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Electrochemical Ionization and Analyte Charging in the Array of Micromachined UltraSonic ElectroSpray (AMUSE) Ion Source

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Abstract

Electrochemistry and ion transport in a planar array of mechanically-driven, droplet-based ion sources are investigated using an approximate time scale analysis and in-depth computational simulations. The ion source is modeled as a controlled-current electrolytic cell, in which the piezoelectric transducer electrode, which mechanically drives the charged droplet generation using ultrasonic atomization, also acts as the oxidizing/corroding anode (positive mode). The interplay between advective and diffusive ion transport of electrochemically generated ions is analyzed as a function of the transducer duty cycle and electrode location. A time scale analysis of the relative importance of advective vs. diffusive ion transport provides valuable insight into optimality, from the ionization prospective, of alternative design and operation modes of the ion source operation. A computational model based on the solution of time-averaged, quasi-steady advection-diffusion equations for electroactive species transport is used to substantiate the conclusions of the time scale analysis. The results show that electrochemical ion generation at the piezoelectric transducer electrodes located at the back-side of the ion source reservoir results in poor ionization efficiency due to insufficient time for the charged analyte to diffuse away from the electrode surface to the ejection location, especially at near 100% duty cycle operation. Reducing the duty cycle of droplet/analyte ejection increases the analyte residence time and, in turn, improves ionization efficiency, but at an expense of the reduced device throughput. For applications where this is undesirable, i.e., multiplexed and disposable device configurations, an alternative electrode location is incorporated. By moving the charging electrode to the nozzle surface, the diffusion length scale is greatly reduced, drastically improving ionization efficiency. The ionization efficiency of all operating conditions considered is expressed as a function of the dimensionless Peclet number, which defines the relative effect of advection as compared to diffusion. This analysis is general enough to elucidate an important role of electrochemistry in ionization efficiency of any arrayed ion sources, be they mechanically-driven or electrosprays, and is vital for determining optimal design and operation conditions.

Keywords

Ion transport; Scaling analysis; Electrochemical ion generation; Analyte charging; Mass spectrometry

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1. Introduction

Development of high throughput and multiplexed ion sources is an emerging trend in modern bioanalytical mass spectrometry, which requires arraying and massively parallel operation of individual devices. One of the promising candidates of such arrayed devices is the AMUSE (Array of Micromachined UltraSonic Electrospray) ion source. Not only enabling massively-parallel sample analysis, AMUSE also conceptually differs from electrospray ionization (ESI) by utilizing mechanically-driven droplet ejection instead of electrically-driven fluidic dispersion of ESI [1–4]. This allows for independent control of analyte charging and droplet/ion formation, enabling low voltage (soft) ionization of a wide range of analytes and flexibility in the choice of solvents [5–8]. Enabled by the array-domain separation of the AMUSE ion source, multiplexed operation has been demonstrated, thus establishing a direct path to a multiplexed ion source for mass spectrometry [2]. AMUSE has also shown superior softness of analyte ionization compared to conventional ESI under certain operating conditions [8]. Enhancements in the mass spectrometric (MS) response (signal abundance, sensitivity, and stability) has been also recently achieved by inducing localized charge separation at the droplet ejection point under static (DC) and dynamic (AC) electric fields [6], and explained using an in-depth fundamental charge transport analysis and simulations [9].

In electrospray ionization (ESI) [10–14] and mechanically-driven, droplet-based (AMUSE) [1–9] ion sources, analyte charging takes place in solution through adduct formation with available ions. Adduct formation typically occurs in the form of protonation and/or adducts formed with various ions from salts in the solution or even electrochemically introduced metal ions [10,15–18]. Electrospray ion sources utilize Taylor cone electric field focusing for both droplet formation and placing net charge on droplets. The application of a large electric field in ESI ion sources induces electrokinetic flow accomplished by charge separation in the course of Taylor cone formation, leading to charged fluid dispersion. Taylor cone formation describes the phenomena by which increasing charge density at the fluid interface creates Coulombic forces that overcome surface tension, resulting in a jet of highly charge droplets [10,13–14, 19]. Once the highly charged droplets are created, the transformation of solute species into free ions in the gas phase (desolvation) occurs by either the charge residue mechanism or the ion evaporation mechanism [11,15,20–21]. These processes are interconnected and difficult to investigate individually in conventional ESI sources [10,13–14,16–17]. The AMUSE ion source allows for analysis of each process independently, uncoupled from the other processes, which is extremely valuable for gaining fundamental insight.

