In Situ Analysis of Organic material with a portable Mass Spectrometer

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ABSTRACT

We have tested a portable mass spectrometer (MS) system, the Mini 10.5, for *in situ* applications including the analysis of volatile organic hydrocarbon (VOC) and water soluble organic components extracted from solid material using an automated sample processing system (ASPS), by doing so we intend to demonstrate the utility of *in situ* analysis compared to sample acquisition and return for analysis on future robotic space missions.

MASS SPECTROSCOPY

Traditionally, mass spectroscopy based analysis has occurred in research labs. This is due to the advantages of laboratory based mass spectroscopy, including minimal limitations on mass, power, and volume. Additionally, laboratory based analysis usually includes human in the loop to perform complicated sample processing and handling. However, there are two reasons why performing *in situ* analysis of samples is preferable to laboratory analysis and they are 1) when collecting, storing and transferring the sample results in a modification of a sample to the point where the scientific value of the sample is decreased, and 2) when returning samples to the laboratory is not possible due to extreme costs or technical risks. We have tested a field portable mass spectrometer, the mini 10.5 developed at Purdue University (Figure 1) in both in the field and in conjunction with an recently developed automated sample processing system (Beegle et al. 2011) to demonstrate the utility of using a fully portable mass analyzer in the field for instant analysis both under terrestrial applications and for future space

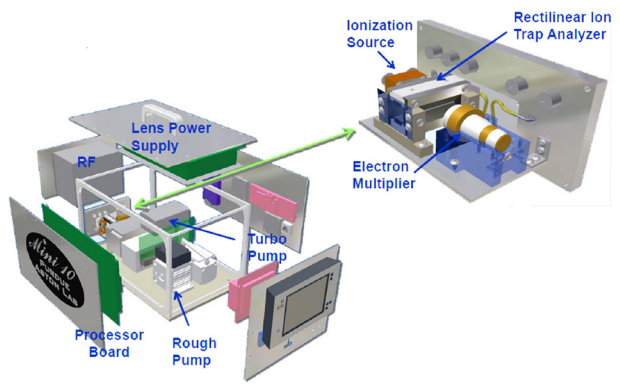

Figure 1: The main components of Mini 10 (10.5) rectilinear ion trap mass spectrometer (Ouyang et al., 2006).

mission.

A portable chemical instrumentation that can demonstrate real-time detection, identification, and quantification of VOCs in the ambient atmosphere can be indication of ongoing bacterial metabolic processes, identify man made chemical species such as pollutants before they can diffuse, identify chemical reactions, and act as ground truth for orbital measurements. VOCs can be produced in unique quantities and combinations which are diagnostic of atmospheric chemical pathways. For instance, indole is responsible for the characteristic odor of E.coli (Lee et al. 2008), making this VOC a common diagnostic marker for the identification of this species. We designed and tested a solid sorbent based sample introduction system in the Mojave Desert to evaluate the capability of the miniature instrument to directly analyze trace atmospheric hydrocarbons. Part of our testing was to evaluate different sorbent traps for their effectiveness on different VOC species. A similar sorbent based sample introduction system has been demonstrated with the Mini 10 instrument for the detection of toxic chemicals (Janfelt et al. 2008) and volatiles from gasoline (Sokol et al. 2008).

Analyzing organic material that is indicative of life is a main goal of NASA. There are two driving science reasons to understand the distribution of organic material in the solar system. One is to understand the chemical processes and history that are ongoing on solar system bodies and the other is to map the distribution of organic material available for the origin of life and determine if life currently exists on such a body. For these types of investigations, organic analyses of near surface material will be of pivotal importance in the astrobiological exploration of targets in the solar system. For bodies such as Enceladus and Europa where organic material is expected to exist due to meteoritic infall and other abiotically derived process, if a highly organized, encapsulated collection of complex molecules analogous to a cell is identified, a detailed analysis of components within it would be the need to uniquely identify biology. However, determining the presence of life not only requires detecting the presence of organics, it is imperative that there is a level of specificity and a method of enumeration.

At its simplest level, life utilizes amino acids as its basic building blocks, however there have been over 70 amino acids and 10's of thousands of different organic structures have been identified in meteorites (Cronin and Pizzarello 1983; Botta and Bada 2002; Schmitt-Kopplin et al. 2010) that have been created through abiotic processes. Life itself utilizes just a small subset of amino acids. One potential life search that primarily utilizes simple quantification techniques is the strategy to inventory the available organic molecules and determine relative compositions (McKay 1997; McKay 2004). When building block organics, such as lipids are created in hydrothermal environments their quantity tends to decrease with increasing carbon number. Life, on the other hand, tends to use lipids with even numbers of carbon atoms, especially those containing 16 and 18 (Simoneit et al. 1998; Simoneit et al. 2004). Identification of large repeating complex molecules resembling Deoxyribonucleic acid (DNA) and the simpler single stranded Ribonucleic acid (RNA), would make a compelling case that either life was present, or true pre-biotic chemistry was taking place (Benner and Hutter 2002; Benner 2004; Benner and Sismour 2005; Yang et al. 2006).

