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Edward D. Hoegg, Tyler J. Williams, Jacob R. Bills, R. Kenneth Marcus, David W. Koppenaal

A novel multi-electrode glow discharge provides increased sensitivity and analytical flexibility for *both* atomic and molecular MS determinations.

A Multi-Electrode Glow Discharge Ionization Source for Atomic and Molecular Mass Spectrometry

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Abstract

A new, multi-electrode, liquid sampling glow discharge ionization source for mass spectrometry is described. This ion source consists of multiple (2-4) counter (anode) electrodes in comparison to prior single counterelectrode designs of this type. In the experiments presented here these ion sources have been interfaced with ThermoScientific Exactive Orbitrap instruments and Advion Expression Compact Mass Spectrometer instruments. Advantages and analytical performance improvements are described. These include ability to use higher plasma currents, resulting in a more robust and energetic plasma exhibiting higher sensitivity, lower spectral background, ppt detection limits, and 2-3x faster washout times. A low-cost, 3D printed version of a dual counter electrode design is also described. The ion source can further be utilized in either atomic (elemental/isotopic) or molecular (molecular ion, fragmentation) ionization modes.

Introduction

This contribution is presented in honor of the retirement of our colleague, mentor, and friend, Professor Gary M. Hieftje of Indiana University. Professor Hieftje's contributions to analytical chemistry in general and atomic spectroscopy in particular are legion. He is responsible for many fundamental insights and advances in flame and plasma spectrochemistry and mass spectrometry. He has been particularly innovative in the development of new instrumentation tools, one of the most prominent and effective ways to accelerate scientific knowledge and contributions. It is in this spirit that we describe this new, multi-electrode glow discharge ionization source for applications in both atomic and molecular mass spectrometry. We can think of no better way to honor

Professor Hieftje than to promote and continue the development of new tools for extraordinary science.

Elemental mass spectrometry (MS) has enjoyed continuous (albeit gradual) development of new ion sources over the century or so of its common use. From electron impact (EI) sources in the earliest days (pre-1950's), to arc and spark discharges (1950-1980's), and then to modern plasma ion sources (1980's-present), new ion source development has been critically important. Among these developments the use of the inductively coupled plasma (ICP) as an ionization source stands tall, as ICP-MS has dominated the field since the mid-1980's. Its principal advantages of high and uniform ionization yields enable the ultimate in sensitivity across the periodic table, and have driven elemental MS to new heights of use and application.

Parallel ion source developments in the organic MS field have also occurred. The predominant ion sources developed include the EI source, electrospray ionization (ESI), and matrix-assisted laser desorption ionization (MALDI). Interestingly, the development of MS ion sources has proceeded along separate, broad organic/inorganic application pathways, with few (if any) common-use ion sources for both organic and inorganic/elemental MS use.

Along these lines, a new ion source capable of both organic and elemental ionization and analysis has been investigated by our research groups (Marcus/Clemson and Koppenaal/PNNL) over the last 9 years. This source, referred to as the liquid-sampling - atmospheric pressure glow discharge (LS-APGD) ion source, is a low-power (<50 W) microplasma (approximate size 1 mm^3), that operates in the abnormal glow discharge regime and is capable of ionizing both molecular and elemental constituents under different operating conditions. First demonstrated as an elemental ion source in 2011, this source was adapted from prior use as an optical emission (photon) source for elemental analysis (see a recent review for its history as both an optical emission source and a mass spectrometry ion source[1]). The first generation 'breadboard' LS-APGD ion source exhibited detection limits in the low ppb range and additionally provided isotope ratio measurement precision of better than 0.1% RSD.[2-5] A subsequent 2nd generation 'production prototype' version has also been described and has exhibited even better analytical performance while providing users with an easily retrofittable ion source chamber that can interchange with many Orbitrap and other types of mass spectrometers.[6] Ionization in either soft (molecular, fragmentation spectra) or hard

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(elemental, isotopic) modes, termed a combined atomic and molecular (CAM) ionization source, have been demonstrated. This aspect has in fact been used to demonstrate atomic mass resolution (R) of over 1 M in a recent report.[8]

The early LS-APGD versions described above used a very simple single cathode/single anode electrode arrangement. This publication describes a novel variation of this design in which multiple (2,3, and 4) anode (counter) electrodes work in concert with a common liquid-carrying cathode electrode. We refer to this design as a multi-electrode LS-APGD, a 3rd-generation of the LS-APGD type. The rationale for adding additional electrodes was prompted by our experiences with increasing plasma power with higher operating currents using a single electrode (i.e., above 30-50 mA), in order to further increase sensitivity and analytical performance. At these higher current levels, the anode (counter electrode) tended to overheat and deform, leading to erratic plasma stability, operation, and even extinguishing of the plasma.[1] Additional counter electrodes allow for distribution of (higher) current among 2, 3, and 4 electrodes. Additional benefits include formation of a larger, more robust and powerful plasma that is capable of higher ionization efficiency and better sensitivity, as well as alleviating plasma positioning and alignment issues. In addition, engagement of multiple electrodes provides a novel level of plasma tunability for the ionization/fragmentation of polyatomic or molecular species/analytes. Development, construction, and improved performance attributes of this design are presented herein.

