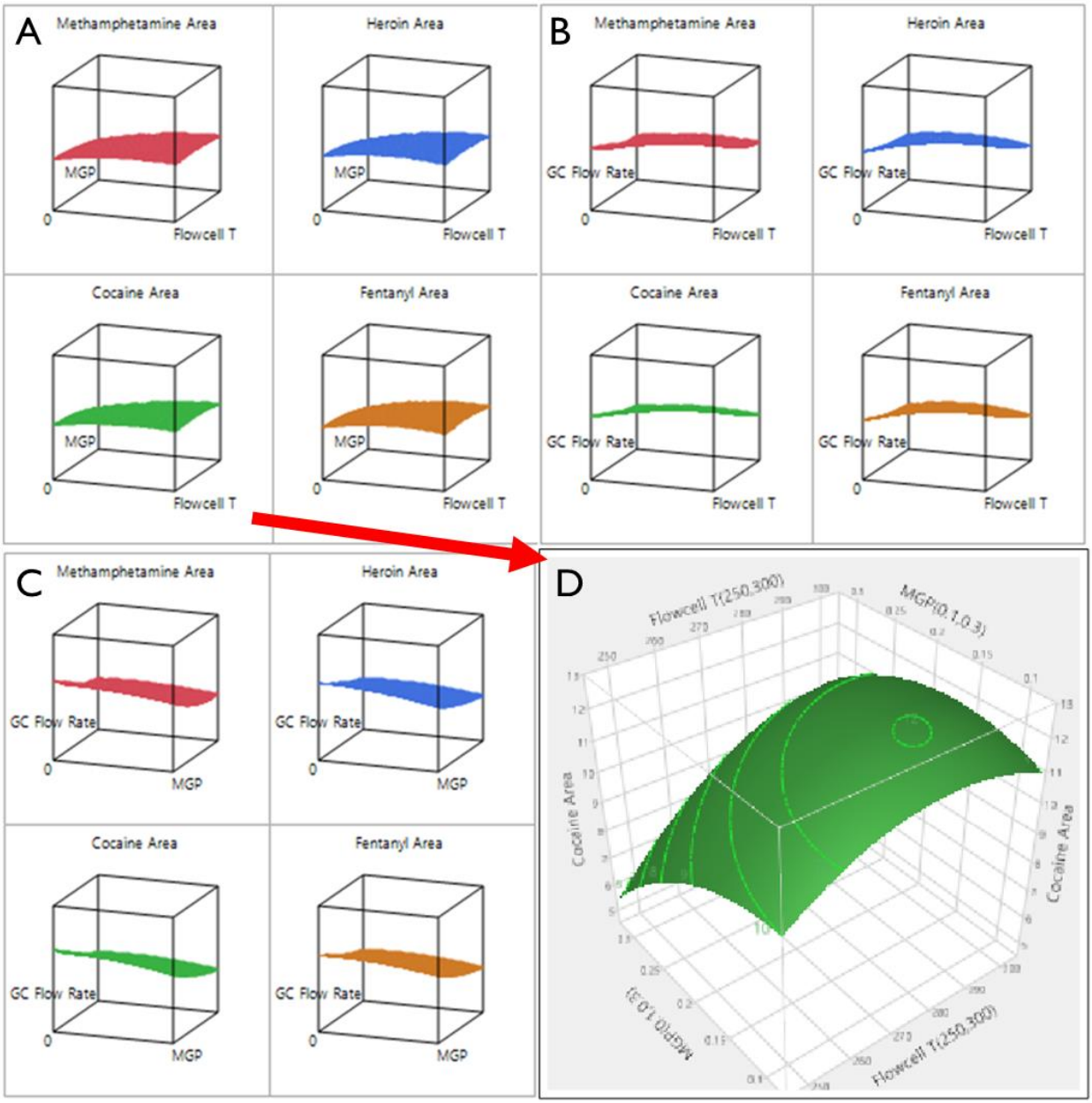

FIGURE 1: PEAK AREA RESPONSE SURFACES FOR METHAMPHETAMINE, HEROIN, COCAINE, AND FENTANYL

The accuracy, precision, linearity, and optimized detection limits for drugs such as cocaine (98.5 %, 1.2%, 0.9998, 1.5 ng), heroin (99.3%, 0.94%, 0.9998, 2.0 ng), and fentanyl (98.5%, 1.7%, 0.9752, 9.7 ng) were reported. In general, the limits of detection for cocaine, heroin, fentanyl, and methamphetamine after optimization were comparable to gas chromatography-mass spectrometry (GC-MS) in "scan mode", which had detection limits of 1.1-38 ng on column.