Simply detecting individual organic material tells us about chemical conditions of the planetary body and potentially about where the material formed, while measuring the amount of different organic material increases the potential for identifying extinct and extant life. By looking at different aspects of an extraterrestrial sample, complementary techniques will lead to as a complete an understanding of the history (geological, chemical, biological, etc.) as possible. An analyzer which is highly sensitive and rugged enough for the harsh conditions on the surface of these bodies would be well suited to serve this purpose. Any instrument capable of this type of investigation requires some sort of sample handling and processing system. There are three prime targets in the solar system for extinct and extant life detection in our solar system, Mars, Europa and Encleadus.

There has been considerable effort from the laboratory of Prof. Graham Cooks to reduce the size and power requirements of mass spectrometry through the development of smaller mass analyzers and compact vacuum pump and electronics.(Ouyang et al. 2009; Xu et al. 2010) The miniaturized MS uses a rectilinear ion trap (RIT) consisting of six planar electrodes as a mass analyzer.(Ouyang et al. 2004) The mass analyzer and detector assembly fit into an area of approximately 500 cm^3. The vacuum system design is akin to the rough-turbo pump configurations found in lab-scale instruments but with small portable pumps (5L/min rough and 10L/s turbo pump).(Ouyang et al. 2009) The entire system including the control electronics and pumps fits into shoebox-size case (0.5 ft^3) and consumes less than 70W. Partially developed through a joint JPL-Purdue University Astrobiology Science and Technology Instrument Development program (ASTID) grant, a Mini-10.5 is in operation at JPL. In this paper we describe two experiments that demonstrate the utility of *in situ* MS.

Field analysis of Volatile Organic Carbon compounds.

To sample VOC analytes from the ambient atmosphere a sorbent trap system was fashioned to preconcentrate organics onto a sorbent bed and introduce them in smaller bolus samples (Figure 2). The sampling system uses cylindrical glass tubes (70 mm, *r* 3 mm) containing 10mg of sorbent placed between solenoid valves (ASCO Valves, Florham Park, NJ). A three way valve is positioned to open the circuit to the atmosphere or to the vacuum manifold and a two way valve opens to allow suction from the sampling tube pump. Pre-conditioned, filled sorbent tubes were purchased from Chemical Agent Monitoring Supply Co., Houston, TX, USA. When the valves are in the open position a miniature sample pump (model NMP015M, KNF Neuberger) draws air over the sorbent bed at a rate of 2.0 L / min. Next, the solenoid valves are both put into the closed position to open the sorbent bed up to the vacuum manifold of the Mini 10.5. The tube can also be heated by passing a current (2 A at 24 VDC for 3.5 s) through 60 cm of 29-gauge nichrome wire wrapped around it, causing the sorbent to reach 240 °C within 4 s.

Air samples were collected during a scouting trip geared toward finding lava rock with lichen growth to see if complex atmospheric organics are a source of potential nutrition. Air was sampled at sites with variable distance from automobile traffic. For air sampling in the desert the sorbent tubes were attached to a sample pump powered by rechargeable batteries. Air was drawn over these tubes at a rate of 2.0 L / min for

at least 15 minutes. Two different sorbents were used to sample air for organics at

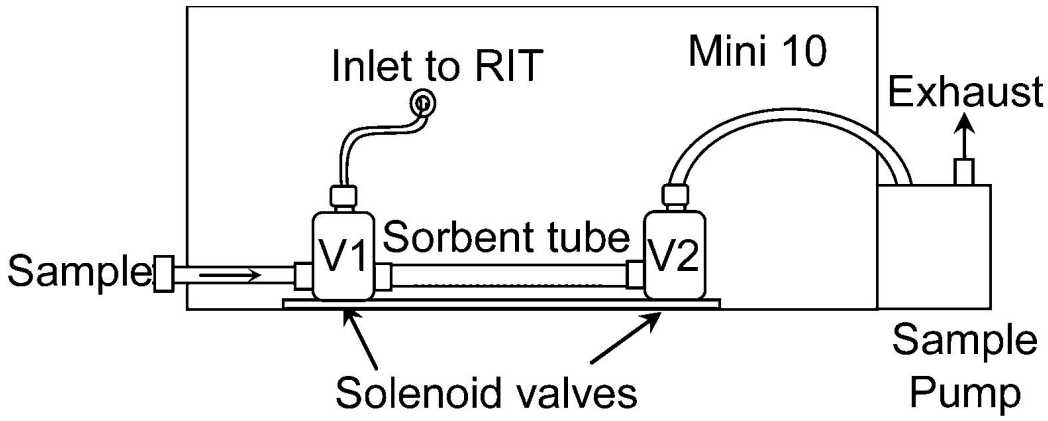

Figure 2: The sorbent trap interface to the Mini 10 uses a sample pump to draw ambient air over the sorbent contained in a tube. When V1 and V2 are opened, sample collects on the sorbent bed as air is pulled by sample pump. V1 is opened to the instrument and V2 is closed to let the sorbent bound analytes outgas into the instrument.

each site. A Hayesep D sorbent tube was used to check for non-polar midsize organics such as benzene. A PoraPak Q tube was used to check for similar compounds that were slightly more polar such as toluene and substituted organics (Figure 3).