Experimental

Source Design & Construction

The original single-electrode LS-APGD MS ion source has been described in previous works.[1-5] The LS-APGD source operates by applying a potential between a nickel or stainless-steel counter (anode) counter-electrode (MDC Vacuum Products, LLC; Hayward, CA) and a grounded solution-carrying (cathode) electrode. A new design for the LS-APGD ion source has been developed that is more durable, robust, user friendly, and reliable. The electrodes have been integrated into a single piece/cartridge of aluminum, of a size slightly larger than a credit card (actual dimensions 10L x 8.4W x 0.75H cm), see Figure 1a. The solution is delivered to the plasma using a concentric capillary system in which the outer capillary (1 mm i.d., 6.35 mm o.d.) delivers a cooling

He sheath gas, and an inner capillary (250 μm i.d., 360 μm o.d., Molex; Lisle, IL) delivers solution to the plasma. The solution flow rate is controlled via a syringe pump (Chemyx OEM 30020; Stafford, TX) and the gas flow is set via a mass flow controller (Alicat BC-C1000-He-232-NPT). Both the counter electrodes and solution/gas flow capillary/electrode are mounted in the card-sized aluminum block, which can be conveniently and firmly mounted, manipulated, and aligned using a complementary aluminum bracket with adjustment mechanisms. The plasma is ignited using a unique auto ignition system (patent pending) that imposes a temporary, controlled high voltage pulse sequence on the counter electrodes, resulting in instantaneous electron emission and plasma formation. The plasma voltage is automatically reduced to a lower operational voltage once the plasma is ignited and the preselected current established. The plasma current is controlled using an Ultravolt high voltage power supply (1C24-P60-I5, Ronkonkoma, NY). All controllers for plasma operation are housed in a control/utility box designed and assembled by GAA Custom Electronics (Benton City, WA). The unit consists of a 10 x 5 x 9" polycarbonate shell (Metcase; Bridgeville, PA), and is controlled using a Raspberry Pi 3 – Model B (New York, NY) system with a 7" diagonal resistive touchscreen display.

Additional source designs employing multiple counter electrodes can be seen in Figs 1b and 1c. We refer to these designs as dual-, tri-, or quad-electrode systems based on the *number of counter electrodes* in the system (a common solution electrode is employed in each case also). The dual-electrode design depicted in Fig 1b uses the same components as the traditional single electrode design, albeit with the addition of a second counter electrode with its own voltage source, with the solution electrode operating at the common, ground. The counter electrodes in this configuration are co-linear and placed perpendicular and equidistant to the solution electrode. The dual-electrode design is conveniently amenable to the same aluminum card-based design described above. The tri- and quad-electrode designs shown in Figure 1c also utilize the same components as the other operating modes, but in this case are integrated into a cross-based aluminum bracket mount design. This design adds the addition of either one or two additional counter electrodes to the dual-electrode mode for a total of three or four counter electrodes. Voltages for all counter electrodes are supplied by separate, independent, current-contolled voltage supplies (ie the exact same current flows to each

of the counter electrodes). Three of the power supplies used here were the Ultravolt model described earlier, while the fourth was a Glassman Model EH (High Bridge, NJ); a fourth Ultravolt supply was unavailable for these experiments and this was only reason for using the Glassman supply . Typical currents of between 25-50 mA are set and controlled for each counter electrode; this ensures a stable, centered plasma within the electrode axes region. In this way, additional electrodes provide greater current density in the plasma glow as well as added heating to affect the vaporization of the analyte-carrying electrolyte solution. There is no wandering or jumping of the plasma from one electrode to the other due to the controlled currents; the voltage changes observed are also insignificant. The system is switched between dual, tri, and quad electrode modes by simply turning one or more of the power supplies on/off. Future power supply designs, under design/development, will utilize a single integrated power supply capable of automated, multiplexed, and independent voltage channel operation, thus enabling use of a single as opposed to multiple separate supplies.