Generation of a Spectral Library

Over the course of the project, the VUV spectra of the following drugs and adulterants were reported:

Cocaine	Morphine	Phentermine
Heroin	3-monoacetylmorphine	Methylphenethylamine
Fentanyl	6-monoacetylmorphine	Methcathinone
Methamphetamine	Caffeine	Ethylamphetamine
PCP	Lidocaine	Dimethylamphetamine
Lorazepam	Quinine	Levomisole
HU-210	Amphetamine	Dimethylsulfone
Heroin	Methamphetamine	

Chemometrics

One of our earliest studies sought to determine the extent to which structurally similar phenethylamines are differentiated using their VUV spectra. Phenethylamines are a common drug class including pseudoephedrine and illicit drugs such as methamphetamine. Several phenethylamines are difficult to analyze by electron impact mass spectrometry due to their fragmentation giving the same mass to charge ratio fragments at similar ratios. While phenethylamines are generally differentiable by retention time, an extra layer of specificity is preferred in forensic analyses. A vacuum UV (VUV) spectrophotometer coupled to a gas chromatograph was used to collect VUV spectra at high frequency between 125 and 430 nm. Eight phenethylamines were analyzed for this work using GC/VUV. The spectra analyzed by Principal Component Analysis (PCA) and Discriminant Analysis, showed that one can reliably differentiate each of the drugs from one another including structural isomers and diastereomers.

A second study focused on GC-VUV analysis applied to naturally occurring (e.g., morphine), semi-synthetic (e.g., heroin), and synthetic (fentanyl) opioids as well as common adulterants

and diluents (e.g., lidocaine and quinine). The specificity of the VUV spectra was examined. visually as well as via descriptive statistical methods (e.g., correlation coefficients. and sums of square residuals). Multivariate pattern recognition techniques (principal component anal. and discriminant anal. (DA)) were used to prove the opioid spectra can be reliably differentiated. The accuracy of the DA model was 100% for a test set of VUV spectra.

REALISTIC SAMPLES

Various samples of "real world" drug exhibits were analyzed to demonstrate applicability to forensic drug analysis. These exhibits originated from the Indiana State Police Drug Chemistry Unit. The main drug of interest in these samples were methamphetamine, cocaine and heroin. These samples contained adulterants such as caffeine, levamisole, as well as byproducts of heroin manufacture.