In order to fully understand the operation of the AMUSE ion source and other droplet-based ion sources an investigation into analyte ionization by electrochemically introduced ions is investigated in this work. In general, the ions used for charging can be introduced in a number of ways. One typical method for bioanalytical MS is the addition of a weak acid (acetic, formic, etc.), reducing solution pH by introducing hydrogen ions resulting in protonation of the analyte molecule. In the case of protonation, the adduct formation is a homogenous reaction which occurs essentially instantaneously and analyte charging is trivial. In other cases, the adducts are formed by the addition of a variety of cations (positive mode), for example, M^+ (metal ions), such as Na^+ , Li^+ , etc. For the case of adducts formed by ions that are obtained from dissociating salts (typically added as a supporting electrolyte), the reactions are homogeneous. When adducts are formed with metal ions obtained from corrosion of the electrode material, the adduct formation is again occurring as a fast homogeneous reaction; however, the cations are introduced to the sample solution through heterogeneous electrochemical reactions occurring at electrode surfaces. For the case of electrochemical reactions occurring at the electrodes, transport processes become important to deliver the ions from the surface to the bulk reservoir where adducts are formed. Several investigations into the importance of

electrochemistry in ESI have been presented in the literature [10,15–18,22–23], in which the ion source is treated as a controlled current electrochemical flow cell [16,18,24–26]. In this electrolytic cell, an oxidation/corrosion reaction is occurring at the electrode surface, consuming electrons and producing positive ions. The ejected droplets/ions carry the excess positive ions to the mass spectrometer. Thus, the reduction reaction is thought of as occurring at the mass spectrometer, which acts as an equivalent of a counter (reduction) electrode. However, instead of this being a continuous electrochemical cell, the electron draw is produced by a power supply. In-depth reviews of electrochemistry in electrospray ionization mass spectrometry are available [10,17].

Recently, we performed a comprehensive analysis of homogeneous analyte charging via protonation for different ion sources, including classical ESI as well as AMUSE [9]. In this contribution, an investigation into an alternative technique for analyte charging in AMUSE by means of heterogeneous electrochemical reactions is completed through an approximate time scale analysis and computational fluid dynamics and charge transport modeling. For positive-mode ionization (Figure 1), the piezoelectric transducer electrode of the AMUSE ion source acts as the oxidizing/corroding anode, where ions are generated and transported to the bulk of the sample reservoir. The analysis of these processes needs to consider the interplay between advective and diffusive ion transport of electrochemically generated ions due to anodic corrosion of a metal electrode, as a function of the source duty cycle (percent of each droplet ejection cycle that the piezoelectric transducer is active) and electrode location. With fundamental modes of ion transport processes being the same in both cases, these results can be generalized to the case of anion oxidation, as well.

2. Time Scale Analysis of Ion Generation and Transport

In evaluation of the electrochemical ion generation and transport, a time scale analysis for associated transport modes is conducted first. The case being considered is for a purely aqueous solution in which the concentration of free charge carriers is low. A schematic of the arrangement considered, the electrode location and associated length and velocity scales, is shown in Figure 2. The top electrode of the piezoelectric element is the location where the electrochemical reaction for production of ions occurs. The relevant length scales for this analysis are the length of the electrode and the height of the fluid reservoir. Order of magnitude approximations for the necessary length scales and other parameters used in the scaling analysis are given as:

$L \sim 1 \times 10^{-2} m$: Maximum horizontal distance fluid must travel to exit the device;

$\delta \sim 1 \times 10^{-3} m$: Maximum distance the analyte species must vertically diffuse to reach the electrode for electrochemical charging or the generated adduct ions must diffuse to reach analyte in the sample as it travels from the electrode to the droplet ejection point;

$u_o \sim 2 \times 10^{-3} m/min$: Mean longitudinal flow velocity in the sample reservoir for 100% duty cycle operation;

$D \sim 10^{-5} cm^2/s$: Typical diffusivity of an analyte in liquid solvent (order of magnitude value).