In addition to the aluminum holder employed at PNNL, a 3D-printed LS-APGD was designed and fabricated at Clemson University out of polylactic acid filament on a Dremel 3D45 printer. The 3D printed model was outfitted with two MHV connectors, PEEK fittings for liquid lines, and stainless-steel fittings for gas lines. The electrodes were connected to the ground and "hot" portions of the MHV connector via internal connections. This design was engineered to be a replacement for the ESI source on an Advion (Ithaca, NY) Expression[L] Compact Mass Spectrometer (CMS). A diagram and photo of the 3D printed ion source is provided in Electronic Supplementary Information Figure 1 (ESI Fig. 1).

Mass Spectrometer Systems

Experiments were carried out using three different mass spectrometer platforms. Proof of concept and initial feasibility studies for the operation of the LS-APGD with multiple electrodes was completed using a ThermoScientific (San Jose, CA) Exactive mass spectrometer at the Environmental Molecular Sciences Laboratory (EMSL) user facility at PNNL. The majority of the work comparing the single electrode and dual-electrode source designs was completed at Clemson University using a

ThermoScientific Q Exactive Focus mass spectrometer and an Advion (Ithaca NY, USA) Expression[L] Compact Mass Spectrometer (CMS).

Interfacing with both Exactive MS platforms has been described previously and was completed by simply removing the commercial ESI source and attaching the plasma source, for which several mounting designs have been implemented and described previously.[3-6] In all system configurations, the solution electrode was mounted in-line with the sampling orifice with the counter electrodes mounted collinearly with each other, but perpendicular to the solution flow axis. Based on a brief optimization experiment, there was no modification, including changes to ion optic potentials or capillary temperatures, made to either Exactive platform. The instruments were operated in positive ion mode and, as in previous experiments, collision induced dissociation was used in order to limit any interfering molecular species. For these experiments, an in-source collision induced dissociation (CID) of 75 eV and a higher energy collision induced dissociation cell (HCD) voltage of 100 eV were used. In experiments conducted at Clemson University using the Q Exactive Focus, the quadrupole filter, located prior to the instrument's C-trap, was set to pass only ions of analytical interest into the C-trap (the C-trap serves to collect and compress the ion packet prior to injection into the Orbitrap mass analyzer).

The experiments completed with the Advion Expression[TM] Compact Mass Spectrometer (CMS) required little modification to the instrument and has been described in detail recently. Either single[7] or dual LS-APGD source designs were mounted inside the Advion source block for direct coupling to the instrument by simply removing the standard ESI source. Different from other instrument couplings, the LS-APGD is held at a 25º angle from the entrance into the mass spectrometer to mimic the angle of the instruments ESI source. Full scan data was acquired using a scan rate of 500 ms across a mass range of 10-250 m/z and data collected using selected ion monitoring (SIM) used a mass window of 0.3 Da and a dwell time of 50 ms.

Test Samples & Standards

Experiments at PNNL were carried out using four test solutions. The first was a multi-element test solution containing Rb, Ag, Ba, Tl and U at a concentration of 500 ng mL^{-1} each. Calibration solutions were made up of 1 ng mL^{-1} - 10,000 ng mL^{-1} containing

Cu, Cs, and Pb. In order to test the ability to make high precision isotope ratio measurements a 500 ng mL^{-1} U solution of natural isotopic abundance was prepared. Finally, a multi-element solution containing Cu, Rb, Ag, Cs, Ba, Pb, Tl, and U was prepared at a concentration of 500 ng mL^{-1} each. Evaluation of the dual-electrode design on the CMS utilized two multi element solutions, one containing Rb, Cs, and Tl, and the other containing Ca, Mg, Cu, K, Na, Pb, Zn, Fe, and Cd. Calibration solutions for the first solution ranged from 50 ng mL^{-1} to 10,000 ng mL^{-1} of each element, and for the second solution ranged from 500 pg mL^{-1} to 1000 ng mL^{-1} of each element.

Organic samples were prepared in a 70:30 MeOH:H_2O mixture. The solvent mixture was prepared using methanol (HPLC grade, EMD Millipore, Billerica MA) and 18.2 MΩ cm^{-1}deionized water from an Elga PURELAB flex water purification system (Veolia Water Technologies, High Wycombe, England). Caffeine was obtained from Aldrich chemical company (St. Louis, MO) and triethyl phosphate was obtained from Alfa Aeser (Ward Hill, MA). Both were dissolved in the 70:30 MeOH:H_2O mixture at a concentration of 1 μg mL^{-1}. The samples were introduced into the ionization source using the MeOH:H2O mixture as the mobile phase an introducing the sample in discrete 20 μL injections.

Results and Discussion

To compare the single and dual electrode designs, preliminary experiments were completed at both PNNL (ThermoScientific Exactive) and Clemson (ThermoScientific Q-Exactive). The first experiments looked at the current-voltage (i-V) relationships of the two designs and the second examined ion intensity/signal comparisons.