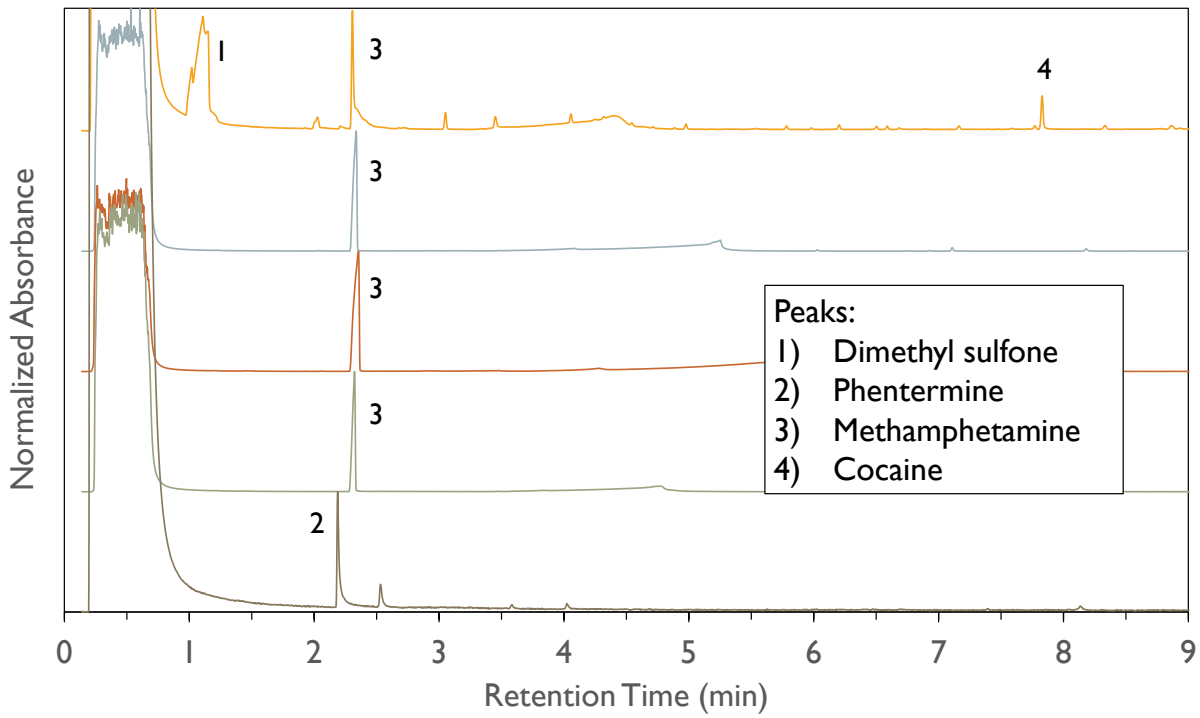

FIGURE 2: ANALYSIS OF SEIZED METHAMPHETAMINE EXHIBITS

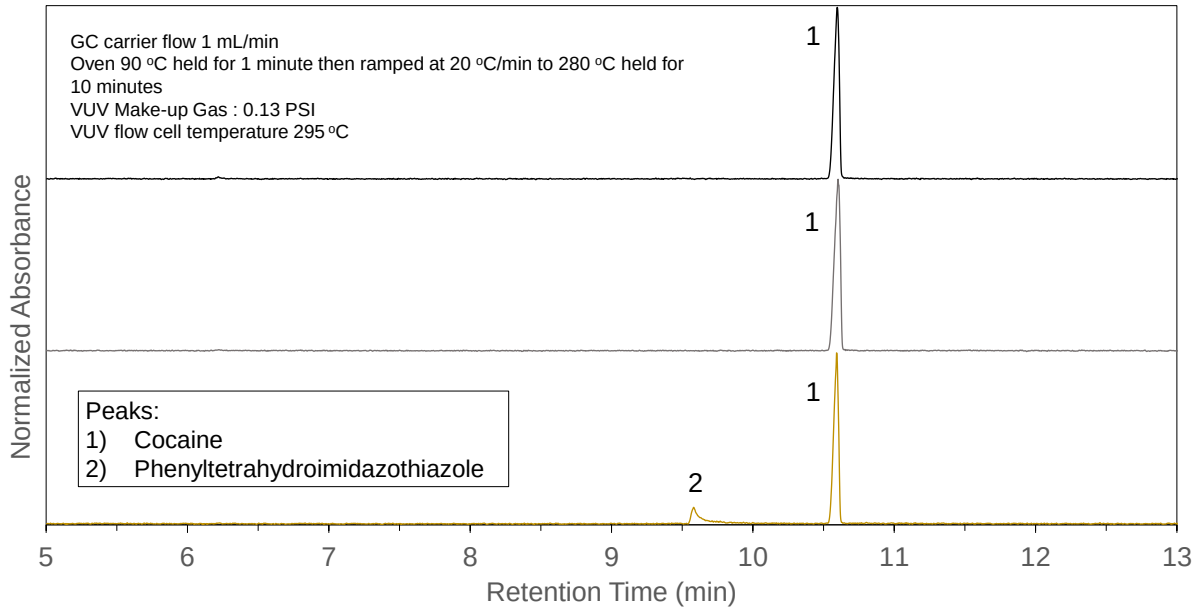

FIGURE 3: ANALYSIS OF SEIZED COCAINE EXHIBITS