For the present analysis, migration effects are neglected (i.e., assuming negligibly small Debye layer and an excess of supporting electrolyte, as it is commonly used in such MS ionization methods [16]).

The two main cases considered are (1) the anodic corrosion (oxidation) of a metal electrode (M), e.g., $M \rightarrow M^+ + e^-$, producing metal ions diffusing into the solution to form adducts with the analyte molecules, and (2) solute/solvent oxidation, e.g. $2H_2O \rightarrow 4H^+ + O_2 + 4e^-$, in which water or other solvents (methanol, buffer (salt), etc) are oxidized removing electrons through

the electrode and leaving positive charges in the solution to form adducts with analyte molecules. The results for these two cases are qualitatively similar, which is expected due to the linearity of the governing equations and boundary condition, and the analysis and discussion presented here apply equally to both cases.

The time scale analysis considers the advection, diffusion, and reaction processes. Efficient electrochemical analyte charging is expected if the following relationship holds for the associated time scales: $t_{rxn} \leq t_{diff} \ll t_{adv}$. For the example of solvent oxidation, if the time scales observed in AMUSE operation fall in this order then, 1) the ion precursor species (e.g., water for protons) are oxidized sufficiently fast as they reach the electrode surface, 2) the electrochemically generated ions have adequate time to reach all/most of the analyte molecules in the bulk solution by diffusion, and 3) the sample has a sufficiently long residence time for the former two processes to be completed. Under these conditions, increased sample ionization is expected by virtue of having an adequate number of generated adduct ions and sufficient time for those ions and analyte to associate in solution (leading to analyte charging) before droplets containing the analyte molecules are ejected from the device. Next, the relevant time scales for the operating conditions which are typically used in AMUSE-MS experiments are analyzed.

The electrode reaction time scale depends on the value of the applied potential with respect to the redox potential (ϕ_{redox}) for the given reaction and electrode material. Thermodynamically, for an applied potential greater than the redox potential, $\phi > \phi_{redox}$, oxidation of the cation-donor species (and cation generation) occurs and electrons, e^- , flow from the solution to electrode. On the other hand, if the applied potential is less than the redox potential, $\phi < \phi_{redox}$, species reduction (and anion generation) occurs and electrons, e^- , flow from the electrode into solution [27]. The redox potential(s) for most redox couples is in the 100s mV range vs. SHE, so the bias potentials typically applied to the AMUSE electrode (1–100V) is significantly greater than the redox potential [27]. Thus, kinetic limitations are removed and the electrode reaction can be treated as infinitely fast reaching equilibrium ($t_{rxn} \rightarrow 0$). It should be noted that a more general formulation would require knowledge of the reaction mechanism and relevant rate constants to properly describe the chemical kinetics of relevant redox reactions [28]. The analysis of “negative” mode operation involving the respective anion production by reduction of appropriate carrier species is fundamentally identical to the discussed case of “positive” mode ionization.

The remaining time scales are derived from the transient advection-diffusion equation for a representative species of interest [e.g., cations (Zn^{2+} , H^+), which are being generated or cation-precursor species, which are being oxidized as a result of electrochemical reaction on the electrode].

$$\frac{\partial C_i}{\partial t} = -\nabla \cdot \left(-D_i \nabla C_i + \vec{u} C_i - \frac{z_i F}{RT} D_i C_i \nabla \phi \right) \rightarrow \frac{\partial C_i}{\partial t} = D_i \nabla^2 C_i - \vec{u} \cdot \nabla C_i \quad (1)$$

The left-hand side of Eq. (1) is the transient change in the concentration of species i (i.e., mass storage term) which is balanced by either/both diffusion or/and advection of species i (the first and the second terms, respectively, in the right hand side). As mentioned, migration effects have been neglected in this analysis in the limit of sufficiently strong buffer electrolyte. Expressing the governing transport equation, Eq. (1), in dimensionless form with the appropriate characteristic scales, enables the analysis of balances between dominant transport mechanisms.