During the first scouting trip air sampling was done near Rainbow Basin near Barstow, CA, Salt Creek ACEC, CA, and Baker, CA. The Rainbow Basin site (*N 35.104181, W -117.136688*) is 12 miles away from the I-15 freeway and 10 miles away from any paved road. Salt Creek Area of Critical Environmental Concern site (*N 35.394088, W -116.127949*) is 8 miles away from the I-15 freeway but adjacent to Hwy 127, a lightly traveled road. During the experiment only light vehicular traffic was seen with approximately 1 auto / 4 min. Baker, CA is a rest stop town on the I-15 freeway where the air sampling was done 100 yds from the freeway (*N 35.265099, W -116.074768*). The air in each location was sampled for 20 minutes at a rate of 2.0

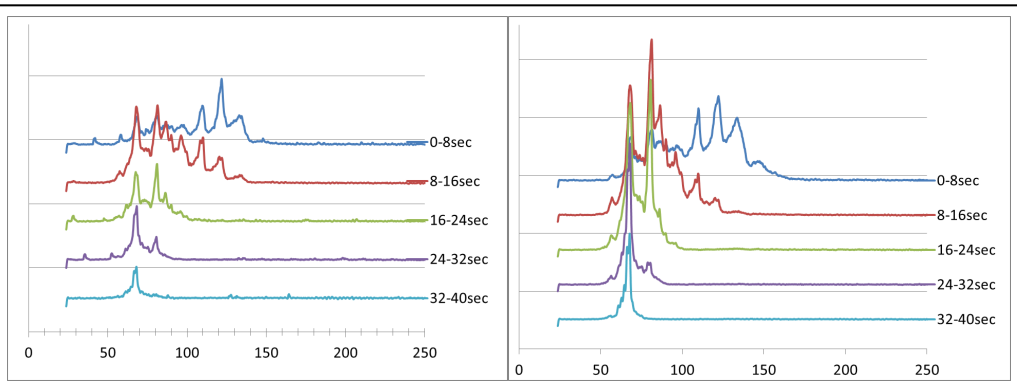

Figure 3: Mass spectra of air sampled at Rainbow Basin (left) and Salt Creek ACEC (right) with PoraPak Q. The three peaks at three peaks in the 0-8 sec most likely correspond to aromatic hydrocarbons commonly found in diesel exhaust: styrene (104amu), naphthalene(128 amu), acenaphthene (154 amu), with the peak at ~140amu unidentified.

L / min.

Air samples collected at Rainbow Basin showed the least overall signal intensity with both the Hayesep D and PoraPak Q resins. Three components were seen eluting from the Hayesep D (Figure 4.3a) and eight from the PoraPak Q (Figure 3). The signal from m/z 72 and m/z 74 in the Hayesep D spectra can be sourced to C3-C4 substituted hydrocarbons. The Hayesep D and PoraPak Q spectra of the Salt Creek had the second highest signal response (maximum 800 counts). Five distinct components were seen in the PoraPak Q spectra and eight from the Haysep D. Peaks seen in the higher mass ranges m/z 108 – 155 likely originate from substituted aromatics. Both Haysep D and Porapak Q tubes gave a maximum signal response over 1400 counts. The trend in signal intensity across the different samples suggests that the amount of organic atmospheric components decrease with increasing distance from automobile thoroughfares.

We also took the Mini 10.5 into the field and directly sampled a sorbent tube near the I-40 near Ludlow Ca. The sorbent material adopted for this experiment was Carbopack C. Carbotrap C gives good recoveries for polyaromatic hydrocarbon (PAH) analytes from naphthalene to chrysene. Air was sampled 10 feet from the freeway using a sample pump to draw the air over the sorbent tubes at a rate of 2 liters/min for 1 hour. The miniature instrument was powered by a Duracell DPP-600HD Powerpack.

The miniature MS system was able to detect the two most abundant components of diesel exhaust, naphthalene and acenaphthene. Background chemical noise was accounted for by taking the spectrum of a preconditioned blank Carbotrap C tube (Figure 4 *left*) before analyzing the sampled tube (Figure 4 *right*). Signal from larger species is also limited in part because thermal desorption was not used during this experiment. The major aromatic components of the exhaust are toluene, phenylacetylene, styrene, indene, naphthalene, and acenaphthalene. The peak at m/z 128 most likely corresponds to the radical cation of naphthalene and the peak at m/z 154 most likely corresponds to acenaphthene. The small peak at m/z 104 is most likely from radical cation of styrene. We plan on further tests during 2012, and will test the ability to perform Ms/MS on mass spectra to uniquely identify the species.