Plasma Operation and Operating Regimes

Glow discharges, such as the LS-APGD, are defined by the i-V relationships for a given plasma size, across their operating regimes. Given the changes made in these designs, confidence was needed that operation in a glow discharge regime was maintained. Accordingly, i-V plots were generated (Fig. 2) where the discharge maintenance voltage is plotted for the current imposed on each electrode; whether single or double. The results of the current voltage plot generated by the single electrode design show a very slightly positive slope which corresponds with the abnormal glow discharge regime, consistent with previous studies[1]. The low extent of a

positive slope is attributed to an increase in the plasma volume as the current increases. Previous studies used a glass sleeve to limit the contact area that the plasma had with the counter electrode, this glass sleeve has been removed in recent designs to limit carryover and simplify operation, however, without the glass sleeve, the plasma grows in size as the current is increased. With the dual-electrode design, there is an initial slight increase in the total voltage (the sum of the two individual supplies) as the current is increased, but at the highest current, beyond which a slight drop is seen. Here again, the plasma is getting visibly larger when dual counter electrodes are operated at higher currents. Somewhat surprising in this data is the fact that there appears to be no sort of cooperative effects in the case of the dual-electrode system. It had been expected that there might be a lessening of the total required voltage, with the increase seen being reflective of the slightly larger interelectrode spacing. The drop in potential at the 50 mA (each) current may be some indication of cooperativity, but beyond this point the system suffers from electrode overheating. The general trends suggest that *electrically* two different plasmas are operating with a common cathode (an interesting observation that might be used to advantage but requires further investigation). As will be seen in the subsequent mass spectrometric responses, the net effects are indeed a reflection of greater amounts (≥2X) of overall power in the plasma. Future experiments that might possibly restrain the plasma size are necessary to obtain a truly valid comparison. However, the initial voltage ramp results indicate that the dual electrode plasma is likely operating in a similar glow discharge regime as the single.

Analyte ion and background improvements

The single counter electrode source geometry has been used as an ionization source for mass spectrometry since 2011,[2] when it was first interfaced with a ThermoScientific Exactive MS. It was reasoned that a larger and more powerful plasma would provide an improvement in ion production, sensitivity, and other analytical figures of merit, and that a simple way to obtain such an improvement would be the addition of plasma current via additional electrodes. Previous attempts at providing more current with a single electrode showed inconsistent and sporadic results owing to electrode heating, deformation, and even destruction[1]. Using separate electrodes carrying additional current resolves the overheating issues, effectively spreading the current. It additionally provides for a larger and more robust plasma, likely alleviating sensitivity to

positioning and alignment. Comparison of improvements with a dual electrode system was completed using a multi-element solution containing 500 ng mL^{-1} each of Rb, Ag, Ba, Tl and U. Spectra (presented as ESI Fig. 2a-d) show signal intensity improvements (up to 150X) with the dual electrode system in comparison to the single electrode system, depending on element. When a wide digitization range is used, Rb is the dominant ion in the spectra and an approximate increase of 6x is observed comparing the two designs. When Rb is removed from the Orbitrap acquisition using a narrower digitization window, Fig 2c and d, a 17X improvement in sensitivity is observed for Ag, and an improvement of over 175X is observed for Ba in comparison to the single electrode system. Similar improvements in response are seen for Tl and UO$_2$. The differences in the level of enhancement reflect their improved efficiencies between the two operation modes. This improved efficiency is also observed in the ion collection time of the orbitrap. During the experiments the maximum injection time (collection time) was set to 100 msec. When the single electrode design was used, the injection time was 100 msec. When the dual electrode was employed not only was the signal intensity improved, but the injection time was only 64 msec for an average of 10 scans signifying an increase in the number of ions being generated, ie a higher ionization efficiency.

An additional advantage with the dual electrode system is observed in background intensities. Significantly fewer molecular background/concomitant ions are observed in the dual electrode system. This advantage can manifest itself in better detection limits and improved sensitivity and precision. The reduction in the number of background molecular ions is likely caused by the higher power and temperatures which leads to greater fragmentation and destruction of concomitant molecular species. Previous studies using the single electrode LS-APGD showed that these background ions are typically solvent-related clusters, taking the general form of $(H_2O)_nH^+$, or perhaps hydrated metal ion forms of these solvent clusters.[2]

A similar set of experiments was run at Clemson University using the Advion Expression[L] Compact Mass Spectrometer (CMS). This instrument is a small, lower-overhead quadrupole MS for laboratory or field-portable applications. A multi-element solution containing Rb, Cs, and Tl at a concentration of 10 µg mL^{-1} each was used to again examine analyte species and background characteristics of the ion source with this MS system. The first experiment considered the ability of the dual-electrode

configuration to reduce the number of molecular background ions, as would be most beneficial on the quadrupole analyzer instrument. As seen in Fig. 3, when the spectrum generated using the single electrode operating at 30 mA is overlayed with the spectrum generated using the dual-electrode of 30 mA each, there is a significant increase in response, as well as a significant decrease in the number and intensity of background ions when using the dual-electrode design. In this case, each of the metals shows an ~4x improvement, while discrete solvent-related background peaks drop in intensity to even greater extents. For example, the ratio of the ^{133}Cs to an adjacent background ion at m/z = 135 Da (equivalent to a species of the form $(H_2O)_4NO_3H^+$), increases from 18 to 262.