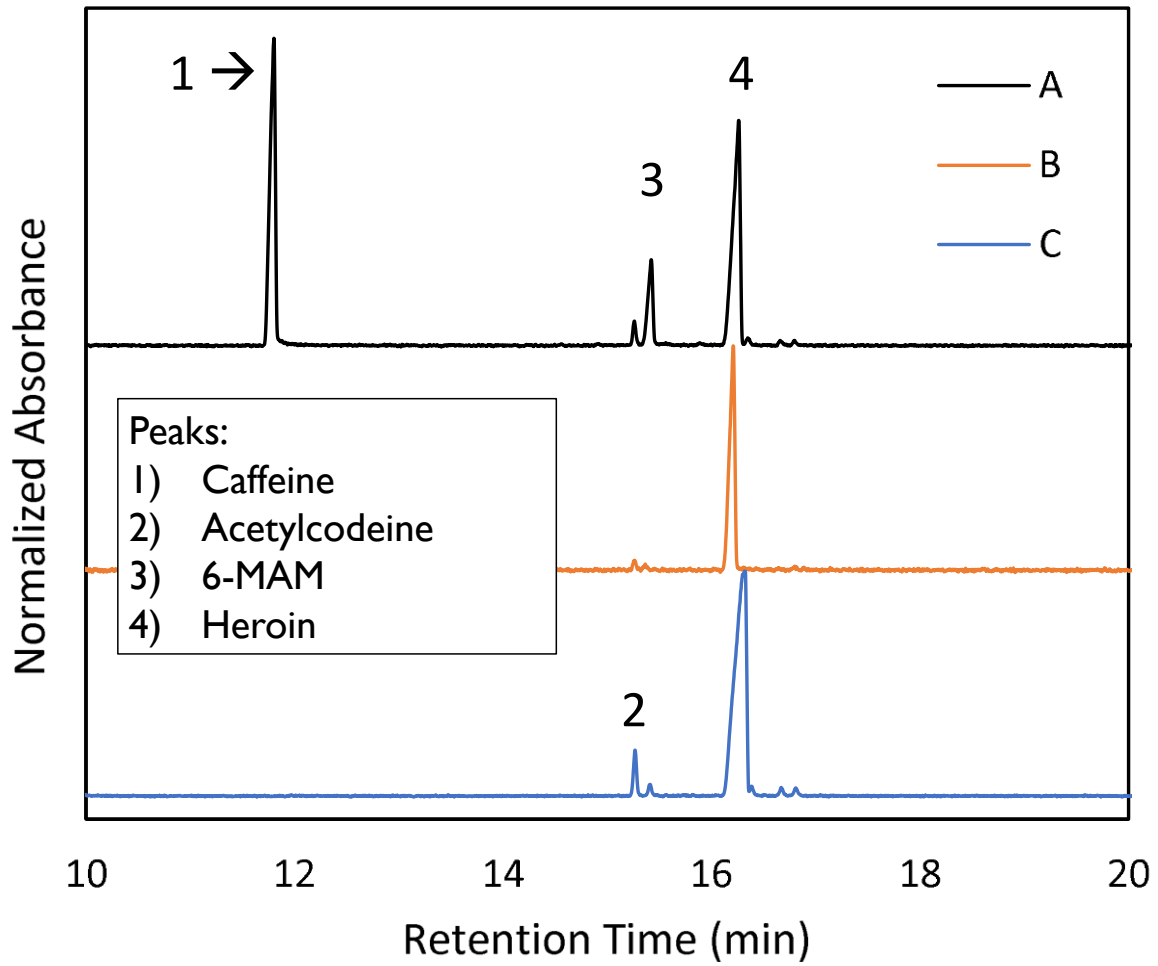

FIGURE 4: ANALYSIS OF SEIZED HEROIN EXHIBITS

LIMITATIONS

The limitations of GC/VUV can be expressed in terms of its sensitivity, selectivity, and specificity.