- Diffusion Time Scale (t_{diff}): $\frac{\partial C}{\partial t} \sim D \nabla^2 C$, $t_{diff} \sim \frac{\delta^2}{D} \sim 1000 \text{sec}$
- Advection Time Scale (t_{adv}): $\frac{\partial C}{\partial t} \sim \vec{u} \cdot \nabla C$, $t_{adv} \sim \frac{L}{u} \sim 300 \text{sec}$

It is now apparent from this approximate examination that one of desired conditions, $t_{diff} < t_{adv}$, is not satisfied for the baseline AMUSE ion source operating with the piezoelectric transducer acting as a charging electrode and operated at 100% duty cycle. Therefore, the sample may be advected (transported) through the device too fast, resulting in insufficient residence time required for efficient diffusion of electrode-generated adduct-forming ions and charging of the analyte before it is being ejected out of the device. One solution to this problem would be to increase the sample residence time by reducing the duty cycle of the device. This would, however, reduce the device throughput. Alternatively, the electrode location (and therefore diffusion length scale) can be easily modified in the realized AMUSE ion source. An additional motivation for considering alternative placement of the charging electrode comes from the “disposable” AMUSE embodiment [1], in which the piezoelectric transducer (electrode surface) is completely isolated from the sample.

One alternate location for the charging electrode is along the pyramidal walls of each individual nozzle in the array of the AMUSE nozzle plate. This can be realized by sputtering or evaporation of thin film metal electrodes onto the AMUSE nozzles. With the electrodes placed on the surface of converging nozzles, the characteristic length scale for diffusion is drastically reduced (from $\delta \sim 1 \times 10^{-3} \text{ m}$ for the baseline AMUSE design down to $\delta_2 \sim 2 \times 10^{-6} \text{ m}$ for the electrodes at the nozzle aperture). This length scale reduction results in significantly faster ion transport from the electrode to the analyte in solution and therefore more efficient ionization. To quantify these advantages, the time scale analysis is repeated for a single AMUSE nozzle with integrated electrode as shown in Figure 3. Estimates of relevant length scales and parameters are summarized below:

- $L \sim 5 \times 10^{-4} \text{ m}$: Maximum distance fluid must travel (be advected) past electrodes to exit nozzle as ejected droplets;
- $\delta_1 \sim 3.5 \times 10^{-4} \text{ m}$: Maximum distance the species must diffuse to reach the electrode or the generated ions must diffuse to reach analyte in the sample;
- $\delta_2 \sim 2 \times 10^{-6} \text{ m}$: Minimum distance the species must diffuse to reach the electrode or the generated ions must diffuse to reach analyte in the sample;
- $D \sim 10^{-5} \text{ cm}^2/\text{s}$: Typical diffusivity of an analyte in liquid solvent (order of magnitude value).

For the new length scales given above and the velocity scale obtained for a single nozzle in the array (based on the total volumetric flow rate and operating frequency), the following value of the time scales are obtained:

- Diffusion Time Scale: $t_{diff, \max} \sim \frac{\delta_1^2}{D} \sim 100 \text{sec}$ $t_{diff, \min} \sim \frac{\delta_2^2}{D} \sim 2 \times 10^{-3} \text{sec}$
- Advection Time Scale: $t_{adv} \sim \frac{L}{u} = \frac{L}{V_{df}/A} = \frac{V_{nozzle}}{V_{df}} \sim 1 \text{sec}$
- Reaction Time Scale: $t_{rxn} \rightarrow 0$

Here, f is the AMUSE operating frequency. Comparing the relevant time scales indicates that, although at the base (large area) of the pyramidal nozzle the diffusion time is still longer than the advection time, as the sample approaches the nozzle orifice, diffusion becomes very fast and a sufficient number of adduct ions are able to reach and charge the analyte before it is

ejected from the device. Thus, the time scale analysis clearly suggests that using the nozzle surface as an electrode should enable much more efficient charging/ionization of the analyte as compared to the baseline case, where the piezoelectric transducer is used for analyte charging in the case of electrochemical charging mode. To further investigate the conclusions reached from an approximate time scale analysis, detailed computational fluid dynamics (CFD) simulations are performed with representative results discussed next.

