Insights into Analyte Electrolysis in an Electrospray Emitter from Chronopotentiometry Experiments and Mass Transport Calculations

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Examining the electrostatic spray ion source used in electrospray mass spectrometry (ES-MS) from an electrical perspective reveals it to be a two-electrode electrochemical cell in a series circuit [1–3]. A recent and thorough evaluation of the equivalent circuit in ES-MS is presented by Enke and co-workers [4]. A metal capillary or other conductive contact (usually stainless steel) placed at or near the point from which the charged ES droplet plume is generated (the ES emitter) is one of two electrodes in the system. In electrochemical terminology, this is the working electrode. The analytically significant reactions (in terms of ES-MS) occur at this electrode. This is also a controlled-current source [2, 3]. The rate of charged droplet production by this source defines the average current (droplet generation rate times average charge per droplet) that flows in the cell (i.e., the ES current, \(i_{\text{ES}}\)) and this rate is determined by several interactive variable parameters including the electric field applied between the electrodes, the solution flow rate, and the solution viscosity and conductivity [5]. The counterelectrode of the circuit is the atmospheric sampling aperture plate or inlet capillary, and the various lens elements and detector of the mass spectrometer.

In a typical ES-MS scenario, a solution containing the analyte of interest is pumped through the ES emitter held at high voltage and sprayed towards the counterelectrode. Under the influence of the applied electric field between the electrodes, ions in solution that are of the same polarity as the voltage applied to the ES capillary build up an excess charge at the surface of the liquid exiting the emitter. When Coulombic forces are sufficient to overcome the surface tension of the liquid, droplets enriched in ions of this polarity are emitted from the capillary and drift toward the counterelectrode. This process produces a quasicontinuous steady-state current [6]. To sustain the build up of an excess of one ion polarity on the surface of the liquid exiting the emitter, heterogenous (electrode-solution) electron transfer reactions (i.e., electrochemical reactions) must occur at the conductive contact to the solution at the spray end of the ES device. Oxidation reactions in positive ion mode and reduction reactions in negative ion mode will occur in the ES emitter. Electron transfer reactions occur at the counterelectrode as the charged droplets and ions arrive to complete the circuit. Thus, electrochemical reactions are inherent to the basic operation of the electrostatic sprayer used in ES-MS.

The electrolysis reactions that take place in the ES emitter may influence the gas-phase ions formed and ultimately analyzed by the mass spectrometer, because they may change the composition of the solution sprayed. These changes include, but are not limited to, analyte electrolysis resulting in ionization of neutral analytes or modification in the mass or charge of the original analyte present in solution [7–18], changes in solution pH through electrolytic H\(^+\) or OH\(^-\) production/elimination [19], and the introduction/elimination...
of specific species to/from solution (e.g., introduction of Fe$^{2+}$ ions from corrosion of a stainless steel emitter [1, 20]). Determining the extent and nature of these solution compositional changes is a complex problem [21]. The extent of any solution compositional change that the electrolytic reactions can impose necessarily increases as flow rate decreases [3, 19], because the magnitude of $i_{f0}$ is only weakly dependent on solvent flow rate [5]. The interfacial potential at the working electrode ultimately determines what reactions in the system are possible as well as the rates at which they may occur. However, in an ES ion source the interfacial potential is not fixed, but rather adjusts to a given level depending upon a number of interactive variables to provide the required current. That is, the ES ion source operates in a fashion analogous to that of a two-electrode, controlled-current electrolytic (CCE) flow cell [2, 3, 22]. The variables that are expected to affect the interfacial electrode potential include the magnitude of $i_{f0}$, the redox character and concentrations of all species in the system, the solution flow rate, the electrode material and geometry, and any other parameters which affect the flux of reactive species to the electrode surface. Potentially more complicating is that the interfacial potential may oscillate in magnitude in response to the charging and discharging of the excess charge at the surface of the liquid (i.e., during and following droplet formation) [6]. In any case, it is clear that a thorough understanding of the electrochemical operation of the ES ion source is essential both to avoid any possible analytical pitfalls it may cause and to fully exploit the phenomenon for new fundamental and analytical applications of ES-MS.

To date, information regarding the interfacial potential along the emitter under various ES-MS operational conditions has been gathered in several ways, but not directly measured. For example, on the basis of the ions observed in the ES mass spectrum of neutral compounds with known redox equilibrium potentials, $E^0$, that are ionized electrolytically in the emitter, the minimum interfacial potentials have been inferred [e.g., 2, 7, 8, 10]. In an elegant experiment, McCarley et al. [15] calculated the interfacial potential on the basis of the flow rate dependent change in the distribution of multiply charged ions observed from redox-active oligomers containing several noninteracting redox sites. Van Berkel et al. [21] used computational simulations to derive both the potential distribution along the length of the emitter and the distribution of the current among those in the ES emitter. The mass transport calculations developed for tubular electrodes. Chronopotentiometry experiments were carried out in a stirred 10 mL batch cell with freshly polished working electrodes, viz., a 2.54-mm diam 304 stainless steel disk (0.05067 cm$^2$), a 1.60-mm diam platinum disk (0.02011 cm$^2$), or a 1.60-mm diam gold disk (0.02011 cm$^2$) each embedded in polyetheretherketone (PEEK BAS). Quoted electrode areas are the geometrical areas. The reference electrode was Ag/AgCl (Model RE-5B, BAS) and the counterelectrode was a platinum wire. The currents applied to each of the respective electrodes in these experiments was that required to generate suggest that the effective electrode area of the ES emitter capillary, that is, the area over which redox reactions actually take place, will be different for analytes with different $E^0$ values.