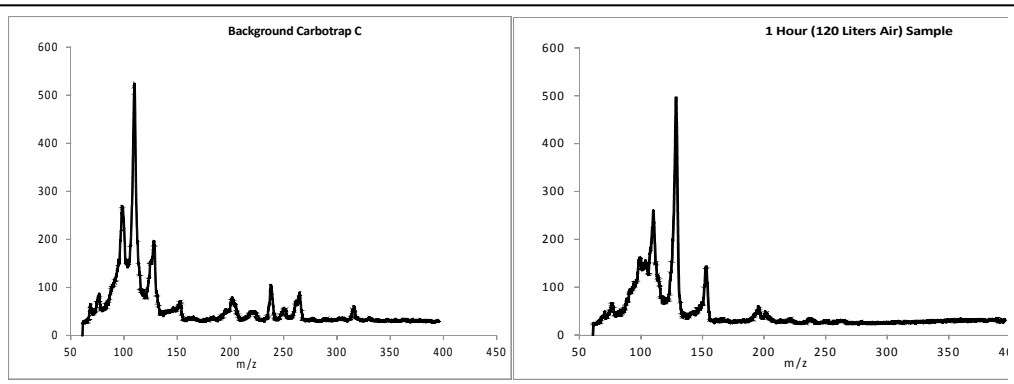

Figure4: *left*- Background signal from blank Carbopak C tube. *Right* Raw signal from a sampling of 120 L of air next to the freeway

Testing an Automated Sample Processing System

In the search for evidence of life in the solar system, analytical instrumentation incorporated onto a spacecraft will be central to the robotic exploration of Mars. A current approach in the study of the biotic potential of the most terrestrial-like planet in our solar system is through the determination of organic compounds in Mars' regolith (Bada et al. 2008). As is the case with most analytical investigations, there is a need to process complex field samples prior to the detection of target analytes, especially when attempting to detect low concentrations. For an astrobiological study, the target analytes are biogenic organic molecules, such as amino acids, that can be used to assess conditions for extant or extinct extraterrestrial life (Sokol et al. 2011).

For most biologically relevant molecules, solvent extraction gently removes organic molecules trapped inside rocks. A common method for isolating amino acids from soils and geological samples starts with a hydrolysis step where the soil sample is boiled in 6 N HCl for up to 24 hours at 100° C (to free up amino acid components of larger molecules) followed by desalting the sample solution on a cation exchange resin(Lee and Hong 1995) column. Amino acids are finally eluted from the column using aqueous NH_3 solution (Degens and Reuter 1964; Cheng 1975). Oxalic acid is sometimes added to remove excess metal interference (Amelung and Zhang 2001). Such steps can be automated for *in situ* life detection (Masuda and Dohmae 2010).

This investigation is focused on an automated wet chemistry preparation system that is being developed at JPL to operate autonomously on Earth in preparation for automated operation under Martian ambient conditions. The system shown in figure 5, the Wet-chemistry Automated Sample Processor (WASP) is being designed as a vehicle to enable a wet chemistry laboratory as part of future missions (Beegle et al. 2011). The WASP will accept either rock chips or fine sediments, submerge them in a solvent, heat to temperatures to dissolve organics, further process the solvent using a cation exchange resin to remove potential masking agents and then transfer that analyte to analytical instruments for analysis. A MS detection system for the WASP has been proposed, but has not yet been implemented. Our goal is to demonstrate a miniature MS for the detection and identification of biogenic molecules, specifically amino acids, from the WASP with the expressed goal of carrying out the same analysis *in situ*.

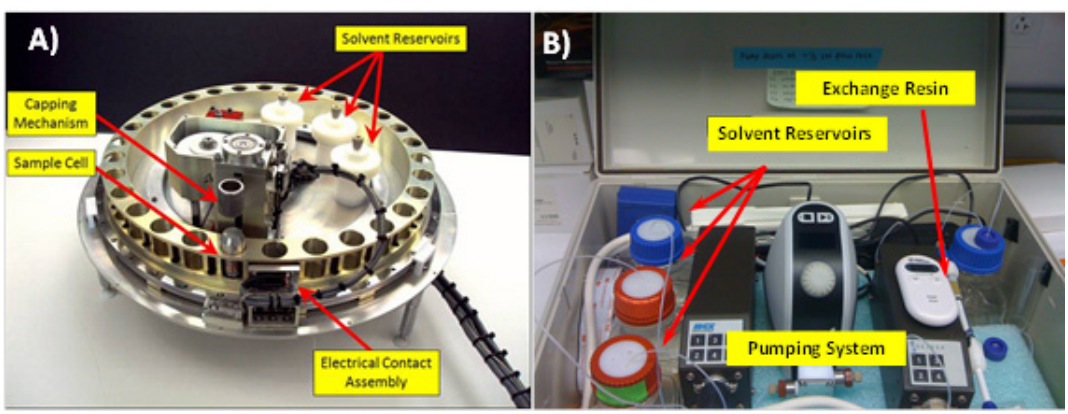

Figure 5: *left* The field portable wet-chemistry automated sample processing (WASP) for solvent extraction. *Right* a lab based automated desalted that was used to provide a desalted sample for MS analysis.

