Evaporation and Discharge Dynamics of Highly Charged Multicomponent Droplets Generated by Electrospray Ionization†

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We investigate the Rayleigh discharge and evaporation dynamics of highly charged two-component droplets consisting principally of methanol with 2-methoxyethanol, tert-butanol, or m-nitrobenzyl alcohol. A phase Doppler anemometer (PDA) characterizes droplets generated by electrospray ionization (ESI) according to size, velocity, and charge as they move through a uniform electric field within an ion mobility spectrometer (IMS). Repeated field reversals result in droplet “ping-pong” through the PDA. This generates individual droplet histories of solvent evaporation behavior and the dynamics of charge loss to progeny droplets during Rayleigh discharge events. On average, methanol droplets discharge at 127% their Rayleigh limit of charge, $q_R$, and release 25% of the net charge. Charge loss from methanol/2-methoxyethanol droplets behaves similarly to pure 2-methoxyethanol droplets which release $\sim 28\%$ of their net charge. Binary methanol droplets containing up to 50% tert-butanol discharge at a lower percent $q_R$ than pure methanol and release a greater fraction of their net charge. Mixed 99% methanol/1% m-nitrobenzyl alcohol droplets possess discharge characteristics similar to those of methanol. However, droplets of methanol containing 2% m-nitrobenzyl evaporate down to a fixed size and charge that remains constant with no observable discharges. Quasi-steady-state evaporation models accurately describe observed evaporation phenomena in which methanol/tert-butanol droplets evaporate at a rate similar to that of pure methanol and methanol/2-methoxyethanol droplets evaporate at a rate similar to that of 2-methoxyethanol. We compare these results to previous Rayleigh discharge experiments and discuss the implications for binary solvents in electrospray mass spectrometry (ESI-MS) and field-induced droplet ionization mass spectrometry (FIDI-MS).

Introduction

Multicomponent solvents are common in the electrospray mass spectrometry of biomolecules, yet questions remain regarding the mechanisms by which analyte-containing single and multicomponent solvents yield unique mass spectra. Electrospray ionization†−3 (ESI) is a popular tool in mass spectrometry because of its ability to generate low-energy, multiply charged biomolecules and molecular clusters.4 In the electrospray process, an applied electric field induces charge separation in a solution flowing from a capillary needle. The resulting electrohydrodynamic forces draw the liquid to a point referred to as the Taylor cone that sprays a fine mist of highly charged droplets.5 Mass spectrometric applications utilize the subsequent evaporation and discharge processes that ultimately yield desolvated gas-phase ions or clusters. Despite the popularity of the technique, recent experiments present conflicting results regarding the dynamics and mechanisms involved.

Current understanding of charged droplet instability and breakup begins with the seminal work of Lord Rayleigh. In 1882, he proposed that the repulsive force due to the net surface charge destabilizes the natural mode oscillations of the droplet. He postulated that these oscillations become unstable when the net charge $q$ on a droplet of radius $r$ and surface tension $\gamma$ exceeds a critical value $q_R$, given by eq 1, where $\epsilon_0$ is the permittivity of the surrounding medium.6

$$q_R = \frac{8 \pi \epsilon_0}{\sigma} \frac{1}{2} \frac{r^{1/2}}{12 r^{3/2}}$$

Rayleigh predicted a droplet emits “fine jets” of charged progeny when $q$ exceeds the limit $q_R$, but his analysis does little to describe the dynamics of the event. Significant experimental7−12 and theoretical13−16 research elucidates these mechanisms for single-component droplets. In the consensus view, solvent evaporates from a highly charged micrometer-sized droplet until $q \approx q_R$, at which point the droplet distorts and emits jets of small, highly charged progeny droplets in an event alternatively termed Coulomb fission or Rayleigh discharge in the literature. Images showing one jet from methanol17 and n-heptane5 and two jets from ethylene glycol droplets11 visually indicate that the progeny droplets are roughly $1−10\%$ the diameter, or $\sim 10^{-6}−10^{-3}$ the mass of the parent droplet. Recent experiments involving field induced droplet ionization (FIDI) in our laboratory suggest that simple jet emission results from external electric fields, either applied directly to or originating from nearby highly charged droplets.18−20 Parent droplets typically release 10−40% of a droplet’s net charge but less than 5% of a droplet’s mass in discharge events that generate tens to thousands of smaller, highly charged progeny droplets.4,21,22 This sequence of evaporation and discharge events is repeated by both the parent and progeny droplet, the latter on a significantly shorter time scale due to their smaller diameter. Over the lifetime of a micrometer-sized charged droplet, significantly more mass is lost due to solvent evaporation than to Rayleigh discharge events and evaporation therefore is critical to understanding droplet behavior and composition. In the nanometer size regime...
(<0.1 μm), researchers propose two competing mechanisms for discharge events. Dole’s original charge residue model (CRM) suggests the process of evaporation and Rayleigh discharge-like events continues until the formation of desolvated ions.25 Conversely the ion evaporation model (IEM) predicts the surface electric field due to excess charge becomes sufficiently large to desorb ions directly from the surface of the nanodroplet.24 Because the CRM and IEM describe nanometer-sized charged droplet phenomena, the present analysis of micrometer-sized droplets does not consider these mechanisms.