A new, interesting observation was made during the CMS experiments regarding washout times. This is the time it takes for the signal to return to baseline after (or between) analyte injections. Washout times were significantly reduced for the dual-electrode system compared to the single electrode system. Figures 4a and 4b show the signal transients of a 20 μL injection of 10 μg mL^{-1} Rb sample for the two powering modes. In principle, the injection peak should be ~40 s wide, though longitudinal diffusion broadening would add somewhat to that. Both transients do indeed reflect the expected general shape. Closer inspection of the trailing edges of the transient reveals that the single electrode does not reach the pre-injection level until approximately 190 s after the initial injection pulse, while the complete washout time for the dual-electrode case is ~90 s. It is hypothesized that the increased energy, plasma temperature, and the operating distance between the microplasma and the sampling orifice decreases analyte deposition there, associated memory effects, and resulting background levels. With the single-electrode system, the plasma is operated at a distance of about 1 mm from the MS orifice while for the dual-electrode design it can be operated farther away (up to ~40 mm) from the orifice with better sensitivity. This again indicates an analytical advantage for the dual- or other multi-electrode systems.

Limits of Detection

The differences in detection limits between the single- and dual-electrode configurations were quantified using a ThermoScientific Q Exactive Focus, located at Clemson University, and were measured using a multi-element solution containing, Cu,

Cs, and Pb. Solutions were diluted to generate response curves that cover a 5 orders-of-magnitude concentration range. While the solution contained multiple elements each one was observed individually by using the quadrupole mass filter to select analyte ion mass ranges passed into the C-trap/Orbitrap. Additionally, a narrow acquisition/digitization range was used to further select said ions. While Cs is monoisotopic, for Cu and Pb, where multiple isotopes are present and thus simultaneously measured by the Orbitrap, only ^{65}Cu and ^{204}Pb were plotted. The response curves for each element/isotope are plotted in ESI Figs. 3a-c, where each data point represents 3 injections of 100 µL each. For most cases the error bars are smaller than the data point itself. In these experiments, the single electrode and each electrode of the dual-electrode designs were operated at 30 mA.

A natural question arises as to whether there is a difference between running two counter electrodes at 30 mA each or running a single counter electrode at 60 mA (total of 60 mA powering the plasma in both cases). Experiments were accordingly also run to address this question and for comparison to the other analytical modes (see again ESI Figs. 3a-c). In the case of Cu and Pb, there is an order of magnitude improvement for both the raw responses and limits of detection when comparing the dual 30 mA electrode results to the 30mA single electrode. The dual 30 mA dual electrode system also outperforms the 60 mA single electrode system, although the 60 mA single electrode system offers improved performance over the 30 mA single electrode system. When analyzing Cs, using the single electrode system at both 30 mA and 60 mA, the response curves become non-linear at the high concentration range (>1,000 ng mL^{-1}). This was not seen for either Cu or Pb even when the most abundant isotope was plotted instead. This response was not seen when using the dual-electrode for any of the samples tested, which suggests that ionization limits may be reached for the easily-ionized Cs at high solution concentrations with the single-electrode design. This, along with the signal response improvement when using the dual-electrode system, suggests that the ionization efficacy of the dual-electrode system is greater than that of the single electrode system.

Based on these response curves, limit of detection (LOD) values were calculated for each element and microplasma powering condition, Table 1. LOD figures were calculated using the equation

$$LOD = \frac{3\sigma}{m}$$

where σ is the standard deviation of the lowest concentration value, m is the slope of the line, and a multiplier of k=3 is used, representing a 99% confidence interval. In the case of Cs the LOD is at the 2 ppt level, with both Cu and Pb having values that extend >3X lower when using the dual-electrode design. When the absolute-mass detection limit is calculated for each of these elements, the quantity ranges from tens to hundreds of femtograms, an impressive performance considering the low (100 μL sample volumes used).