In this paper, qualitative insights into the average emitter interfacial electrode potential, the effective electrode area of the ES emitter, and the efficiency of analyte electrolysis are gleaned from off-line chronopotentiometry experiments and mass transport calculations developed for tubular electrodes. Chronopotentiometry is a controlled-current technique in which a current step to a fixed level is maintained at the working electrode, and the resulting potential response at the working electrode is measured versus a reference electrode as a function of time [22]. The measured interfacial electrode potential is dependent upon the current density, the electrode material, and the mass transport to the electrode. Mass transport to a planar electrode in a batch cell is different than that expected for the ES system, which is a flow-through tubular electrode. Nonetheless, the trends in the measured interfacial potential in the off-line chronopotentiometry experiments, when the limiting reactions involve species that are not diffusion limited (electrode corrosion) or involve the major species in the solution (solvent oxidation/reduction), are expected to be similar to those in the ES emitter. The mass transport calculations reveal the electrode area required for complete analyte electrolysis at a given volumetric flow rate. On the basis of the insights gained from these electrochemical studies and calculations, the design of ES emitters to assure maximum or minimum analyte electrolysis during ES-MS are discussed.

Experimental

Samples were prepared using deionized H$_2$O (Milli-RO 12 Plus, Millipore, Bedford, MA). The electrolyte in all solutions was 0.1 M KNO$_3$ (EM Science, Gibbstown, NJ), a 1.0 M HCl solution in H$_2$O prepared from 37 wt% HCl in H$_2$O (99.999%, Aldrich, Milwaukee, WI) or a 1.0 M KOH solution in H$_2$O (reagent grade, Aldrich) were used to titrate sample solutions to the desired pH. A Corning M106 pH meter (Corning, NY) was used to measure pH. Electrochemical experiments were controlled with a CH Instruments Model 660 Electrochemical Workstation (Austin, TX) interfaced to a C-2 Cell Stand [Bioanalytical Systems, (BAS), West Lafayette, IN]. Chronopotentiometry experiments were carried out in a stirred 10 mL batch cell with freshly polished working electrodes, viz., a 2.54-mm diam 304 stainless steel disk (0.05067 cm$^2$), a 1.60-mm diam platinum disk (0.02011 cm$^2$), or a 1.60-mm diam gold disk (0.02011 cm$^2$) each embedded in polyetheretherketone (PEEK BAS). Quoted electrode areas are the geometrical areas. The reference electrode was Ag/AgCl (Model RE-5B, BAS) and the counterelectrode was a platinum wire. The currents applied to each of the respective electrodes in these experiments was that required to generate
current densities of 0.0032, 0.032, 0.32, 3.2, and 32 mA/cm², accounting for their different geometrical areas. These current densities are equivalent to the average current density calculated for a 100-µm i.d. metal ES emitter with an effective electrode length of 1.0 cm (area = 3.14 × 10⁻² cm²), 1.0 mm (area = 3.14 × 10⁻³ cm²), 100 µm (area = 3.14 × 10⁻⁴ cm²), 10 µm (area = 3.14 × 10⁻⁵ cm²), and 1.0 µm (area = 3.14 × 10⁻⁶ cm²), respectively, for an ES current of 0.1 µA. Electrodes were preconditioned at -1.0 V for 20 s just prior to the start of an experiment to remove any surface oxides. Individual experiments started with the application of a given anodic current that was maintained for 60 s. At 60 s, a cathodic current of the same magnitude was applied for 60 s (total time 120 s). The five individual chronopotentiograms in each set of chronopotentiometry experiments were acquired in order from lowest to highest current density.

Results and Discussion

Electrochemists often speak in terms of the "potential window" or potential range within which redox reactions can be carried out with high efficiency in a particular solvent system using a particular working electrode. This "window" represents the maximum anodic (oxidation) and cathodic (reduction) interfacial electrode potential that can be applied to an electrode before a significant electrode current is generated due to oxidation or reduction of the major components of the solvent system (solvent and/or electrolyte) or the electrode. In the current-limited situation of ES, the occurrence of redox reactions of the solvent or any other species sufficient to supply all the required current are expected to effectively maintain or "buffer" the interfacial potentials of the emitter electrode at or near the E⁰ values for those particular reactions. The interfacial potential in the emitter is expected to be only that magnitude necessary to supply the required current for a given availability of material for reaction [3]. The electrolysis of analytes with E⁰ values at or beyond the potential window limits will either be inefficient or will not occur.