A prototype lab based system was used instead of the flight model to provide a desalted sample for MS analysis (Figure 5 right). The system consisted of a two valve actuators; injection valve 1 is an IDEX 6-valve actuator, and injection valve 2 is a 3-way SCIVEX 4-valve actuator driven by a KNF STEPDOS-03 pump (Trenton, NJ, USA). The desalting resin was packed into an Omnifit column (Diba Industries, Danbury, CT, USA) and all connections between valves used 1/16" OD peek tubing (Idex, Lake Forest, IL, USA), mounted within a rugged plastic container, measuring 38 W x 49 L x 21 D cm. Power cords from each valve actuator and pump were mounted to a power strip within the container. The container has a locking lid for transportation for field use. Eluents (HCl, oxalic acid, NH_4OH, and water) were placed in 500 ml square glass bottles (Corning, NY, USA) that fit compactly within the container. The system output and the eluate in ammonia solution were collected in disposable 15 ml polypropylene tubes (Corning, NY, USA). The desalting column consisted of a glass chromatography column (10x100mm adjustable bed volume, with PTFE frits) packed with strong acid cation exchange (H+ type) resin, AG 50W – X8, 100-200 mesh (Biorad labs, Hercules, CA, USA). A slurry of resin in water was used to pack 0.75 g AG 50W-X8 resin in 2 cm length of column with a bed volume of 1.57 cm^3.

A reagent sequence for extraction can be implemented by the switching of valve actuators and controlling the flow rates with the pump. The system is prepared by flushing the column with 3 M HCl (15 ml, 10 ml/min) to fully protonate the sulfonic acid residues. This is followed by a rinse that removes excess acid from column in a wash step (15 ml water, 10 ml/min). If desalting is not done during extraction, it is also possible to wash with 0.1 M oxalic acid (10 ml, 1 ml/min) followed by a wash step (15 ml water, 10 ml/min). The collection of the amino acid sample from the column is achieved by an elution with ammonia solution (2 ml, 1 ml/min). Finally the instrument is prepped again (15 ml water, 10 ml/min) in preparation for the start of the sequences. The flow of reagents was activated using the 'Prime' setting on the KNF pump.

Sample ionization was achieved by placing 15 µL of sample extract in a commercial nanoelectrospray (nanoES)(Wilm and Mann 1996) tip (outer diameter 1.0 mm ; inner diameter 0.78 mm; tip 4 µm) obtained from New Obejective (Woburn, MA, USA) and inducing electrospray through the application of 4 kV on the tip holder.

Sample collected from 15 cm underground at the Cima site underwent hand-organic extraction because the WASP was not completed at time of analsys. 3.0 g of soil was placed in a sterile container heated to 100° C in 3 ml 1.0 M oxalic acid for 24 hours to extract amino acids potentially present in the soil sample. After 24 hours oxalic acid supernatant was collected and the soil sampled was rinsed with DI H_2O. The final pH was 4.5. The rinse water was collected and added to the extract to equal a total volume of 9 ml. The 9 ml of extract/rinse represent an extraction of 3 g of soil. The final solution was split into 3 equal portions of 3 ml, each representing 1 g of soil. Two 3 ml portions were desalted using the automated de-salter cation exchange column and one 3 ml portion was left unprocessed. The 3 ml portions were eluted from the cation exchange resin with 2 ml of NH_4OH. 1 ml of DI H_2O was added to bring all solutions back to 3 ml to keep the concentration at 1 g soil / 3 ml extract.

Preliminary testing of the salted and desalted solutions was done by spiking them with 2.5 µM arginine and analyzing them using a commercial electrospray ionization (ESI) source coupled to an LCQ-MS (Thermo Scientific, San Jose, CA, USA). The protonated arginine peak at m/z 175 can be seen much more clearly in the spectrum of the desalted extract (Figure 6). The desalting step removes metal oxalates and a variety of interfering organic substances present in the soil from the final amino acid eluate.