Sensitivity and LOD experiments were again run using both the 30 mA single electrode and the dual 30 mA electrode systems on the CMS quadrupole instrument. The data was taken using triplicate injections, 20 μL each, of the multi-element solution, diluted to cover 4+ orders of magnitude, 500 pg mL^{-1} to 1000 ng mL^{-1}. The CMS system was operated in selected ion monitoring (SIM) mode with a mass range centered on the most abundant isotope of each element with a mass range of 0.3 Da and a dwell time of 50 ms. Table 2 compares the results from this study and shows nearly universal improvement in the calculated LODs when using the dual-electrode system, with only Ca curiously breaking the trend. In this instance, and also the case for Na and K, the presence of molecular isobars is the likely limiting feature. That said, a significant decrease in the number of background ions when using the dual-electrode system compared to the single-electrode system was again observed in these experiments. While the CMS system is clearly less sensitive than the Orbitrap MS system, the results are still impressive for this low cost and small footprint system.

Isotope Ratio Measurement Precision

One of the more interesting applications of the LS-APGD has been as a new ionization source for measuring isotope ratios when coupled with orbitrap mass spectrometers. Our work,[3-5] as well as that of Eiler and colleagues (low mass stable isotope and oxyanion isotope ratio work),[11-14] indicate that excellent analytical ratio precision can be achieved with Orbitrap MS systems, contrary to conventional wisdom. Although our research is relatively recent, it has already met or exceeded traditional elemental mass spectrometer performance when measuring U or other isotope ratios.[3-5]

By harnessing the resolving power of orbitrap instruments, it is also possible to measure isotope ratios of samples, even those that typically suffer from interelement isobaric interferences. In order to show that there is no degradation of performance when performing high precision isotope ratio measurements using the dual-electrode ion source, a test solution containing CRM-129a ($^{235}U/^{238}U$ = 0.0072614) was analyzed (Table 3). When these results are compared to measurements taken using the single electrode, the measurement precision remains excellent, with no statistical difference observed. There is however a slight improvement in the accuracy with the dual-electrode system. This is most likely due to the reduction of background ions that lead to the noise levels (even though the noise level is lowered by software treatment in the Exactive MS system, see earlier work by our group[3-6]). Note that these values are not corrected for mass bias, which is typical with many other MS systems. When compared to the International Target Values (ITV) for Measurement Uncertainties in Safeguarding Nuclear Materials,[15] the uncertainty measured here falls below the acceptable random uncertainty component of the ITV, as had previous single-electrode efforts.[16-17]

Molecular Species Analysis

While the LS-APGD was originally implemented as an atomic ion source, it has been shown as a viable ion source for molecular analysis as well. This is accomplished by simply changing the sample preparation to use an organic solvent, such as a MeOH:H_2O solution, which effectively "cools down" the plasma which yields molecular mass spectra with a high degree of information about the compound. Previous studies have shown that the discharge current, and resulting number of available electrons generated, corresponds with the amount of fragmentation with high currents yielding more fragmentation.[3,10] By doubling the power density of the plasma, the resulting electron density will be higher suggesting a greater degree of ionization/fragmentation. The concept of using single and dual electrode operation to affect predominately chemical ionization (CI) versus electron ionization (EI) spectral features is illustrated in Figs. 5a and b. In this case, the common organic mass spectrometry standard, caffeine and triethyl phosphate (a chemical warfare simulant), are used as demonstrations, respectively. These samples were run as discrete 20 µL injections on the Advion CMS using the 3D-printed LS-APGD ion source. As can be seen, the mass spectra obtained using the single electrodes are very much akin to chemical ionization sources, where

proton donation yields large amounts of the (M+H)$^+$ pseudo-molecular ion, where the dual electrode results in a larger degree of fragmentation for both compounds. Similar to the atomic analysis presented above, the number of solvent-related background ions is also reduced when using the dual electrode source. Further investigation is required to deduce and optimize the exact ionization mechanisms and resulting fragmentation pathways. However, an advantage of the multi-electrode LS-APGD system is that one could rapidly pulse (ms) the second counter electrode to produce alternating CI/EI spectra on time scales of relevance for liquid chromatography elution peaks. In this way, a single quadrupole analyzer could affect many of the desired functions of triple-quadrupole instruments.