Recent mass spectrometry studies illustrate a variety of interesting but disparate ionization behaviors for analytes dissolved in multicomponent solvents. Iavarone and Williams correlate solution surface tension and the electrospray mass spectrometry (ESI-MS) charge-state distribution of polymers and biomolecules in the gas phase.25 26 Terming the phenomenon “supercharging”, they note the addition of m-nitrobenzyl alcohol (γ = 50 mN m⁻¹)25 affects the charge-state distributions of the amine-functionalized dendrimers poly(propyleneimine)hexadecammine DAB-16 with 16 amino groups, and poly(propyleneimine)tetrahexacontaamine DAB-64 with 64 groups. The addition of 5 vol % m-nitrobenzyl alcohol to DAB-16 in methanol (γ = 22 mN m⁻¹)27 increases the weighted ESI-MS average charge state to 4.2 from 3.3 in the methanol electrospray. Conversely, adding 1 vol % m-nitrobenzyl alcohol to DAB-16 in water (γ = 72 mN m⁻¹)27 decreases the average ESI-MS charge state to 3.8 from 4.7 when sprayed from water. In finding similar results for DAB-64, poly(ethylene glycol), and cytochrome c, they conclude that the charge-state distribution of multiply charged species correlates with the surface tension of the lowest volatility solvent.25 26 28 In contrasting experiments, Šamalikova and Grandori report no change in the ESI-MS charge-state distribution of denatured proteins upon the addition of n-propanol (γ = 23 mN m⁻¹) to aqueous solutions.29 They further characterize a range of protein charge-state distributions from water—alcohol—acid mixtures and conclude that factors other than solvent surface tension play a significant role.29

The conflicting results suggest that more research is necessary to understand the processes that govern Rayleigh discharge processes in multicomponent solvents and the resultant charging of analytes in electrospray mass spectrometry.

This manuscript reports the evaporation and discharge dynamics of the multicomponent solvent systems listed in Table 1. Methanol/tert-butanol mixtures from 95 vol %/5% to 50%/50% explore the droplet behavior when the components have similar evaporation rates and bulk surface tensions. Droplets of methanol and 2-methoxyethanol provide insight when components differ in both evaporation rates and bulk surface tension values. m-Nitrobenzyl alcohol is added at 1 vol % and 2% in methanol to classify discharge and evaporation phenomena from “supercharging” solvents. Additionally, studies of both neat methanol and neat 2-methoxyethanol provide comparison for the multicomponent solvents. Electrospray ionization generates highly charged droplets for each pure or binary solvent system, while the droplet “ping-pong” experiment developed in our laboratory provides a temporal history of droplet size and charge.10 12 Droplet generation by ESI is tuned away from the standard cone—jet mode of spraying to generate highly charged 10—50 μm diameter droplets for analysis of their Mie scattering patterns as they travel through an ion mobility spectrometer (IMS). These droplet diameters are somewhat larger than the 1—2 μm droplets generated by cone—jet electrospray, and significantly larger than the <200 nm droplets generated from a nanoelectrospray or nanospray ion source.12 For each system, percent charge lost and percent qₘ at discharge characterize Rayleigh events. Interestingly, experimental evaporation rates fit the shape and behavior predicted by single-component evaporation models. A quasi-steady-state evaporation model corroborates this finding and enables correlations between discharge characteristics and time-dependent droplet composition. These results constrain the interpretation of recent electrospray mass spectrometry experiments and provide further insight into the behavior of evaporating charged droplets.

### Experimental Section

**Droplet Ping-Pong.** Figure 1 shows a schematic diagram of the experimental apparatus. Previous reports of single component microdroplets detail the hardware, experimental methodology, and data analysis for the ping-pong technique.10 12 In brief, an electrospray source generates micrometer-sized droplets that enter the ion mobility spectrometer cell for characterization by the phase Doppler anemometer (PDA). A 35-gauge polished stainless steel capillary (R-HTX-35, 64 μm i.d., 150 μm o.d., Small Parts, Inc.) sprays upward at two sequential transfer apertures. Capillary biases of +800 to 1500 V, capillary—aperture distances of 0.5—5 mm, and flow rates of 0.5—2 μL min⁻¹ maintain the positive-ion electrospray in a vibrating spindle or pulsed cone—jet mode.33 The first 500 μm diameter aperture is biased at +100 V. Mounted 1 cm above the first, the second aperture is 1.5 mm in diameter and maintained at earth ground. Solvents methanol (HPLC grade, EM Science), 2-methoxyethanol (99.5%, EM Science), tert-butanol (99%, Sigma Aldrich), and m-nitrobenzyl alcohol (98%, Sigma Aldrich) are used without further purification.

Eight resistively coupled stainless steel rings define a linear, 50 V cm⁻¹ electric field within the IMS. A laminar 3 cm s⁻¹ downward flow of nitrogen ensures that droplets evaporate in a
approximately 50 cm s\(^{-1}\) nascent droplets drift upward antiparallel to gravity at aperture. Under normal operating conditions, volume of the PDA at the center of the IMS, \(V \) is the measurement volume of the phase Doppler anemometer (PDA) and successive field reversals enable PDA characterization of droplet size, velocity, and charge with time.