One might postulate the potential window limits that might be achieved for a particular ES experiment by recourse to tabulated equilibrium potentials for reactions of the various species present. Table 1 lists many of the reactions and the corresponding potentials for the components one finds in a typical ES solvent system including H₂O, CH₃OH, HOAc, NH₃OH, or NH₄OAc [23]. For example, one might anticipate that the potential window will be significantly limited in the cathodic direction if CH₃OH is the solvent rather than H₂O, because CH₃OH (eqs 13 and 17, Table 1) is much easier to reduce than H₂O (eqs 14 and 19, Table 1). On the other hand, the exact potentials for CH₃OH or H₂O reduction, or for any of the other reactions in Table 1, are influenced by the nature of the electrode and by solution additives (e.g., pH and electrolytes). Furthermore, because a stainless steel working electrode and the solvents typical in ES-MS are somewhat unusual for electrochemical studies, pertinent data from which to postulate the potential window may not be readily available.

Chronopotentiometry is an electrochemical experiment that can be used to qualitatively assess what the emitter interfacial potential might be under conditions particular to ES-MS. Chronopotentiometry, like the ES ion source, is a controlled-current technique. A current is maintained at the working electrode, and the resulting potential response at the working electrode is measured versus a reference electrode as a function of time producing a chronopotentiogram [22]. To mimic the ES situation with chronopotentiometry one needs to know the appropriate current density to apply to the working electrode. The current density is a function of the electrode area for a fixed current, which begs the question, "What is the effective electrode area in an ES emitter?" Effective electrode area is defined here as the internal surface area of the ES emitter capillary, from the spray-tip upstream into the capillary, over which redox reactions actually occur. This area will be the same or less than the physical area of ES emitter

### Table 1. Major electrolytic reactions anticipated in typical ES solvent systems employing stainless steel or platinum capillary emitters [23]

<table>
<thead>
<tr>
<th>Reaction</th>
<th>E⁰ (V vs. Ag/AgCl)</th>
<th>Eq. no.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxidation (positive ion mode)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>solvent system reactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4OH⁻ = 2H₂O + O₂ + 4e⁻</td>
<td>0.204</td>
<td>1</td>
</tr>
<tr>
<td>2OH⁻ = H₂O₂ + 2e⁻</td>
<td>0.683</td>
<td>2</td>
</tr>
<tr>
<td>2H₂O = O₂ + 4H⁺ + 4e⁻</td>
<td>1.03</td>
<td>3</td>
</tr>
<tr>
<td>2NH₄⁺ = N₂H₆²⁺ + 3H⁺ + 2e⁻</td>
<td>1.08</td>
<td>4</td>
</tr>
<tr>
<td>NH₄⁺ + H₂O = NH₄OH⁺ + 2H⁺ + 2e⁻</td>
<td>1.15</td>
<td>5</td>
</tr>
<tr>
<td>2H₂O = H₂O₂ + 2H⁺ + 2e⁻</td>
<td>1.57</td>
<td>6</td>
</tr>
<tr>
<td>OH⁻ = OH⁺ + e⁻</td>
<td>1.80</td>
<td>7</td>
</tr>
<tr>
<td>emitter electrode reactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fe + 2OH⁻ = Fe(OH)₂ + 2e⁻</td>
<td>-1.07</td>
<td>8</td>
</tr>
<tr>
<td>Fe = Fe²⁺ + 2e⁻</td>
<td>-0.64</td>
<td>9</td>
</tr>
<tr>
<td>Fe = Fe³⁺ + 3e⁻</td>
<td>-0.23</td>
<td>10</td>
</tr>
<tr>
<td>Pt + 2OH⁻ = Pt(OH)₂ + 2e⁻</td>
<td>-0.037</td>
<td>11</td>
</tr>
<tr>
<td>Pt + 2H₂O = Pt(OH)₂ + 2H⁺ + 2e⁻</td>
<td>0.78</td>
<td>12</td>
</tr>
<tr>
<td><strong>Reduction (negative ion mode)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>solvent system reactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH₃OH + 2H⁺ + 2e⁻ = CH₄ + H₂O</td>
<td>0.38</td>
<td>13</td>
</tr>
<tr>
<td>2H₂O + O₂ + 4e⁻ = 4OH⁻</td>
<td>0.204</td>
<td>14</td>
</tr>
<tr>
<td>2H⁺ + 2e⁻ = H₂</td>
<td>-0.197</td>
<td>15</td>
</tr>
<tr>
<td>CH₃COOH + 2H⁺ + 2e⁻ = CH₃CHO + H₂O</td>
<td>-0.33</td>
<td>16</td>
</tr>
<tr>
<td>CH₃OH + H₂O + 2e⁻ = CH₄ + 2OH⁻</td>
<td>-0.45</td>
<td>17</td>
</tr>
<tr>
<td>2NH₄⁺ + 2e⁻ = 2NH₃ + H₂</td>
<td>-0.75</td>
<td>18</td>
</tr>
<tr>
<td>2H₂O + 2e⁻ = H₂ + 2OH⁻</td>
<td>-1.02</td>
<td>19</td>
</tr>
<tr>
<td>emitter electrode reactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pt(OH)₂ + 2e⁻ = Pt + 2OH⁻</td>
<td>-0.037</td>
<td>20</td>
</tr>
<tr>
<td>Fe(OH)₂ + e⁻ = Fe(OH)₂ + OH⁻</td>
<td>-0.76</td>
<td>21</td>
</tr>
<tr>
<td>Fe(OH)₂ + 2e⁻ = Fe + 2OH⁻</td>
<td>-1.07</td>
<td>22</td>
</tr>
</tbody>
</table>
capillary. The effective electrode area might be less than the physical area because of limited electric field penetration into the liquid at the spray tip and because of other limits to ionic transport in the solvent.