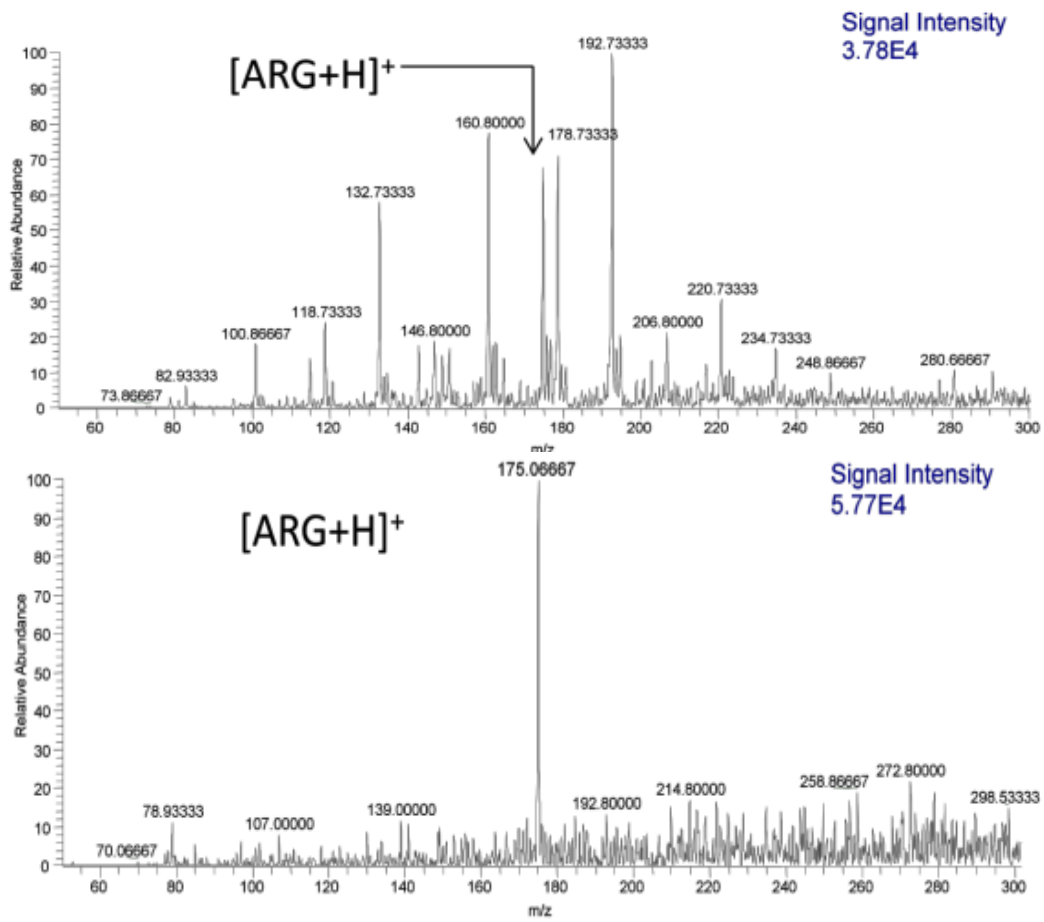

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Figure 6 Mass spectra of 2.5 uM arginine including salted (top) and desalted (bottom). Arginine can be seen as $[ARG+H]^+$ at m/z 175.

One concern of using the automated sample processing system is the interference of high pH in subsequent MS analysis. After the cation exchange column of AG50W-X8 resin is prepped with 3.0 M HCl, solution containing a mixture of salts and amino acids is introduced. Amino acids in solution bind to the resin in the column. The column is then desalted using oxalic acid. The amino acids are finally extracted from the resin using 2.5M NH_4OH. Therefore the final solution of amino acids is at pH of 11.9. For MS analysis, any analyte species must bear a net charge. Unfortunately, at this pH protonation of most amino acids via electrospray method is inhibited. One solution is to reduce the pH using acid. Adding a strong acid, HCl, results in a reduced pH but the concentration of the resulting NH_4Cl is very high. The sensitivity of ESI-MS is typically lowered by the presence of high concentration

of salts due to charge completion (Ikonomou et al. 1990; Tang and Kebarle 1993; Wang and Cole 1994). For the ESI of solutions with high salt content, the addition of ammonium acetate has been shown to improve signal stability and reproducibility, and can significantly lower adduction and background signals (Sterling et al. 2010). Since the eluate is already in a solution of 2.5 M NH_4OH, an ammonium acetate (NH_4Ac) buffer can be generated in the solution by simply adding acetic acid as $NH_4OH + CH_3COOH \rightarrow [CH_3COO]^- + [NH_4]^+ + H2O$.