3. Computational Modeling of Ion Transport and Electrochemistry

3.1. Model Formulation

The commercial computational fluid dynamics (CFD) package, FLUENT [29], is used for model implementation. The two-dimensional simulations are performed for a domain consisting of the fluid reservoir and an array of 20 nozzles, with the fluid inlet on the left hand side and the piezoelectric transducer electrode along the bottom (Figure 4). Since the ejection time scale, $t_{eject} \sim 1/f$, based on the frequency of operation ($\sim 1\text{MHz}$), is much faster than the diffusion and advection time scales, a time-averaged, quasi-steady-state advection-diffusion equation can be used to describe the time-averaged concentration field of electrochemically generated ions.

$$\vec{u} \cdot \nabla C_i = D_i \nabla^2 C_i \quad (2)$$

No homogeneous reactions are considered in the analysis, limiting consideration to only the heterogeneous electrochemical reactions taking place at the electrode surface. The bulk velocity, $\vec{u}$, is calculated from momentum conservation by solving the full set of incompressible Navier-Stokes equations of motion using a standard (semi-implicit method for pressure-linked equations, SIMPLE) computational method.

The heterogeneous electrochemical reaction considered is the anodic corrosion of a zinc (Zn) electrode; however, this could be generalized to represent corrosion of other electrode materials or solute/solvent oxidation of a cation-precursor species. Equation (2) is numerically solved for concentration of zinc cations produced as a result of the electrochemical oxidation reaction at the transducer electrode. The following boundary conditions are used to complete the model formulation.

$$\text{All Non - Reacting Solid Surfaces: } \nabla_n C_{Zn^{2+}} = 0 \quad \text{and} \quad \vec{u} = 0 \quad (3)$$

$$\text{Nozzle Exits: } \nabla_n C_{Zn^{2+}} = 0 \quad \text{and} \quad p = p_{atm} \quad (4)$$

where, $\nabla_n = \vec{n} \cdot \nabla = \partial/\partial n$, is a projection of the gradient operator on the outer normal to the boundary. This boundary condition indicates that zinc ions can leave the nozzles through only advective transport, which is associated with ejection of a charged droplet. The model considers ejection of droplets of radius equal to the nozzle aperture radius from each nozzle, corresponding to the ejection cycle, resulting in the following boundary conditions.

$$\text{Inlet: } C_{Zn^{2+}} = 0 \quad \text{and} \quad \vec{u} = u_{in} = NV_d f A_{in} \quad (5)$$

Here N is the total number of nozzles in the array, f is the frequency of the drive signal, V_d is the volume of a single ejected droplet, and A_{in} is the inlet cross sectional area. The concentration of zinc cations is set to zero at the inlet. The fluid velocity at the inlet is an input parameter, which is varied depending on the sample flow rate based on the operational duty cycle. Assuming infinitely fast kinetics of the electrochemical reaction results in instantaneous production of Zn^{2+} at the electrode surface, yielding the following (scaled) boundary condition for concentration.

$$\text{Electrode Surface: } C_{Zn^{2+}} = 1 \quad \text{and} \quad \vec{u} = 0 \quad (6)$$

The concentration of Zn^{2+} throughout the domain is scaled by the equilibrium value at the electrode surface for a given electrode potential determined by the Nernst equation [27]. For a generic redox reaction, $R \leftrightarrow O + ze^-$, the Nernst equation relates the electrode potential to the equilibrium concentrations of the oxidized (O) and reduced (R) species at the electrode surface. The system operates at a constant applied potential. In this scenario, a constant bias voltage is applied to the top electrode of the piezoelectric transducer (facing the solution) with respect to the opposite (bottom) electrode of the piezoelectric transducer, which is maintained at the common electric “ground” with the bulk solution in the far field (i.e., before it is introduced into an ionization/sample reservoir of the ion source).

$$E = E^o + \left(\frac{RT}{zF}\right) \ln\left(\frac{C_o}{C_R}\right) \rightarrow C_o = C_R \exp\left(\frac{zF(E - E^o)}{RT}\right) \quad (7)$$

Here, E^o is the standard potential and depends on the reaction pair and electrode material, R is the universal gas constant, T is the absolute temperature, F is the Faraday constant (the charge on one mole of electrons), and z is the number of electrons transferred in the reaction. This equation can be used to find the concentration of zinc cations produced at the surface of the electrode under equilibrium conditions for a given electrode potential. It is this value that is used to scale the metal ion concentration throughout the simulation domain, resulting in a dimensionless value of 1 at the electrode surface and 0 at the fluid reservoir inlet.