In an ES ion source providing a given current, $i_{ES}$, in which the emitter and high voltage contact is a conductive tubular capillary of radius $r$, an average current density $j$, for an effective electrode length $l$, can be calculated using

$$j \text{ (mA/cm}^2) = \frac{i_{ES} \text{(mA)}}{[2\pi r(cm)]l(cm)}$$  \hspace{1cm} (23)

Consider, for example, the typical nano-ES versus normal ES emitter design (Figure 1). With a metal-coated, pulled-glass capillary emitter used in nano-ES there is a finite, small electrode (e.g., 10 $\mu$m i.d. and a few micrometers length) [24]. With a metal ES capillary there is the possibility of a much larger electrode area (e.g., 100 $\mu$m i.d. and several centimeters long), because reactions might occur some distance back into the capillary. For a fixed current, a smaller electrode area translates to a higher current density. For the experiments performed in this work, five current densities were used that were equivalent to the average current density calculated (eq 23) for a 100-$\mu$m i.d. ES emitter with an effective electrode length of 1.0 cm ($j = 0.0032$ mA/cm$^2$), 1.0 mm ($j = 0.032$ mA/cm$^2$), 100 $\mu$m ($j = 0.32$ mA/cm$^2$), 10 $\mu$m ($j = 3.2$ mA/cm$^2$), and 1.0 $\mu$m ($j = 32$ mA/cm$^2$), respectively, given an ES current of 0.1 $\mu$A. Note that the current was considered to be distributed evenly along the length of electrode, and is therefore only a first order approximation of the ES current density situation [21].

Figure 2 shows a series of chronopotentiograms acquired using either a 304 stainless steel (Figure 2a–c) or a platinum (Figure 2d–f) working electrode in water under acidic (pH = 2.4), neutral (pH = 6.5), and basic (pH = 11.6) conditions. Individual experiments started with the application of an anodic current for 60 s (0–60 s) and then a cathodic current of the same magnitude was applied for an additional 60 s (60–120 s). The five different anodic–cathodic chronopotentiogram plots within each of the six sets of experimental results shown were acquired in order from the application of the lowest to highest current density (thinnest to thickest plot lines).

An initial glance at the data in Figure 2 reveals substantial differences in the potential response for a given applied current density, anodic or cathodic, among the two electrodes under identical pH conditions. These differences are most apparent at low current density (thinnest plot lines) and diminish as current density increases (thicker plot lines). There are also differences in the potential response for a given electrode as the pH of the solution is altered, but again these differences diminish as current density increases. In general, with the application of the low anodic current densities (equivalent to the current densities for emitter electrode lengths of 1.0 cm and 1.0 mm), the interfacial potentials at the stainless steel electrode had negative values which ranged between −0.2 and −0.6 V (Figure 2a–c). These values of the potential indicate that the major reactions supporting the current involve corrosion of the stainless steel (eqs 8–10, Table 1). In both acidic and basic solution, the potential values are unchanged. Application of the intermediate current density of 0.32 mA/cm$^2$ (corresponding to the current density for an emitter electrode length of 100 $\mu$m), results in a substantial change in the potential recorded over the 60 s the anodic current was applied, under all three pH conditions. This indicates that a change in the redox reactions supplying the current takes place during the course of the experiment. Corrosion alone can no longer support the current at this increased current density or perhaps changes in the chemistry of the electrode (passivation) prohibit corrosion. In any case, the electrode potential increases to a more positive value to oxidize other species in the system at a rate sufficient to satisfy the current demand. At the highest current density (32 mA/cm$^2$), corresponding to an emitter electrode length of 1.0 $\mu$m, the same potential (about 1.8 V) is reached under the three different pH conditions. At this potential, water oxidation producing protons and oxygen (eq 3, Table 1), and possibly reactions creating reactive molecular species like H$_2$O$_2$ (eq 6, Table 1), are taking place to support the current. Under basic conditions (Figure 2c), the potentials obtained at the intermediate current densities appear to be buffered near 0.8 V. This is most likely due to oxidation of hydroxide anions, which may also create H$_2$O$_2$ (eqs 1 and 2, Table 1).