Tri- and Quad-Electrode Systems

In an effort to further improve the LS-APGD performance, experiments focused on increasing the number of counter electrodes were conducted at PNNL. A multi-element solution containing 500 ng mL^{-1} of Cu, Rb, Ag, Cs, Ba, Pb, and U was analyzed using a dual-electrode, tri-electrode, and quad-electrode LS-APGD configuration, as described in the Experimental Section and Fig. 1c above. Results are shown in Figs. 6a-c, where an approximate order of magnitude increase for Rb, Ag, and Cs ion intensities is observed as each additional plasma counter electrode is engaged. The previous studies comparing the single and dual electrodes observed a decrease in the recorded ion injection times on the Orbitrap in the latter case, owing to higher ion currents. In the studies that compared the dual, tri, and quad electrode designs, a decrease was only observed when using the quad electrode, a 77 msec average injection time for 10 scans. For the dual and tri electrode systems the injection time was recorded to be 100 msec, the maximum allowable injection time for these experiments. Additionally while there was improvement between the dual, tri, and quad electrode systems, the sensitivity of the dual electrode system is a factor of 10 less in these experiments than those presented above, reflecting some variance between experiments. Given the increase in sensitivity, and the normal voltage observed on each of the power supplies during the experiments it is not like that the problem is with the ion source but rather with the interface or the MS itself. In fact in later servicing of the instrument it was observed that the ion source inlet had significant soot built up on the ion optics reducing the ion transmission efficiency. This suggests that an even greater

improvement may be realized in future experiments. At the same time, while perhaps not of an issue with the outstanding mass resolving power of the Orbitrap, the spectral background species become effectively non-existent.

The physical characteristics of the multi-electrode plasma of course change significantly. The size and shape of the plasma increases with addition of counterelectrodes, to the point with the quad-electrode system that the plasma adopts a tail flame of sorts with an appearance akin to a mini-ICP (see photograph, Fig. 7). In this case the primary plasma is a coalesced, 4x cylindrical-to-spherical/toroidal, shape of nominal 3 x 3 mm cross-sectional size (not including tail flame). This quad electrode configuration has the benefit of being used as a single-, dual-, tri-, or quad electrode system according to sensitivity or other analytical needs. This configuration allows active, or "hot", selection of the single/dual/tri/quad modes (i.e., the plasma can be increased or decreased in power by simply powering or de-powering each electrode sequentially). This feature may have future advantage for selective ionization of certain elements, use or avoidance of interferent ions, or use in a combined atomic or molecular analysis mode, results of which will be reported in a subsequent work. It is also presumed that designs using additional multi-electrodes might result in even better performance.

Conclusion

A new multi-electrode LS-APGD ion source has been demonstrated to show significant analytical advantages for both elemental and molecular mass spectrometry. In the atomic mode, increased analyte ion yields (approximately an order of magnitude improvement for each counter electrode added) and lower detection limits are achieved. In addition, spectral background contributions and analyte washout (memory) times are reduced. These improvements are due to higher plasma powers (and likely temperatures) being achieved with the multi-electrode design. In the molecular mode, using multiple electrodes also shows higher degrees of ionization and fragmentation, indicating that this source can be capable of both soft and hard ionization modes. A key development in the course of this work is the ability to assemble LS-APGD sources of various geometries using straight forward 3D printing techniques. At this point, materials costs for the source bodies, exclusive of commercial high voltage

feedthroughs and the like, are less than $10 per device. Future work will seek to demonstrate the efficacy of this ion source for specific applications, and there are many fundamental questions to be addressed in terms of the coupling of higher power densities into the microplasma. This work demonstrates a significant addition to the repertoire of available ion sources for mass spectrometry, and it is hoped that this development will spur adoption and additional investigations and applications by new research groups and instrument manufacturers. A US patent covering portions of this work is pending.

Acknowledgements

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Table 1. Comparison of single vs dual electrode LS-APGD results. Single electrode held at either 30 mA or 60 mA; Dual electrodes held at 30 mA (each). 100 mL injections. Exactive Orbitrap MS system utilized.

Electrode Configuration	(Isotope)	(ng mL^{-1})	(pg)
Dual Electrode (30 mA)		**0.00068**	**0.07**
Single Electrode (60 mA)	^{65}Cu	0.02249	2.25
Single Electrode (30 mA)		0.09864	9.86
Dual Electrode (30 mA)		**0.00217**	**0.22**
Single Electrode (60 mA)	^{133}Cs	0.01062	1.06
Single Electrode (30 mA)		0.01443	1.44
Dual Electrode (30 mA)		**0.00068**	**0.07**
Single Electrode (60 mA)	^{204}Pb	0.00563	0.56
Single Electrode (30 mA)		0.01180	1.18

Table 2. Comparison of single vs dual electrode LS-APGD LOD's. Single electrode held at 30 mA and dual electrodes held at 30 mA (each). 10 mL injection. Advion Expression^{TM} CMS system utilized.

Element	Single Electrode (ng mL^{-1})	Dual Electrode (ng mL^{-1})	Dual Electrode (ng)
Na	424	134	1
Mg	500	6	0.06
K	797	103	1
Ca	35	50	0.5
Fe	310	72	0.7
Cu	140	66	0.7
Zn	948	26	0.3
Rb	28	2	0.02
Cd	106	0.5	0.005
Cs	18	5	0.05
Tl	20	6	0.06
Pb	128	24	0.2

Table 3. Comparison of $^{235}U/^{238}U$ isotope ratio measurements using single vs dual electrode LS-APGD ion source with Exactive MS system.