Figure 1. Schematic of the “ping-pong” apparatus. An electrospray source generates micrometer-sized droplets that travel through two transfer apertures into the drift region of the ion mobility spectrometer (IMS). Droplet ping-pong commences when a droplet passes through the measurement volume of the phase Doppler anemometer (PDA) and successive field reversals enable PDA characterization of droplet size, velocity, and charge with time.

Evaporation and Discharge Dynamics of Droplets

Evaporation Models\(^{27,36}\) Evaporation temperatures represent a depression from an ambient temperature \(T_\infty\). Table 2 lists the calculated solvent parameters for methanol, 2-methoxyethanol, and tert-butanol.

### Table 2: Physical Parameters Employed for the Evaporation Models\(^{27,36}\)

<table>
<thead>
<tr>
<th>Parameter/Units</th>
<th>Methanol</th>
<th>2-Methoxyethanol</th>
<th>tert-Butanol</th>
</tr>
</thead>
<tbody>
<tr>
<td>(T_\text{surf} / \text{K})</td>
<td>266</td>
<td>289</td>
<td>282</td>
</tr>
<tr>
<td>(\varepsilon)</td>
<td>33</td>
<td>17.2</td>
<td>12.47</td>
</tr>
<tr>
<td>(\gamma / \text{mN m}^{-1})</td>
<td>22.07</td>
<td>30.84</td>
<td>19.96</td>
</tr>
<tr>
<td>(\mu / \text{Pa s})</td>
<td>5.46 \times 10^{-3}</td>
<td>1.36 \times 10^{-3}</td>
<td>4.15 \times 10^{-3}</td>
</tr>
<tr>
<td>(c_{p,d} / \text{J mol}^{-1} \text{K}^{-1})</td>
<td>81.1</td>
<td>171.1</td>
<td>218.6</td>
</tr>
<tr>
<td>(c_{p,g} / \text{J mol}^{-1} \text{K}^{-1})</td>
<td>45.2</td>
<td>99.8</td>
<td>115.2</td>
</tr>
<tr>
<td>(V / \text{m}^3 \text{mol}^{-1})</td>
<td>4.05 \times 10^{-5}</td>
<td>7.88 \times 10^{-5}</td>
<td>9.40 \times 10^{-5}</td>
</tr>
<tr>
<td>(p^i(T_\text{surf}) / \text{Pa})</td>
<td>2.59 \times 10^3</td>
<td>6.50 \times 10^2</td>
<td>1.77 \times 10^3</td>
</tr>
<tr>
<td>(D_{i,\text{air}(T_\text{surf})} / \text{m}^2 \text{s}^{-1})</td>
<td>1.20 \times 10^{-6}</td>
<td>8.26 \times 10^{-6}</td>
<td>7.72 \times 10^{-5}</td>
</tr>
<tr>
<td>(\Delta H_{vap}(T_\text{surf}) / \text{J mol}^{-1})</td>
<td>4.00 \times 10^4</td>
<td>4.56 \times 10^4</td>
<td>4.89 \times 10^4</td>
</tr>
<tr>
<td>(κ_{\text{air}} )</td>
<td>1.87 \times 10^{-3}</td>
<td>1.24 \times 10^{-3}</td>
<td>1.53 \times 10^{-3}</td>
</tr>
</tbody>
</table>

\(s\) Parameters are functions of temperature and are listed at the respective evaporation surface temperature, \(T_\text{surf}\), of the pure solvent. Evaporation temperatures represent a depression from an ambient temperature \(T_\infty\) = 293 K.

Surface Tension. A NIMA model PS4 pressure sensor (Coventry, U.K.) ascertains how small additions of \(m\)-nitrobenzyl alcohol affect the bulk surface tension of methanol using the Wilhemy plate method.

Modeling Droplet Evaporation. Hinds presents a model for single-component micrometer-sized droplets evaporating at ambient pressure.\(^{35}\) Equation 3 characterizes the time-dependent diameter \(d\) that depends on the initial diameter \(d_0\), time \(t\), and solvent parameters \(s\) defined by eq 4.

\[
d^2 = d_0^2 + st
\]

\[
s = -\frac{8D_{i,\text{air}(T_\text{surf})}M p^i(T_\text{surf})}{R\rho} \frac{T_\text{surf}}{T_\infty}
\]

Solvent parameters include the gas constant \(R\), the bulk molar mass \(M\) and density \(\rho\), and the temperature-dependent binary diffusivity of solvent vapor \(i\) in air \(D_{i,\text{air}(T_\text{surf})}\) and equilibrium vapor pressure \(p^i(T_\text{surf})\). Equation 4 simplifies the more rigorous model by not considering the inhibiting effect of solvent vapor in the ambient gas. Counter-flowing nitrogen gas within the IMS allows for this simplification. Thus \(s\) is constant for a pure droplet of fixed temperature and qualitatively relates evaporation rates of different droplets. As the value of \(s\) is always negative for an evaporating droplet, we refer to \(-s\) as the evaporation rate. Because evaporation is spontaneous and endothermic, the droplet surface cools from the ambient gas temperature \(T_\infty\) to an equilibrium value \(T_\text{surf}\) given by eq 5.\(^{35}\)

\[
T_\text{surf} = T_\infty - \frac{D_{i,\text{air}(T_\text{surf})}\Delta H_{vap}(T_\text{surf}) p^i(T_\text{surf})}{Rκ_{\text{air}}} \frac{T_\text{surf}}{T_\text{surf}}
\]