3.2. Simulation of Effect of Ejection Duty Cycle

First, a base case simulation is run for operation at 100% duty cycle considering the ion generating electrode as the piezoelectric transducer’s top electrode in contact with the solution. From Figure 4, the solution flows into the domain from the fluid inlet, on the left hand side of the reservoir, and out through the 20 nozzles. As clearly seen in Figure 5(top) showing the zinc ion concentration within the fluid reservoir at 100% duty cycle, the incoming solution and analyte are ejected prior to coming into contact with the cations produced at the electrode surface. This result was also predicted by the time scale analysis, showing the diffusion time to be much longer than the advection time. From a charging standpoint, very little of the bulk solution and analyte experience contact with the generated adduct ions before being ejected. Figure 5(bottom) also shows the concentration contours for a 1% duty cycle. By decreasing the duty cycle, the advection and residence times are increased allowing for improved ionization of the analyte due to a greater penetration zone of electrochemically generated adduct ions.

Figure 6 is another representation of the concentration of zinc cations at the exit of each individual nozzle. From Equation (1) and boundary condition Equation (4), it is clear that Figure 6 also represents the distribution of ionic current, scaled by the ejection velocity, exiting

each nozzle across the array. Again, it is apparent that for 100% duty cycle, the majority of nozzles are ejecting droplets without the presence of any zinc ions. Reducing the duty cycle does improve adduct ion penetration in the nozzles further downstream from the inlet, but still leaves insufficient time for ion diffusion in the upstream nozzles, resulting in inefficient ionization. An alternate electrode location, instead of reduced duty cycle, is considered next as a means to improving analyte charging via heterogeneously produced adduct ions.

3.3. Simulation of Effect of Electrode Location

While reducing the duty cycle increases residence time and improves analyte charging, it decreases throughput and still fails to produce complete analyte charging. To circumnavigate this problem, instead of increasing the advection time, the diffusion time can also be decreased. By moving the electrode location from the surface of the piezoelectric element to the walls of each nozzle, the diffusion distance the ions must travel from the surface to the bulk is greatly reduced. This results in a much faster diffusion time scale, smaller than the residence time of the analyte. Figure 7 compares the concentration contours for electrode locations for the AMUSE device operated at 50% duty cycle. Moving the electrode to the nozzle surface provides a dramatic increase in the concentration of cations (and ionic current) ejected from the array, Figure 8. This in turn provides a greater opportunity for adduct formation with the analyte and improved charging and ionization.

To compare variations in both parameters (duty cycle and electrode location), an ionization “efficiency” parameter is defined. Since the adduct formation is not modeled, a reasonable metric for ionization “efficiency” is the total concentration of ions generated and made available for analyte charging. Specifically, for the foregoing discussion, the ionization “efficiency” of zinc ion production is defined as the rate of zinc cations exiting the device (encompassed into ejected droplets) normalized by the total mass flow rate:

$$\varepsilon = \frac{\dot{m}_{Zn^{2+}}^{exit}}{\dot{m}_{total}} \quad (8)$$

This value is computed and compared for various duty cycles, as well as for both electrode locations. Figure 9 plots the ionization “efficiency” as function of a single dimensionless parameter, the Peclet number, which expresses the effects of both the duty cycle reduction and charging electrode location in a generalized fashion. The Peclet number is defined as the ratio of relevant diffusion and advection time scales:

$$Pe = \frac{t_{diff}}{t_{adv}} = \frac{\delta^2/D}{L/u} = \frac{u\delta^2}{DL} \quad (9)$$

Figure 9 summarizes the results and shows that for all cases considered, i.e., with variable duty cycle and the charging electrode placed on the piezoelectric transducer, the Peclet number is always greater than unity ($Pe > 1$). From Equation (9), these flow conditions are characterized by longer diffusion times relative to advection, $t_{diff} > t_{adv}$. As the duty cycle (and throughput) is decreased and the advection time approaches the diffusion time, the ionization “efficiency” increases steadily. The only exception is a case when the electrodes are placed on the nozzle surface (given by clear symbols in Figure 9), which results in the advection time longer than the diffusion time yielding $Pe < 1$. This leads to a dramatic increase in the ionization “efficiency” without a sacrifice in the device throughput.