The sensitivity of VUV reaches into the low part-per-million range, which is comparable to a GC/MS operating in "scan" mode. If the technique is intended for seized drugs analysis, where sample sizes are in the milligram to gram range, then its sensitivity is not an issue.

The selectivity of GC/VUV depends upon the use of spectral filters, where specific wavelength ranges are used to re-construct a chromatogram. In general VUV is not as selective as MS given that extracted ion profiles can be constructed from single ions that are well resolved from other fragment ions.

The specificity of GC/VUV is best realized when coupling the technique to chemometric data analysis. Pattern recognition techniques such as Principal Components Analysis (PCA) and Discriminant Analysis (DA) were impressive and even allowed for differentiation of diastereomers. The VUV spectra obtained from drug molecules were not highly structured and not as specific as an EI mass spectrum.

ARTIFACTS

LIST OF PRODUCTS

PRESENTATIONS

"Coupling Gas Chromatography and Vacuum UV Spectroscopy for Forensic Applications" John Goodpaster, Centre College (Danville, KY), April 19, 2018. Oral presentation.

"Coupling Gas Chromatography and Vacuum UV Spectroscopy for Forensic Applications" John Goodpaster, Eastern Kentucky University (Richmond, KY), April 20, 2018. Oral presentation.

"Analytical Challenges in Identifying Structural Isomers of Drugs " John Goodpaster, Mitigating the Emerging Drugs of Abuse Epidemic (VUV Analytics) (Indianapolis, IN), June 6, 2018. Oral presentation.

"Analytical Challenges in Identifying Structural Isomers of Drugs " John Goodpaster, Mitigating the Emerging Drugs of Abuse Epidemic (VUV Analytics) (Chevy Chase, MD), August 18, 2018. Oral Presentation.

"Detection and Differentiation of Controlled Substances by GC-VUV and Chemometrics" Zackery Roberson and John V. Goodpaster, AAFS 71st Annual Scientific Meeting, February 22, 2019. Oral presentation.

"Performance of a Vacuum Ultraviolet Spectrophotometer as a Gas Chromatography detector applied to controlled substances detection" Zackery Roberson and John V. Goodpaster, 2019 PittCon Analytical Chemistry Conference, March 19, 2019. Poster presentation.

"Coupling Gas Chromatography (GC) and Vacuum Ultraviolet (VUV) Spectroscopy for Forensic Applications" John Goodpaster, Forensic Technology Center of Excellence (NIJ Webinar), April 4, 2019. Oral Presentation.

"Optimizing GC-VUV for Drug Detection through Response Surface Methodology" Zackery R. Roberson and John V. Goodpaster, 2020 PittCon Analytical Chemistry Conference, March 3, 2020. Poster presentation.

PUBLICATIONS

Roberson, Z.R., Goodpaster, J.V. Differentiation of structurally similar phenethylamines via gas chromatography–vacuum ultraviolet spectroscopy (GC–VUV), Forensic Chemistry 2019; 15:100- 172.

Roberson, Z.R.; Gordon, H.; Goodpaster, J.V.. Instrumental and Chemometric Analysis of Opiates via Gas Chromatography – Vacuum Ultraviolet Spectrophotometry (GC – VUV). Analytical and Bioanalytical Chemistry 2020, 412, 1123–1128.

Roberson, Z.R.; Goodpaster, J.V. Optimization of the quantitative and qualitative analysis of cocaine and other drugs of abuse via gas chromatography-Vacuum ultraviolet spectrophotometry (GC-VUV), Talanta 2021, 222, 121461.

DATA SETS GENERATED

We generated spectra for over 25 different drug molecules over the course of this project. This data has been shared with VUV Analytics for inclusion in their VUV library that is distributed with their instrument software.

DISSEMINATION ACTIVITIES

Our dissemination activities have focused upon oral presentations at regional and national venues as well as peer-reviewed publications.