	Single Electrode	Dual Electrode
Average	0.006802	0.006855
Std Dev	5.2E-06	3.9E-06
%RSD	0.076	0.057

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Figure Captions

Figure 1. a) New LS-APGD design showing electrodes along with electrical and solution connections integrated into a compact, solid aluminum card/cartridge. This card can be easily mounted, manipulated, and deconstructed/rebuilt. b) Dual-electrode design with two counter electrodes. c) Quad electrode design with up to 4 counter electrodes, using a cross-shaped variant of the card design.

Figure 2. Current-voltage plot for the new LS-APGD dual-electrode design compared to the traditional single electrode design, both affected on the aluminum card source assembly. Solvent = 2 % HNO3, solution flow rate 30 μL min^{-1}, He sheath flow = 0.5 L min^{-1}.

Figure 3. Comparison of single- vs dual-electrode signal response for elements Rb, Cs, and Tl, showing ~3-5x increased signal response for dual-electrode LS-APGD, using Advion Expression^{L} CMS system.

Figure 4. Rb signal washout times for single (a) vs dual (b) electrode LS-APGD runs using Advion Expression^{L} CMS system. Faster washout by ~3.5x is noted for the dual electrode source.

Figure 5. Molecular spectra for caffeine (a) and triethyl phosphate (b) acquired using single and dual electrode 3D printed LS-APGD ion source, Advion Expression^{L} MS. Note higher fragmentation levels and decreased background with dual electrode ion source use.

Figure 6. Cu, Rb, Ag, Cs, Ba, Pb, and U intensity plots for dual (a), tri (b), and quad (c) electrode LS-APGD runs using Exactive Orbitrap MS system. An approximate 10x increase is observed with addition of each counter electrode.

Figure 7. Photograph of quad-electrode LS-APGD ion source, showing 4 counter electrodes in vertical axis, along with horizontal solution electrode and ion sampling capillary of PNNL/EMSL Exactive Orbitrap MS.

Electronic Supplementary Information – Figure Captions

Electronic Supplementary Information Figure 1. Photograph of 3D-printed LS-APGD dual-electrode ion source. This ion source was used in Advion Expression Compact MS experiments.

Electronic Supplementary Information Figure 2. Spectra of a multi-element solution containing 500 ng mL-1 of Rb, Ag, Ba, Tl and U taken using the single and dual electrode designs on a Q Exactive Orbitrap mass spectrometer. A) Single electrode LS-APGD and a wide digitization range, B) dual electrode LS-APGD and a wide digitization range, C) Single electrode LS-APGD and a narrow digitization range, d) dual electrode LS-APGD and a narrow digitization range. Wide digitization range includes Rb ions, narrow range excludes Rb ions.

Electronic Supplementary Information Figure 3. Response curves generated using the single electrode design operated at 30 and 60 mA and the dual electrode design with each electrode operated at 30 mA. Three elements were analyzed, and the minor isotope was plotted; A) ^{204}Pb, B) ^{65}Cu, and C) Cs.

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Multi Electrode Paper, Koppenaal
Figure Legends

Figure 1. a) New LS-APGD design showing electrodes along with electrical and solution connections integrated into a compact, solid aluminum card/cartridge. This card can be easily mounted, manipulated, and deconstructed/rebuilt. b) Dual-electrode design with two counter electrodes. c) Quad electrode design with up to 4 counter electrodes, using a cross-shaped variant of the card design.

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Figure 7. Photograph of quad-electrode LS-APGD ion source, showing 4 counter electrodes in vertical axis, along with horizontal solution electrode and ion sampling capillary of PNNL/EMSL Exactive Orbitrap MS.

Liquid Flow

Gas Inlet/ Flow

Inner Capillary

Electrical Connection

Outer Capillary

Counter Electrode

Solution Electrode

Figure 1a

Solid Counter Electrode

Outer Capillary

Inner Capillary

Liquid Flow

Gas Inlet/ Flow

Figure 1b

Outer Capillary

Liquid
Flow

Inner
Capillary

Solution Electrode

Gas Inlet/ Flow

Electrical
Connection

Solid
Counter
Electrode

Figure 1c

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Figure 2

Figure 3

Figure 4A

Figure 4B

Figure 5A

Figure 5B

Triethyl Phosphate
(1 μg mL^{-1}),
70:30 MeOH:H$_2$O

— Dual Electrode
— Single Electrode

Figure 6a

Figure 7