A 100 µM mixture of 5 amino acids, histidine, arginine, lysine, phenylalanine, and therionine, was spiked into to the desalted eluate (2.5 M NH_4OH). The spiked extract was electrosprayed and analyzed with the Mini 10.5 as the concentration of acetic acid was increased. Initially, it was only possible to see protonated lysine, $[LYS+H]^+$ at m/z 175 and histidine, $[HIS+H]^+$ at m/z 156. As the concentration of acetic acid was increased up to 1.5 M, signal corresponding to the other amino acids, $[ARG+H]^+$ at m/z 175, $[PHE+H]^+$ at m/z 166, and $[THR+H]^+$ at m/z 147 became apparent (Figure 7). It is suggested that increased ionization efficiency of analyte

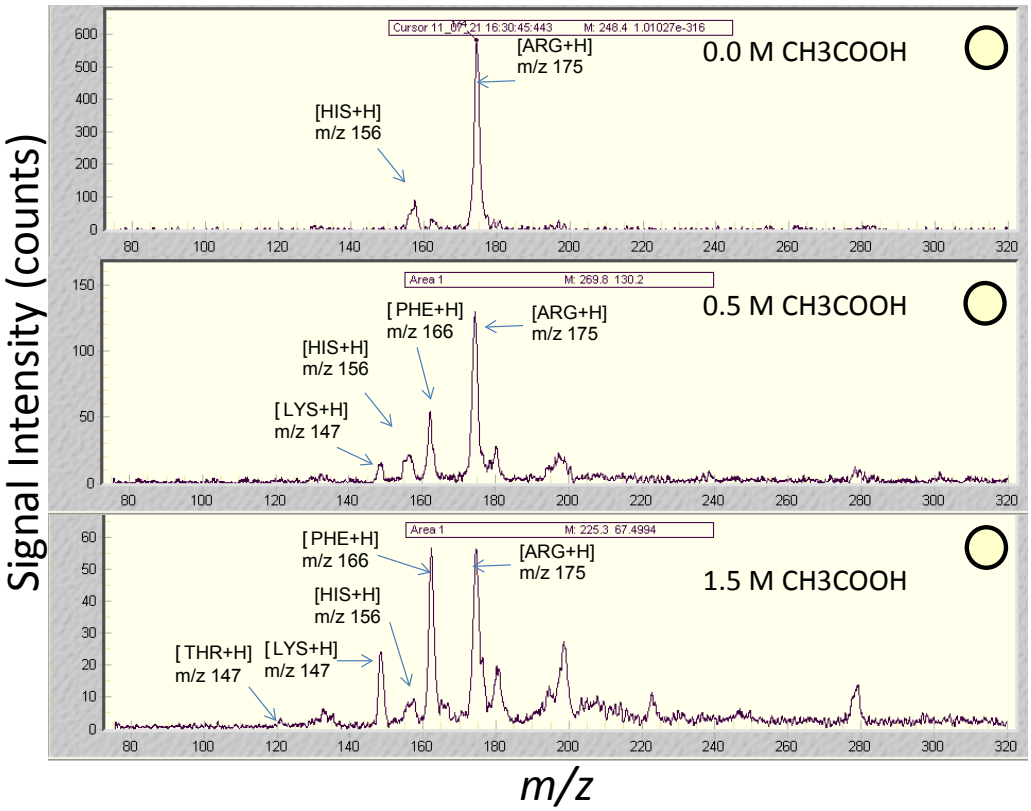

Figure 7: A 100 µM mixture of 5 amino acids, histidine, arginine, lysine, phenylalanine, therionine, was spiked into to the desalted eluate (2.5 M NH_4OH). The spiked extract was nanosprayed and analyzed with the Mini 10.5 as the concentration of acetic acid was increased. Initially, it was only possible to see protonated lysine, $[LYS+H]^+$ at m/z 175 and histidine, $[HIS+H]^+$ at m/z 156. As the concentration of acetic acid was increased up to 1.5 M, signal corresponding to the other amino acids, $[ARG+H]^+$ at m/z 175, $[PHE+H]^+$ at m/z 166, and $[THR+H]^+$ at m/z 147 became apparent.

molecules is achieved by the precipitation of NH_4Ac (and other ionic species) within the evaporating electrospray droplets (Iavarone et al. 2004). There is also a decrease in overall signal observed with the addition of acetic acid. Due to the increased concentration of ionic species, there is a reduced rate of droplet evaporation. This negative effect can be overcome by increasing the voltage applied to induce electrospray. This process performs a preparative step inside the electrospray droplet instead of at a lab bench. Future work will expand on this research by optimizing the chemistry of extraction while simultaneously developing an interface between the ASPS and Mini 10.5.

CONCLUSION

We have started the process of developing a system that can analyze atmospheric, liquid and solid samples in the field for organic molecules. This system, once completely completed, would serve as a field demonstration for future flight missions to bodies such as Mars, Europa and Enceladus. Currently the many of the components are fully field portable and able to perform unique scientific investigations.

ACKLODGEMENTS

This research was carried out at the Jet Propulsion Laboratory, California Institute of Technology under a contract from the National Aeronautics and Space Administration (NASA).

REFERENCES

Amelung, W. and X. Zhang (2001). "Determination of amino acid enantiomers in soils." Soil Biology & Biochemistry **33**(4-5): 553-562.