Additional values in eq 5 include the temperature-dependent enthalpy of vaporization \(\Delta H_{vap}(T_\text{surf})\), and the thermal conductivity of air \(κ_{\text{air}}\). Equation 5 must be iteratively solved for \(T_\text{surf}\) as many parameters are temperature-dependent. Table 2 lists the calculated solvent parameters for methanol, 2-methoxyethanol, and tert-butanol. The superscript \(a\) denotes temperature-depen-
dent parameters listed at the respective \( T_{\text{surf}} \) relative to \( T_c = 293 \) K. Lide\(^{27}\) and Yaws\(^{36}\) provide all pertinent physical constants. Even with \( T_c = 298 \) K, eq 5 predicts the tert-butanol evaporation temperature below its 298 K freezing point.

Droplet evaporation models rely on balancing energy and mass transfer between the droplet and the gas. In the case of single-component droplets, eqs 3–5 provide analytical solutions for this balance. In the case of multicomponent droplets, more rigorous evaporation models allow only numerical solutions. Following a derivation by Newbold and Amundson,\(^ {37}\) Hopkins and Reid implement a quasi-steady-state evaporation model that accurately describes micrometer-sized alcohol/water droplets.\(^ {38}\)

This model quantifies the rate of change in the droplet radius, \( \frac{dr}{dt} \), the change in mole fraction \( dx/dt \) of pure species \( i \) within the droplet, and the surface temperature depression \( dT_{\text{surf}}/dt \). In further simplification, this equilibrium surface temperature \( T_{\text{surf}} \) is taken as the temperature throughout the droplet volume.

\[
\frac{dV}{dt} = -\sum_{i=1}^{n} N_i V_i 
\]

(6)

In eq 6, \( V_i \) is the molar volume of pure species \( i \) while \( N_i \) is the flux of species \( i \) diffusing away from the droplet according to eq 7.\(^ {38}\)

\[
N_i = \frac{C_T D_N}{r_p} \ln(\chi) \left[ \frac{x_p \phi_i(T_{\text{surf}}) \Delta H_{\text{vap}}}{\chi \Delta H_{\text{vap}} - 1} \right] 
\]

(7)

This is a simplification from Hopkins and Reid in which \( C_T \) is the gas concentration above the droplet surface; \( D_N \), the self-diffusivity of nitrogen gas, approximates the diffusion coefficient of inert gas in the vapor mixture above the droplet surface; \( x_i \) is the mole fraction of species \( i \); and \( p \) is the ambient pressure.\(^ {38}\) As with the single-component evaporation model in eqs 3–5, this simplification does not consider the flux-inhibiting contribution of ambient solvent vapor. The parameter \( \chi \) is the ratio of the ambient inert gas concentration to the concentration of inert gas above the droplet surface. We approximate \( \chi \) using Raoult’s law as shown in eq 8.

\[
\chi = \left[1 - \sum_{i=1}^{n} \frac{x_p \phi_i(T_{\text{surf}}) \Delta H_{\text{vap}}}{\chi \Delta H_{\text{vap}} - 1} \right]^{-1} 
\]

(8)

From a calculation of mass balance, the quasi-steady-state model calculates the change in mole fractions by eq 9 where the droplet molar volume, \( V_m \) is defined in eq 10.

\[
\frac{dx_i}{dt} = \frac{3V_m}{r} \sum_{j=1}^{n} N_j \left( x_j - \frac{N_i}{\sum_{j=1}^{n} N_j} \right) 
\]

(9)

\[
V_m = \sum_{j=1}^{n} x_j V_j 
\]

(10)

Similarly, energy balance accounts for the temperature depression due to the spontaneous, endothermic evaporation. Equation 11 models the rate of change in droplet temperature, \( dT_{\text{surf}}/dt \).

\[
\frac{dT_{\text{surf}}}{dt} = \frac{3V_m}{r c_{p,\text{air}}} \left\{ \frac{k_{\text{surf}} A}{(e^\lambda - 1)r} (T_c - T_{\text{surf}}) - \sum_{i=1}^{n} N_i \left[ \Delta H_{\text{vap},i}(T_{\text{surf}}) + \Delta c_{p,i}(T_{\text{surf}} - T_c) \right] \right\} 
\]

(11)

The droplet temperature depends on the heat capacity of air \( c_{p,\text{air}} \), the enthalpy of vaporization of the \( i \)th droplet species at the droplet surface temperature, \( \Delta H_{\text{vap},i}(T_{\text{surf}}); \) the difference between the liquid-phase and vapor-phase heat capacity of the \( i \)th droplet species, \( \Delta c_{p,i} \), and the ambient temperature, \( T_c \). Equation 12 defines \( A \).

\[
A = \frac{r}{k_{\text{air}}} \sum_{i=1}^{n} N_i \Delta c_{p,i} 
\]

(12)

These equations model the evaporation behavior for a binary droplet. Table 2 lists the additional pertinent physical constants employed in the calculations. Constants for air include \( D_{N_2} = 2.03 \times 10^{-5} \text{ m}^2 \text{ s}^{-1} \), \( c_{p,\text{air}} = 29.1 \text{ J mol}^{-1} \text{ K}^{-1} \), \( K_\text{air} = 0.0253 \text{ W m}^{-1} \text{ K}^{-1} \), and \( C_T = 42.3 \text{ mol}^{-3} \text{ K} \). Because there is no analytical solution to the quasi-steady-state model, a fourth-order Runge–Kutta numerical method computes droplet sizes with an ambient temperature of 293 K, an initial droplet diameter of 50 \( \mu \)m, and a 0.5 ms time step. Smaller timesteps do not show observable differences in the computed evaporation characteristics.