When a cathodic current is maintained at the stainless steel electrode, negative potentials result. At the lowest current density, the potential is least negative, $\sim −0.4$ V, indicating the current is supported by proton reactions creating reactive molecular species like H$_2$O$_2$ (eqs 1 and 2, Table 1).
reduction (eq 15, Table 1) and possibly reduction of surface oxides (eq 21, Table 1). As current density is increased, the potentials achieved are more negative, ultimately reaching magnitudes of about $-1.6 \, \text{V}$. At these potentials, the current is probably supported in large part by water reduction (eq 19, Table 1).

**Figure 2.** Chronopotentiograms acquired using a stainless steel electrode in (a) acidic ($\text{pH} = 2.4$), (b) neutral ($\text{pH} = 6.5$), and (c) basic ($\text{pH} = 11.6$) $\text{H}_2\text{O}$ or a platinum electrode in (d) acidic ($\text{pH} = 2.4$), (e) neutral ($\text{pH} = 6.5$), and (f) basic ($\text{pH} = 11.6$) $\text{H}_2\text{O}$. Increasing plot line thickness corresponds to increasing current density applied, viz., 0.0032, 0.032, 0.32, 3.2, and 32 mA/cm$^2$, respectively, which is equivalent to the average current density that would be expected in a 100-$\mu \text{m}$ i.d. ES metal emitter with an effective electrode length of 1.0 cm, 1.0 mm, 10 $\mu \text{m}$, and 1.0 $\mu \text{m}$, respectively, for an ES current of 0.1 $\mu \text{A}$. 

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**ANALYTE ELECTROLYSIS IN AN ES EMITTER**
Corrosion of the platinum electrode does not occur so the potentials recorded at the low anodic current densities are almost a full 1.0 V more positive than under the same conditions with the stainless steel electrode (Figure 2d–f). Application of low anodic current densities (0.0032 and 0.032 mA/cm²) for solutions of pH 2.4 and 6.5 (Figure 2d, e), resulted in initial electrode potentials of roughly 0.2 to 0.8 V, respectively. The potential remained relatively constant at its initial value (0.0032 mA/cm²), or gradually increased over the course of the 60 s experiment to a level no higher than \(~0.8\) V (0.032 mA/cm²). For the basic solution (Figure 2f), the trends in the chronopotentiograms were the same, but the potentials were shifted slightly negative of values recorded for pH 2.4 and 6.5. The potential levels at low current density are probably maintained by formation of surface oxides on the platinum (eqs 11 and 12, Table 1) or under basic conditions, by the oxidation of hydroxide anion (eqs 1 and 2, Table 1).

Application of an anodic current of 0.32 mA/cm² resulted in a changing potential, at all three pH values, that started at about 0.4 V and increased to a stable value of about 1.2–1.3 V within 10 s. At this current density, surface oxide formation or hydroxide oxidation cannot provide enough current and the potential increases to that level sufficient to oxidize H₂O (eq 3, Table 1). At the highest current density of 32 mA/cm² (corresponding to the current density for an emitter electrode 1.0 µm long), the potential rapidly attained a magnitude of about 2.1 to 2.3 V and remained constant for the remainder of the anodic portion of the experiment. At the highest current densities, reactive species like H₂O₂ are probably created at the electrode, and in this case, because the potentials are sufficiently positive, also highly reactive radicals (e.g., eq 7, Table 1).

In contrast to the stainless steel electrode, the potentials at the platinum electrode for the application of cathodic current have a positive value of about 0.4 to 0.5 V at the lowest current densities, in both acidic and neutral solution. This is the same interfacial potential range that was obtained at this electrode with the application of anodic current of equal magnitude. It is well known that the overpotential for reduction of protons at platinum is low [22] and this reaction (eq 15, Table 1) supports the current under these conditions. As current densities are increased, the potentials achieved do eventually become negative, ultimately reaching magnitudes of about \(-1.6\) V. There is some delay in reaching constant potential levels for current densities of 0.32 and 3.2 mA/cm². This is probably due in part to the reduction of surface oxides (eq 20, Table 1) formed on the platinum electrode during the previous anodic cycle. Thus, at the lowest cathodic current densities, the potentials at the platinum electrode are significantly more positive than at stainless steel. However, at the highest cathodic current density, the potentials achieved are nearly the same (\(-1.5\) to \(-1.7\) V).

Chronopotentiometry data not shown for the application of an anodic current at a gold electrode, under neutral pH conditions, resembles the data obtained with the platinum electrode under the same conditions. The major difference is that at the lower current densities, the potentials attained are more positive than that for platinum. This relates to differences in oxide formation on the two different materials. Nonetheless, at the highest current densities the maximum potential is, as for platinum, about 2.0 V. Unlike the other two electrodes, for each of the three lowest current densities, the potential when a cathodic current is applied changed over time or underwent a transition during the 60 s period of current application. At first the potentials were positive, which was an indication that surface oxides were being reduced to supply the current. Once the oxides were reduced the potentials reached a constant, slightly negative value. At the highest cathodic current density (32 mA/cm²), the magnitude of the potential recorded, \(\sim2.0\) V, was the most negative of the three electrode systems studied.