4. Conclusions

The results of electrochemical cell analysis of the AMUSE ion source demonstrate that for 100% duty cycle operation with the electrochemically “hot” electrode on top of the piezoelectric transducer, the majority of the analyte solution is ejected prior to coming into contact with the cations produced at the electrode surface. In other words, the majority of AMUSE nozzles are ejecting droplets lacking the analyte-charging ions, which will lead to very poor ionization efficiency. While reducing the duty cycle allows for improved ion transport from the electrode to the bulk by diffusion, it greatly reduces throughput which may be undesirable in some applications. Also, operation of the device in multiplexed format [2] with a smaller sample reservoir would impose an even more stringent requirement on the sample residence time (and, thus, will put a severe limit on device throughput) if the change of the duty cycle was the only way to improve analyte charging. To circumnavigate this challenge, the electrode location needs to be moved from the surface of the piezoelectric element to the walls of each nozzle, making the diffusion length scale the ions must travel from the electrode surface to the bulk greatly reduced. This results in much faster diffusion, occurring on a time scale smaller than the residence time of the analyte within the AMUSE chamber prior to its ejection. Indeed, moving the electrode to the nozzle surface shows a dramatic increase in the concentration of ejected cations. This in turn provides a greater opportunity for adduct formation with the analyte (typically a very fast process) and improved charging and ionization. It is important to emphasize that this gain in ionization efficiency, enabled by moving the electrode, comes with no sacrifice of the device throughput. In order to compare the ion production for each case, an ionization “efficiency” parameter is introduced as the rate of cations exiting the device (encompassed into ejected droplets) normalized by the total mass flow rate. This value is compared for various duty cycles, as well as for both electrode locations. The ionization “efficiency” is computed as a function of a single dimensionless parameter, the Peclet number, which expresses the effects of both the duty cycle reduction and charging electrode location in a generalized fashion.

When analyte charging is accomplished by homogeneous protonation, due to dissociation of a weak acid as in the case of ESI of biomolecules, electrochemistry still plays an important role in the ion source operation. This is because upon ejection of positively-charged analyte molecules from the solution (positive mode ionization), net negative charge remains in the bulk reservoir [6]. Electrochemical oxidation of this excess charge to maintain electroneutrality in the bulk reservoir is imperative for steady state operation of an ion source. Lastly, it should be noted that although this analysis has been applied to the AMUSE ion source, the methodology and the conclusions on the effect of operation duty cycle and electrode location are general and can be applied to any planar array of ion sources wherein electrochemistry contributes to ion generation or consumption. Thus, the developed understanding of electrochemistry in the AMUSE ion source is sufficiently general and vital for optimal design and operation of any MS ion sources.

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Fig. 1. Schematic representation of the AMUSE ion source as a controlled-current electrolytic cell, including relevant components.

Fig. 2. AMUSE schematic showing relevant length scales and velocities used in the time scale analysis.

Fig. 3.
Schematic representation of relevant length scales for electrode location at the pyramidal surfaces of each nozzle.

Fig. 4.
Simulation domain for electrochemically generated ion transport model.

Fig. 5. Simulated results of Zn^{2+} concentration throughout fluid reservoir for 100% (top) and 1% (bottom) duty cycle operation.

Fig. 6.

Simulated results of Zn²⁺ concentration at each of the 20 nozzle orifices along the nozzle array for changing duty cycle. These results also represent the distribution of ionic current at each nozzle along the array.

Fig. 7. Simulated results of Zn^{2+} concentration throughout the fluid reservoir for an electrode at the piezoelectric transducer top surface (top) and at the pyramidal nozzle surfaces (bottom). Both results are for 50% duty cycle operation.

Fig. 8. Simulated results of Zn^{2+} concentration at each of the 20 nozzle orifices along the nozzle array for electrode locations at the piezoelectric element and the nozzle surface. These results also represent the distribution of ionic current at each nozzle along the array.

Fig. 9.
Ionization “efficiency” for all simulated cases as a function of the Peclet number