Experimentally, linear regressions of \( d^2 \) versus \( t \) determine \( s \) values for all of the binary and pure systems studied according to eq 3. For multicomponent systems \( s \) is not strictly defined because the component concentration profiles change due to differential evaporation rates. However, regressions show a good fit to eq 3 for the binary droplets studied, making \( s \) a useful parameter to compare evaporation for both multicomponent and single component droplets.

**Results**

At least 100 Rayleigh discharge events were recorded for binary solvent mixtures consisting of methanol/2-methoxyethyleneol, methanol/tert-butanol, and methanol/1 vol % \( m \)-nitrobenzyl. Characterized droplets are initially 30–50 \( \mu \)m in diameter and carry a nascent charge of 60–90% \( q_d \) from the electrospray source. Methanol droplets with 2 vol % \( m \)-nitrobenzyl alcohol seldom demonstrate Rayleigh discharge events, but more often evaporate down to a fixed size and charge that remains constant for up to one second, the maximum acquisition duration for a single droplet. These nonvaporizing droplets are generally 5–10 \( \mu \)m in diameter and carry a 20–50% \( q_d \) nascent charge. Calculations based on the quasi-steady-state model guide these interpretation of the “ping-pong” results.

**Quasi-Steady-State Evaporation Model**. Figure 2 presents the model evaporation lifetime of 50 \( \mu \)m diameter droplets of (A) 75% methanol/25% 2-methoxyethyleneol and (B) 75% methanol/25% tert-butanol. The solid line indicates the droplet diameter and the dashed line indicates the component mole fraction as a function of time. As previously mentioned, highly charged droplets initially travel upward at \( \sim 50 \text{ cm} \text{ s}^{-1} \), taking approximately 0.2 s reach the PDA measurement volume after generation by electrospray. The dotted line in Figure 2 denotes this experimental 0.2 s delay between generation and characterization. Thus the ping-pong experiment only “sees” droplets to the right of the dotted line.
Figure 2. Time evolution of droplet diameter (solid line, left axis) and component mole fraction (dashed line, right axis) as modeled by quasi-steady-state evaporation for a droplet of (A) 75 vol % methanol/25% 2-methoxyethanol, and (B) 75% methanol/25% tert-butanol. Because of the experimental delay between droplet generation and PDA characterization, the dotted line at 0.2 s indicates the first time these droplets would be detected by the ping-pong experiment.

Figure 3. Representative (A) size, (B) velocity, (C) charge, and (D) percent $q_R$ of a highly charged 75 vol % methanol 25% 2-methoxyethanol droplet acquired by the ping-pong experiment. Large decreases in velocity and charge indicate Rayleigh discharge events, indicated with arrows. Discharge events are characterized by ~30% charge loss at ~100% the Rayleigh limit of 2-methoxyethanol with no detectable loss of mass. In (A) the dotted line represents diameter values from a linear regression of $d^2$ versus $t$ with a slope $s \approx 1200 \mu m^2 s^{-1}$.

Droplets with Observed Rayleigh Discharge Events. Figure 3 shows a representative history of (A) diameter, (B) speed, (C) charge, and (D) charge as a percent of its Rayleigh limit (% $q_R$) for a single droplet of 75% methanol/25% 2-methoxyethanol undergoing multiple Rayleigh discharges. When first characterized, the droplet is roughly 32 $\mu m$ in diameter (A) with $\sim 4.2 \times 10^9$ elementary charges (C). This corresponds to roughly 81% $q_R$ for 2-methoxyethanol (D). In repeated observations through the first 0.2 s of measurement, the droplet’s diameter (A) decreases, the speed (B) increases, and the charge (C) remains constant. The speed increase is due to the constant electrical force, $qE$, becoming proportionally greater than the force of gravity $mg$, which steadily decreases as the droplet loses mass to evaporation. The small oscillations in speed are due to the droplet traveling upward antiparallel to gravity more slowly than traveling downward parallel to gravity. The oscillations in the diameter measurement are propagated from oscillations in the Doppler phase shift data that in turn may be due to an unresolved asymmetry in the signals acquired by the split diode detector. The resulting ±2 $\mu m$ oscillation is most pronounced in the small droplet diameter in Figure 6A but is also evident in the larger droplet diameter data presented in Figure 3A as well. As such, these oscillations do not adversely impact the conclusions we draw regarding droplet evaporation.
and discharge dynamics. The oscillations in charge and percent Rayleigh limit in Figure 6C and D, are a consequence of the small oscillations in measured droplet diameter. As the diameter decreases and the charge remains constant, the ratio $q/q_R$, increases, as reflected in the $\% \Delta q/q_R$ plot in Figure 3D. At $\sim 0.2$ s after the initial characterization, the charge decreases suddenly, resulting in a decrease in velocity and the percent Rayleigh limit. This is not accompanied by a concomitant decrease in mass. We interpret this sudden charge loss to be a Rayleigh discharge event. Over the acquired evaporation and discharge history, the droplet presented in Figure 2 shows six well-defined events denoted by arrows. With an initial recorded diameter of 32 $\mu$m and a final diameter of $\sim 5 \mu$m, this history represents the loss of 99.6% of the droplet’s initial mass and 90% of the nascent charge.