The nature of mass transport to the electrode surface in the chronopotentiometry experiments described above is certainly not the same as in the tubular capillary electrode of the ES system. Also, the chronopotentiometry experiments are of uniform current density and potential, whereas both current density and interfacial potential are expected to change along the length of the emitter electrode in ES-MS [21]. This means that the absolute magnitudes of the potential measured in the chronopotentiograms at a given current density might be different than those actually present in an ES emitter electrode. However, the trends in the average interfacial potential with current density should be very much the same. On the basis of these trends one obtains an insight into the interfacial potentials achieved in the ES emitter under different conditions.

The chronopotentiograms in Figure 2 show that different interfacial potentials are to be expected for different electrode materials under identical solution conditions. Differences in the interfacial potential at the different electrodes will be minimal at high current densities and accentuated at low current densities. The distribution of current among various reactions, particularly at low current density, may be significantly different among different electrode materials. If one physically limits the area of a tubular ES emitter, as is done, for example, with a metal-coated (e.g., gold), pulled glass capillary in nano-ES [24], the high resultant current densities may push the magnitude of the interfacial potential to the extreme values where solvent electrolysis occurs. The emitter electrode area can be physically much larger, which is normally the case with a conductive tubular ES emitter capillary (Figure 1). The area of the electrode used for redox chemistry depends, however, on a complicated interaction of parameters including penetration of the electric field into the capillary, ionic transport in the solution, and flux of reactive material to the electrode surface. Nonetheless, one can assume that the system will tend toward the lowest
energy state and that the magnitude of the interfacial potentials will be minimized.

Modeling indicates that the effective electrode length of the emitter capillary may be no more than three times the diameter of the capillary or 300 μm for a 100 μm i.d. capillary [21]. The average current density for an electrode of this seemingly short length, for 0.1 μA of current, is only about 0.1 mA/cm². This is between the magnitude of the second and third lowest current densities studied in the chronopotentiometry experiments. Thus, the differences in interfacial potential among the various metal capillaries that might be used as the ES emitter should be significant. This circumstance is supported by experimental evidence. Oxidation of analytes or solution composition changes in positive ion mode ES/MS are boosted with the use of a platinum capillary compared to a stainless steel capillary [10, 12, 16, 19]. For a given “low” current density, the interfacial electrode potential is expected to be more positive at the platinum electrode than that at the stainless steel electrode.

An interfacial potential of sufficient magnitude is required if an analyte is to undergo an electrolysis reaction. The magnitude of the potential necessary will of course depend on the redox character of the analyte under study. If the potential is less than that required, no reaction can occur. Provided the potential is sufficient for reaction, the efficiency of the reaction will depend on the magnitude of the current and on the “availability” of the analyte for reaction, compared to the availability of everything else in the system that can also react.

The magnitude of \( i_{ES} \) must be at least sufficient for oxidation/reduction of the molar equivalent of the analyte flowing through the emitter, which can be calculated from Faraday’s law as expressed in

\[
C_A = \frac{i_{ES}}{(nFv_f)}
\]

where \( C_A \) is the bulk solution concentration of the analyte, \( n \) is the molar equivalent of electrons involved in the redox reaction of the analyte, \( F \) is the Faraday constant, and \( v_f \) is the volumetric flow rate through the emitter. A greater magnitude of current than calculated in eq 24 will be necessary for efficient electrolysis if another reaction also occurs (e.g., emitter corrosion or solvent electrolysis). If necessary, the magnitude of \( i_{ES} \) can be increased. In practice, a simple means to substantially increase \( i_{ES} \) over that current obtained under optimized ES conditions (e.g., 4–5 kV voltage drop between electrodes with a fixed solvent system, capillary size, and ES source geometry) is to increase solution conductivity by addition of an “ES friendly” electrolyte to the solvent system [2, 10].

Even if the required potential and current are proper, complete analyte electrolysis will not occur unless all of the analyte is transported to the electrode surface and reacts on passage through the capillary emitter (Figure 1b, R → O). The fraction of analyte that can contact the inner walls of a tubular electrode and react on passage through the tube, \( f_A \), can be calculated using eq 25. This equation developed by Chen et al. [25] assumes diffusive-convective flux to the inner wall of the tubular electrode under parabolic flow and total concentration polarization conditions,

\[
f_A = \frac{i}{(nFv_fC_A)} = 1 - 0.8191 \exp\left(-3.657 \frac{\pi Dl}{v_f}\right) - 0.09753 \exp\left(-22.30 \frac{\pi Dl}{v_f}\right) - 0.0325 \exp\left(-56.96 \frac{\pi Dl}{v_f}\right)
\]

In this equation, \( i \) is the current measured at the electrode, \( D \) is the electrolyte diffusion coefficient, and the other parameters are the same as previously defined. Only the first three terms of the equation are used here which is sufficient for \( f_A > 0.1 \) (10% electrolysis) [25]. Note that the value of \( f_A \) is independent of the electrode radius.