Bada, J., P. Ehrenfreund, F. Grunthaner, D. Blaney, M. Coleman, A. Farrington, A. Yen, R. Mathies, R. Amudson, R. Quinn, A. Zent, S. Ride, L. Barron, O. Botta, B. Clark, D. Glavin, B. Hofmann, J. Josset, P. Rettberg, F. Robert and M. Sephton (2008). "Urey: Mars Organic and Oxidant Detector." Space Science Reviews **135**(1): 269-279.

Beegle, L., J. P. Kirby, A. Fisher, R. Hodyss, A. Saltzman, J. Soto, J. Lasnik and S. Roark (2011). "Sample handling and processing on Mars for future astrobiology missions." Aerospace Conference, 2011 IEEE (5-12): 1-10.

Beegle, L., J. P. Kirby, A. Fisher, R. Hodyss, A. Saltzman, J. Soto, J. Lasnik and R. S. (2011). Automated Sample Handling and Processing on Mars for Future Astrobiology Missions. Aerospace Conference. Big Sky, Mt., IEEEE. **Paper #1602**.

Cheng, C. N. (1975). "Extracting and desalting amino acids from soils and sediments: Evaluation of methods." Soil Biology and Biochemistry **7**(4-5): 319-322.

Degens, E. T. and J. H. Reuter (1964). "Analytial techniques in the field of organic geochemistry." Advances in Organic Geochemistry, Proceeding of International Meeting **1962**: 377-402.

Iavarone, A. T., O. A. Udekwu and E. R. Williams (2004). "Buffer Loading for Counteracting Metal Salt-Induced Signal Suppression in Electrospray Ionization." Analytical Chemistry **76**(14): 3944-3950.

Ikonomou, M. G., A. T. Blades and P. Kebarle (1990). "Investigations of the electrospray interface for liquid chromatography/mass spectrometry." Analytical Chemistry **62**(9): 957-967.

Janfelt, C., N. Talaty, C. C. Mulligan, A. Keil, Z. Ouyang and R. G. Cooks (2008). "Mass spectra of proteins and other biomolecules recorded using a handheld instrument." International Journal of Mass Spectrometry **278**(2-3): 166-169.

Lee, J., X.-S. Zhang, M. Hegde, W. E. Bentley, A. Jayaraman and T. K. Wood (2008). "Indole cell signaling occurs primarily at low temperatures in Escherichia coli." Isme Journal **2**(10): 1007-1023.

Lee, K. and J. Hong (1995). "Nonionic adsorption of aromatic amino acids on a cation-exchange resin." Reactive and Functional Polymers **28**(1): 75-80.

Masuda, A. and N. Dohmae (2010). "Automated Protein Hydrolysis Delivering Sample to a Solid Acid Catalyst for Amino Acid Analysis." Analytical Chemistry **82**(21): 8939-8945.

Ouyang, Z., R. J. Noll and R. G. Cooks (2009). "Handheld Miniature Ion Trap Mass Spectrometers." Analytical Chemistry **81**(7): 2421-2425.

Ouyang, Z., G. X. Wu, Y. S. Song, H. Y. Li, W. R. Plass and R. G. Cooks (2004). "Rectilinear ion trap: Concepts, calculations, and analytical performance of a new mass analyzer." Analytical Chemistry **76**(16): 4595-4605.

Sokol, E., K. E. Edwards, K. Qian and R. G. Cooks (2008). "Rapid hydrocarbon analysis using a miniature rectilinear ion trap mass spectrometer." Analyst **133**(8): 1064-1071.

Sokol, E., R. J. Noll, R. G. Cooks, L. W. Beegle, H. I. Kim and I. Kanik (2011). "Miniature mass spectrometer equipped with electrospray and desorption electrospray ionization for direct analysis of organics from solids and solutions." International Journal of Mass Spectrometry **306**(2-3): 187-195.

Sterling, H., J. Batchelor, D. Wemmer and E. Williams (2010). "Effects of buffer loading for electrospray ionization mass spectrometry of a noncovalent protein complex that requires high concentrations of essential salts." Journal of The American Society for Mass Spectrometry **21**(6): 1045-1049.

Tang, L. and P. Kebarle (1993). "Dependence of ion intensity in electrospray mass spectrometry on the concentration of the analytes in the electrosprayed solution." Analytical Chemistry **65**(24): 3654-3668.

Wang, G. and R. B. Cole (1994). "Effect of Solution Ionic Strength on Analyte Charge State Distributions in Positive and Negative Ion Electrospray Mass Spectrometry." Analytical Chemistry **66**(21): 3702-3708.

Wilm, M. and M. Mann (1996). "Analytical Properties of the Nanoelectrospray Ion Source." Analytical Chemistry **68**(1): 1-8.

Xu, W., N. E. Manicke, G. R. Cooks and Z. Ouyang (2010). "Miniaturization of Mass Spectrometry Analysis Systems." **15**(6): 433-439.