**Evaporation Dynamics.** In the micrometer regime, evaporation dominates mass loss of charged droplets and the contribution of Rayleigh discharge events is negligible. In agreement with the consensus view on Rayleigh discharge phenomena, Figure 3A shows no measurable mass loss associated with discharges but rather a smoothly decreasing mass due to evaporation. Other experiments lead to an expectation of approximately 2% of droplet mass loss in a discharge event,$^7$ corresponding to a $\sim 0.7\%$ diameter change that is smaller than the $\sim 2 \mu$m measurement error in the ping-pong experiment. The dashed line in Figure 3A follows a fit to eq 3 with $-s = 1200 \mu m^2 s^{-1}$. This is somewhat smaller than the predicted evaporation rate of pure 2-methoxyethanol of 1925 $\mu m^2 s^{-1}$ from Table 2 but significantly smaller than the evaporation rate of 4750 $\mu m^2 s^{-1}$ for methanol. This suggests that 2-methoxyethanol dominates the observed droplet composition. This agrees with the results of the quasi-steady-state evaporation model shown in Figure 2 that indicate significant methanol depletion before initial PDA observation.

Table 1 lists experimentally determined average $-s$ values with the corresponding standard deviations for each system studied. Droplets consisting of methanol/2-methoxyethanol show evaporation similar to that for pure 2-methoxyethanol, and the mixed methanol/tert-butanol droplets evaporate with rates similar to those of both pure methanol and tert-butanol. These relative rates are in excellent agreement with the predicted results from the quasi-steady-state model. Methanol droplets with 1% m-nitrobenzyl alcohol evaporate at a rate similar to that of pure methanol. This suggests that this concentration of $m$-nitrobenzyl alcohol has no significant effect on the evaporation of methanol droplets in the micrometer regime.

**Discharge Dynamics.** For droplets such as the 75% methanol/25% 2-methoxyethanol characteristic example in Figure 3, the percent charge in average charge before and after a discharge event, $\% \Delta q/q_R$, quantifies the charge loss. The percent of the Rayleigh limit at discharge, $\% q/q_R$, is simply the last recorded value before the sharp decrease characteristic of a discharge event. In the case of binary solvents, the exact $q_R$ value is unknown a priori due to the droplet surface tension being unknown a priori due to the droplet surface tension being composition- and time-dependent. Since the evaporation model suggests the methanol/2-methoxyethanol droplets are predominantly composed of 2-methoxyethanol during the ping-pong experiment, we use the 2-methoxyethanol Rayleigh limit value. The methanol $q_R$ quantifies the Rayleigh limit of methanol/tert-butanol droplets since the similar surface tension values introduce a maximum 5% error in $q_R$. Lastly, the methanol $q_R$ quantifies the Rayleigh limit of the methanol droplets with added $m$-nitrobenzyl alcohol as the addition of up to 2 vol % does not change the bulk surface tension of methanol within the 0.1 mN m$^{-1}$ error of measurement.

Table 1 lists the averages and standard deviations for the percent charge lost and the percent Rayleigh limit at discharge for the solvent systems studied. On average, events from pure methanol droplets release 25% of the droplet net charge, in good agreement with previous results from our laboratory.$^{10}$ Increasing concentrations of tert-butanol raises the percent charge lost from 25% up to 37% average charge loss for 50/50% mixtures. In contrast, droplets containing increasing concentrations of 2-methoxyethanol show little concentration dependence in the discharge dynamics. These results support the evaporation model in which the methanol/tert-butanol droplets change composition throughout their characterized lifetime while the detected methanol/2-methoxyethanol droplets are principally composed of 2-methoxyethanol. Although the standard deviation is large, methanol droplets with 1% m-nitrobenzyl alcohol appear to release slightly less charge, 21%, than pure methanol droplets, but with large standard deviations. The methanol/2% m-nitrobenzyl alcohol droplets release a larger fraction of their net charge, $\sim 35\%$. While this is greater than the neat methanol and 1% $m$-nitrobenzyl alcohol charge loss, the small sample size limits rigorous statistical comparisons.

Size-charge correlation diagrams more fully highlight the discharge dynamics. Figure 4 presents the percent charge lost, $\% \Delta q/q_R$, as a function of droplet diameter at discharge for (A) 75% methanol/25% 2-methoxyethanol, (B) 50%/50%, and (C) pure 2-methoxyethanol droplets. Figure 5 represents similar size-charge correlations for methanol/tert-butanol compositions of (A) 95%/5%, (B) 90/10%, (C) 75/25%, and (D) 50/50%.
Discharge events from methanol/2-methoxyethanol droplets are consistent across the concentration ranges studied. There is a slight trend suggesting a larger fraction of charge loss from smaller droplets, although this is small compared to the range of scatter in the data. That the discharge dynamics remain relatively size-independent also suggests that the composition of these droplets remains constant, consistent with the conclusion above that these droplets are principally composed of 2-methoxyethanol. This agrees well with previous research in our laboratory that found no significant variation in the fraction of charge loss with droplet size for water, methanol, and acetone, as well as pure hydrocarbon solvents with up to 1 vol % of a conductivity enhancing agent.