The relationship in eq 25 is shown graphically in Figure 3 as a plot of the fraction of analyte reacting \( f_A \) versus the tubular electrode length \( l \) for volumetric flow rates \( v_f \) of 0.01, 0.1, 1.0, 10, and 100 μL/min and diffusion coefficients \( D \) of 5 × 10⁻⁶ and 2.4 × 10⁻⁵ cm²/s. The former value of \( D \) is typical for an organic analyte in aqueous solution [22], whereas the latter value is more typical of an organic analyte in a non-aqueous solvent (e.g., ferrocene in acetonitrile) [26]. Complete electrolysis will be defined here as \( f_A = 0.99 \) or 99% electrolysis. For an ES emitter of 100 μm i.d., operated at 1.0 μL/min (the lowest operational flow rate for a capillary of this diameter), reference to eq 25 and the plots in Figure 3 find that an electrode length of 1.28 cm is required for complete electrolysis given \( D = \)
5 \times 10^{-6} \text{ cm}^2/\text{s}. The length needs to be only 2.67 mm for \( D = 2.4 \times 10^{-5} \text{ cm}^2/\text{s} \). If the flow rate was 100 \( \mu \text{L}/\text{min} \), electrodes 128 cm and 26.7 cm long would be needed for complete electrolysis of analytes with these two different diffusion coefficients, respectively.

Metal capillary ES emitters are normally at least several centimeters in length. Thus, the physical electrode length required for complete electrolysis at the low flow rate end of their operational range is available. However, complete electrolysis at flow rates of 100 \( \mu \text{L}/\text{min} \) or more appears improbable. The physical length of the ES emitter electrode required for complete electrolysis (tens of centimeters) is not usually available on commercial ES ion sources. Van Berkel and Zhou [12] showed complete electrolysis of \( \approx 10 \) \( \mu \text{M} \) nickel octaethylporphyrin (\( E^0 \approx 0.88 \text{ V vs Ag/AgCl} \)) was possible using a 6.5-cm long platinum capillary at a flow rate of 1.5 \( \mu \text{L}/\text{min} \) in nonaqueous solvents [methylen chloride/acetonitrile (1/1 v/v)]. As mentioned above, computational simulations of the ES process indicate that the majority of the current in a metal emitter of these dimensions occurs only about 300 \( \mu \text{m} \) back into the capillary, or roughly a distance three times the diameter of the capillary. Under the conditions of those simulations, the predicted electrolysis efficiency of the analyte (ferrocene, \( E^0 \approx 0.35 \text{ V vs Ag/AgCl} \)) in \( \text{CH}_3\text{CN/H}_2\text{O} \) (9/1 v/v) was low (15%). Using the equations from Chen et al. [25] with \( D = 2.4 \times 10^{-5} \text{ cm}^2/\text{s} \) (the same value used in the simulations), the efficiency of analyte electrolysis for a 300 \( \mu \text{m} \) long electrode at a flow rate of 1.5 \( \mu \text{L}/\text{min} \) is calculated to be about 40%. From these same equations it is determined that an electrolysis efficiency of 99% would require an electrode 4.0 mm long. As a whole these data indicate that a reexamination of the simulations [21], which predict a very short effective electrode length (several hundred micrometers or less) within the metal ES emitter, may be warranted.

Consider next a metal-coated, pulled-glass nano-ES glass capillary with a 10-\( \mu \text{m} \) i.d. tip. Operated at its normal lowest flow of 10 \( \text{nL}/\text{min} \), reference to eq 25 and Figure 3 reveals that an electrode length of 128 \( \mu \text{m} \) would be required for complete electrolysis of an analyte with a diffusion coefficient of \( D = 5 \times 10^{-6} \text{ cm}^2/\text{s} \). An electrode length of 26.7 \( \mu \text{m} \) would be required for complete electrolysis of an analyte with \( D = 2.4 \times 10^{-5} \text{ cm}^2/\text{s} \). In a typical nano-ES capillary of this type, the maximum physical length of the electrode at the spray tip is no more than a few micrometers. Thus, precluding phenomena like through-glass conduction and turbulent flow or eddy currents in the Taylor cone [27], that may affect mass transport to the electrode, one predicts that direct analyte electrolysis in a metal-coated nano-ES emitter (or other extremely short tubular electrode configuration) will be much less efficient (particularly in the aqueous solvent) than in a typical metal capillary ES emitter. This prediction awaits experimental verification.