In contrast, Figure 5 shows a significant correlation between droplet size and charge loss for the methanol/tert-butanol droplets. For each concentration studied, smaller droplets release a larger fraction of their net charge than the larger droplets. We attribute this to changing component concentrations as these droplets evaporate. As the model predicts in Figure 2B, methanol/tert-butanol droplets become more concentrated in tert-butanol over the observed droplet lifetime. Considering droplets with larger initial concentrations of tert-butanol undergo greater average charge loss as shown in Table 1, this suggests that the droplets become more concentrated in tert-butanol as they evaporate, and this concentration results in greater net charge loss in Rayleigh discharge events. As can be seen in Figure 5 this approaches 50% for droplets below 5 µm.

Size-charge correlations for methanol with 1% m-nitrobenzyl alcohol (not shown) display a size dependence similar to that for the methanol/tert-butanol droplets. This similarly suggests a size and time-dependent composition change implying that m-nitrobenzyl alcohol concentrates in droplets as methanol preferentially evaporates.

**Droplets with No Observed Rayleigh Discharged Events.** Methanol droplets with 2 vol % m-nitrobenzyl alcohol show only a few Rayleigh discharge events at most, and evaporate down to a “core” size that remains fixed for the duration of analysis, ~1 s. Figure 6 shows a characteristic acquisition. Unlike the methanol droplets with 1% m-nitrobenzyl alcohol that display more typical discharge behavior, the 2% addition to methanol has a profound effect on the evaporation and...
discharge dynamics. We attribute the different behavior to a change in the electrospray dynamics for this solvent system and the related difficulty in generating 30–50 μm droplets with sufficiently high net charge. The droplet examined in Figure 6 has a significantly smaller initial size with significant oscillations in the diameter measurement. Figure 6C shows that the characteristic droplet carries an order of magnitude less charge than the characteristic droplet in Figure 3C, and its initial speed is half that of the droplet shown in Figure 3. Therefore, this droplet undergoes significantly more evaporation before it reaches the PDA measurement volume. Despite the extended period of evaporation, these droplets show no discharge events because the evaporation ceases before the charge approaches the $q_R$ of m-nitrobenzyl alcohol (Figure 6D). The halt in evaporation is likely due to complete methanol depletion, leaving only the low volatility m-nitrobenzyl alcohol component. A 50 μm diameter methanol droplet evaporates in ~0.5 s, suggesting that these slow moving droplets undergo nearly complete methanol loss before detection. Additionally, the 6 μm droplet in Figure 6A is only 0.1% the volume of a 50 μm droplet, and 1% the volume of a 25 μm droplet. This also suggests that the droplet has lost nearly its entire methanol component as well as a significant fraction of its m-nitrobenzyl alcohol component by the time it reaches this nonevaporative domain.

The morphology of the nonevaporating droplet in Figure 6 is unclear from present experiments. As Table 2 shows, evaporative cooling significantly reduces the temperature of methanol droplets. These droplets easily cool below the freezing point of pure m-nitrobenzyl alcohol (304 K),27 suggesting the nonevaporating droplet may be a crystallized m-nitrobenzyl alcohol particle. This may explain the oscillation in diameter values shown in Figure 6A. As droplet size is calculated on the basis of PDA Doppler bursts due to refractive Mie scattering, a solid particle or droplet with a crystallized surface may scatter light very differently compared to a Mie analysis that assumes a liquid droplet. As the derived diameters affect charge (Figure 6C) and percent Rayleigh limit (Figure 6D) plots, these data show similar oscillations. These persistent “frozen” droplets are likely not an issue in traditional electrospray mass spectrometry experiments where heated capillaries typically desolvate analyte ions at 100–300 °C, well above the 31 °C freezing point of m-nitrobenzyl alcohol.

**Discussion**

**Comparison with Single Component Experiments.** Previous research from our laboratory on pure droplets shows a correlation between solvent surface tension and the percent charge lost in a Rayleigh discharge event. This correlation extends from traditional electrospray solvents10 to hydrocarbon solvents with a conductivity-enhancing additive.12 In the case of the binary systems presently studied, methanol/2-methoxyethanol droplets continue this trend. Table 1 indicates that droplets containing 2-methoxyethanol release more of their net charge than pure methanol droplets on average and 2-methoxyethanol has a higher surface tension than methanol. However, this trend breaks down when considering both methanol/tert-butanol and methanol/1 vol % m-nitrobenzyl alcohol droplets. Although tert-butanol has a bulk surface tension similar to that of methanol, increasing tert-butanol concentration in binary droplets results in greater charge transferred to progeny droplets in discharge events (i.e., a greater $\Delta q/q$). Conversely, charge loss from methanol with 1 vol % m-nitrobenzyl alcohol is slightly smaller than charge loss from pure methanol. While there is considerable evidence for surface tension involvement, present results suggest that other factors contribute to the discharge dynamics. Fernandez de la Mora theorizes that current flow during a discharge event is proportional to solvent surface tension, dielectric constant, and conductivity.15 Solvent dielectric constants listed in Table 2 for 2-methoxyethanol and tert-butanol are roughly half that of methanol, indicating that the differing dielectric constant alone does not explain the inconsistency.36 Similarly, solvent viscosity does not appear responsible as Table 2 shows the coefficient of viscosity for tert-butanol is lower than the value for methanol, while 2-methoxyethanol is higher. Our results for binary solvents show interesting discharge phenomena that highlight the need for further research to quantify the relationship between solvent properties and Rayleigh events.

**Implications for Electrospray Ionization Mass Spectrometry.** In their discussion of analyte charging and supercharging mechanisms in ESI-MS from multicomponent solvents, Lavaron and Williams note a correlation between analyte charge levels and the surface tension of the least volatile solvent.23 Results from the ping-pong experiment support this conjecture. Methanol and 2-methoxyethanol have drastically different evaporation rates, and there is time for significant methanol evaporation between electrospray generation and Rayleigh discharge events detected for droplets containing these components. This phenomenon may become more pronounced in smaller electrospray droplets due to decreasing solvent diffusion time scales, making it easier for droplets to “refresh” the high-volatility species as it evaporates from the surface. Similarly, small changes in m-nitrobenzyl alcohol concentration have a significant impact on the discharge phenomena. At ambient temperatures, methanol with 1 vol % m-nitrobenzyl alcohol shows evaporation and discharge dynamics similar to those of pure methanol whereas 2% shows significantly different behavior. This indicates that small changes in the m-nitrobenzyl alcohol concentrations profoundly affect droplet evaporation and discharge dynamics.

The implications of the present results for electrospray ionization are less clear for droplets with components of similar evaporation rate. In the present study, discharge events from methanol/tert-butanol show a correlation between size and charge loss, indicating time-dependent composition changes as the droplets evaporate. This implies that progeny ejected in successive events are chemically and physically unique and may result in a broader distribution of ion charge states in ESI-MS. Additionally, these systems release more of the droplet net charge as the concentration of tert-butanol increases. Because the pure components have similar bulk surface tension values, the increase in charge loss cannot be rationalized through droplet surface tension alone. Šamalikova and Grandori note the converse effect in the charge-state distribution of proteins in ESI-MS experiments. They find the addition of 1- or 2-propanol ($\gamma = 24.74$ and 22.40 mN m$^{-1}$, respectively)36 to aqueous myoglobin and cytochrome c does not significantly affect protein charge-state distributions. These results suggest a need for additional research to elucidate the chemical processes involved in Rayleigh discharge events. Studies conducted by Agnes and co-workers39,40 in which the progeny of Rayleigh discharge events are separated from parent droplets suspended in an electrodynamic balance may provide further insights. In addition, the technique of field-induced droplet ionization-mass spectrometry (FIDI-MS)18,20 may provide further elucidation into these processes. The FIDI technique generates what are essentially dual, highly controlled electrospray ionization events from a single droplet. Online droplet mass analysis following a well-defined period of binary solvent evaporation enables
correlations between analyte mass spectra and the parent droplet composition. Experiments such as these and further rigorous characterization of the physical and chemical differences between progeny and the parent is needed to complete the picture of Rayleigh discharge and its effect on electrospray mass spectrometry.

Conclusions

Insight into the evaporation and discharge dynamics of multicomponent solutions is critical for understanding the mechanism by which electrospray produces charged droplets that ultimately yield desolvated ions for mass analysis. In the present study, the ping-pong technique is employed to examine microdroplet evaporation and Rayleigh discharge of 10 one- and two-component solvent mixtures comprising methanol and 2-methoxyethanol, tert-butanol, or m-nitrobenzyl alcohol. Discharge dynamics for methanol/2-methoxyethanol droplets follows previous research that note a correspondence between droplet surface tension and charge loss. Conversely, charge loss from methanol/tert-butanol droplets do not follow this trend as the components have similar bulk surface tension values but increasing tert-butanol results in greater charge loss. Charge loss in methanol with 1% m-nitrobenzyl alcohol is similar to that with pure methanol.

Evaporation models accurately describe the evaporation dynamics and provide further insights into discharge behavior. Charge loss in discharge events from methanol/tert-butanol droplets increases as size decreases in agreement with changing component concentration throughout the droplet evaporation lifetime. In contrast, methanol/2-methoxyethanol droplets show no significant correlation between droplet size and charge loss suggestive of significant methanol evaporation prior to droplet ping-pong. These results agree with the quasi-steady-state evaporation model and support its viability in future studies of Rayleigh discharge phenomena of multicomponent droplets.

Future experiments may utilize the phenomena of persistent frozen droplets for further insight into discharge and evaporation mechanisms relevant to electrospray mass spectrometry. Because these droplets evaporate to a fixed size, independently manipulating the initial droplet composition, size, and charge would allow for designer droplets that undergo exactly one Rayleigh discharge event. This is difficult in electrospray ionization where droplet size and charge are coupled to the spray mechanism. However, a vibrating orifice aerosol generator (VOAG) can produce droplets with uniform size and charge where these parameters may be independently modified.18,19 Experiments comparing a VOAG source to a standard electrospray source might reveal interesting differences in ions originating from progeny droplets formed in early discharge events.

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References and Notes

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