Note that the above discussion does not preclude indirect oxidation or reduction of the analytes by homogeneous solution reactions. As previously stated, the current density at the small nano-ES emitter electrode is expected to be of sufficient magnitude to form reactive peroxides or radicals (e.g., eqs 6 and 7, Table 1). If produced, these species would diffuse from the electrode into the solution where they could react with the analytes, producing the same analyte oxidation products as the direct (electrode–solution) electron transfer reactions. This same basic phenomenon is used to advantage in coulometric titrations [22] to increase overall “titration efficiency.” The efficiency of the direct oxidation of the analyte at the electrode may be low, but the overall redox efficiency (direct plus indirect reactions) may be high. In fact, Bateman [17] has provided evidence that peptide oxidation in capillary electrophoresis/nano-ES-MS can result from a chemical reaction of the peptides with reactive oxygen, peroxide, or hydroxyl radicals formed electrochemically from \( \text{H}_2\text{O} \) at the nano-ES spray tip. The estimated current density in Bateman’s experiments was about 150 mA/cm\(^2\), or roughly 4.5 time greater than the highest current density investigated here using chronopotentiometry. The interfacial electrode potentials measured in the chronopotentiograms at the highest current density (32 mA/cm\(^2\)) were already sufficient (\( \approx 1.8 \text{ V} \), Figure 2) to generate most of these suspected reactive species. Under typical ES-MS conditions with a metal capillary emitter, peptide oxidation is rare [28].

### Conclusions

The results from chronopotentiometry experiments carried out with current densities in the range that might be found in an ES emitter, and the results from mass transport calculations for flow through tubular electrodes, provide insight into analyte electrolysis in an ES emitter during ES-MS. Chronopotentiograms indicate the magnitudes and trends in the interfacial potential one might anticipate in an ES emitter under different solution conditions and current densities, using different electrode materials. The magnitude of the interfacial potential at the electrode ultimately determines which reactions can occur and at what rate. If the emitter electrode area is physically limited (high current density), as in a metal-coated, pulled-glass capillary used in nano-ES, or in another extremely short tubular electrode configuration, the emitter electrode interfacial potential under a given set of conditions will tend toward the extremes in magnitude where solvent electrolysis occurs. The actual potential limits will be influenced then by the redox character of the particular solvents and additives in solution. The efficiency of electrolytic reactions involving analytes in the system that occur at potentials at or beyond these potential limits will be diminished because the reactions involving the solvent system can supply the major fraction of the current. Also, the interfacial potential may be essentially “buffered” below that necessary for analytic reac-
tion. If one wishes to avoid a particular electrolysis reaction this can be used to advantage and in fact “redox buffers” (sometimes called depolarizers [22]) might be added to solution for this purpose [19, 29]. If one does not physically limit the electrode area to such a degree, the interfacial electrode potentials are expected to be lower under otherwise identical conditions, because of the decreased current density (larger effective electrode area). Such might be the case with the typical metal capillary ES emitter. A “sacrificial electrode” (one that anodically corrodes), such as stainless steel or another metal (e.g., zinc, copper, or silver), might be used to maintain the emitter electrode potentials below that necessary for analyte redox chemistry in positive ion mode ES-MS. Of course, it must be recognized that it is fortuitous that Fe²⁺ ions in solution from stainless steel corrosion do not readily form gas-phase ions or otherwise interfere in analyses of most analytes by ES-MS. The same may not be true for other metal ions added to solution via corrosion. In negative ion mode, the low overpotential for hydrogen generation on platinum might be one means to maintain the interfacial potential relatively positive and limit analyte reduction.

The interfacial potential at the ES emitter electrode is only one aspect of analyte electrolysis to consider. The other aspects are the magnitude of the ES current and the mass transport of the analyte to the electrode (both of which also influence the interfacial potential). To maximize analyte electrolysis, the magnitude of the ES current must be sufficient for complete electrolysis of the molar equivalent of the analyte flowing through the emitter electrode. The minimum current required can be calculated from Faraday’s law (eq 24). In addition, all the analyte must contact the electrode surface on passage through the electrode. In general, operating at slower flow rates with physically long (noncorrodible) electrodes (≫1 mm long), should enhance electrolysis efficiency (via direct heterogenous electron transfer) by increasing the time available (electrolysis time) for analyte transport to the electrode via convective-diffusive flux. Changing from the normal tubular geometry electrode to emitters containing conductive frit electrodes, a thin-layer channel electrode or other geometry might be investigated as means to enhance mass transport and increase analyte electrolysis. To limit analyte electrolysis, high flow rates and physically short tubular electrodes that can corrode (like stainless steel), will decrease the efficiency of direct heterogenous electron transfer reactions (short electrolysis time). However, the small electrodes facilitate extremes of potential and redox reactions creating reactive species. These reactive species may react with the analyte in solution (indirect, homogenous electron transfer reactions) producing the same net products as the direct electrochemical reactions. This means that the time the analyte remains in solution, past the point on the emitter electrode where redox chemistry is taking place, could be a factor in determining the extent of analyte oxidation or reduction in ES-MS.

A way in which both direct and indirect electrochemical alteration of solution species can be avoided is to design the ES emitter electrode so that is has no direct contact to the flow stream. This has been done for other purposes in the coupling of capillary electrophoresis and ES-MS [30, 31]. The electrode–solution contact is made by ionic transport across an ion permeable barrier membrane that isolates the electrode from the flow stream in a separate buffer/electrolyte containing reservoir. If the electrode reservoir is large enough, or if it is continually renewed, the products of electrolysis at the electrode will not enter the flow stream.

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