Millisecond Coulometry via Zeptoliter Droplet Collisions on an Ultramicroelectrode

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Abstract: We show that discrete collisions of zeptoliter emulsion droplets on an ultramicroelectrode (UME) can be used as individual controlled potential coulometry experiments, lasting between 100 and 500 milliseconds. By loading a highly hydrophobic toluene droplet with a hydrophobic analyte of interest and knowing the volume of the droplet to a high degree of precision, Faraday's Law can be employed to calculate the number of electrons passed during the electrolysis. Monodisperse ($\pm15\%$ of the average size) emulsion systems were created by ultrasonication followed by filtering through a 200 nm porous filter. Discrete droplet collision events were observed in the amperometric i-t curve. Each of these collisions are interpreted as individual coulometry experiments, implying that several bulk electrolyses can be carried out over the course of one collision experiment. Herein, we show calculations of the electron stoichiometry for the ferrocene oxidation reaction, which agrees well with the expected value of 1 electron. We further extend the methodology to more complicated systems, such as the oxidation of tetrathiafulvalene (TTF), tertiary aliphatic amines, such as tripropylamine (TPrA), and a 1,2-diphenylhydrazine (DPH) molecule. This electroanalytical methodology allows for fast, nanoscale electrolysis in low dielectric media.

Keywords: Collisions · Coulometry · Electrochemistry · Emulsion · Zeptoliter

1 Introduction

Controlled potential coulometry is a powerful tool in electroanalysis due to its ability to directly derive the quantity or electron stoichiometry of a substance without use of a calibration curve [1]. The technique has also been employed for mechanistic considerations; however, the general long experimental times (minutes to hours) are not conducive to such studies because of possible follow-up reactions. When a sample is electrolyzed at a constant potential, the i-t response, limited by the rate of mass transfer of a redox species to the electrode surface, can be modeled by the following equation (assuming that the concentration of electroactive species remains uniform over the solution volume) [1].

$$i(t) = i_0 e^{-pt} \qquad \text{Eq.1}$$

where $i(t)$ is the current at time t, i_0 is the initial current, and p, the electrolysis time constant, is given by the following expression

$$p = m_o A V^{-1} \qquad \text{Eq.2}$$

where m_o is the mass transfer coefficient, A is the electrode area, and V is the solution volume. Therefore, fast electrolysis can be achieved with a high A/V ratio. Furthermore, in solutions with low dielectric constants, and, thus, lower conductivities, it is necessary to design an electrolysis where low currents are passed in order to minimize ohmic drop [2]. To the best of our knowledge, bulk electrolysis experiments have not been explored in low dielectric media, such as toluene [3]. Experimental methods have been developed to overcome the challenges outlined above. For instance, thin layer electrochemistry, where the dimensions of the electrolysis cell are less than the diffusion layer thickness, has been developed as a non-convective means of controlled potential coulometry with a high A/V ratio[4]. Electrolysis-scanning electrochemical microscopy (e-SECM) has also been proposed as a means of doing quick (~5 minute) electrolysis [5].

In the last decade, the study of stochastic collisions at ultramicroelectrodes has been expanding [6]. Most recently, there has been interest in collisions of soft nanoparticles, such as emulsion droplets [7–11], vesicles [12,13], viruses [14], and biological macromolecules [15]. Previously, we have found that a toluene droplet can be stabilized in water using an ionic liquid as a surfactant and supporting electrolyte for the toluene [7]. Dynamic Light Scattering (DLS), showed that the droplets displayed volumes of attoliter to zeptoliter and a size distribution spanning hundreds of nanometers. Collisions of emulsion droplets on UMEs have been observed by loading the droplet with an electroactive material sufficiently

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hydrophobic to dissolve in the low dielectric oil phase, such as ferrocene in a droplet of toluene. If the potential of the electrode is held sufficiently positive to oxidize ferrocene in the toluene droplet, a current response, or "blip," will manifest upon a collision event, indicating that each droplet is an individual electrolysis reactor. In these previous experiments the polydispersity of the emulsion system prepared by ultrasonication was high as determined by collisions and DLS [7]. However, if the droplets are to be used for analytical coulometry, a high level of uniformity in size must be achieved (*vide infra*).

Figure 1 gives a schematic representation of the oil droplet, filled with electroactive material, on the electrode surface, and the usual *i*-t response achieved for each oil droplet collision. Upon collision with the electrode surface, the contents in the droplet are electrolyzed and the product of the electrochemical reaction, slightly more soluble in the aqueous phase compared to the uncharged parent molecule, dissolves into the aqueous phase to maintain charge balance [7]. With the reactor experiments, a current blip response is integrated to yield the total charge passed in the system. From this integral, Faraday's Law, as displayed in Figure 1, can be employed to calculate a size distribution of droplets, assuming the contents are completely electrolyzed, which was previously shown to be true [7]. The following equation can be used to calculate the size of the droplet:

$$r_{drop} = [0.75Q(nFC\pi)^{-1}]^{1/3} \qquad \text{Eq.3}$$

where Q is the charged passed in the collision, *n* is the stoichiometric number of electrons, F is Faraday's Constant, and C is the concentration of redox active species within the droplet. A size distribution of droplets based on electrochemical collisions can be attained and evaluated against known techniques. The use of a droplet system makes very small volumes achievable, which would be advantageous in bulk coulometry experiments, increasing the A/V ratio and decreasing the electrolysis time.

In this article, we show that when the size dispersion of the droplet system is minimized, Faraday's Law can be employed to calculate the electron stoichiometry in a system. The electron stoichiometry can also give insight into possible mechanistic pathways. Bulk coulometry in low dielectric media (i.e., toluene) in 500 milliseconds or less is achieved with this method. In principle, several bulk electrolysis experiments can be recorded during one collision experiment. The millisecond time scale of the proposed methodology is competitive with microscale electrochemical transient techniques [16].

2 Experimental

2.1 Materials and Instrumentation

All chemicals were reagent grade and used as purchased without further purification. The ionic liquid trihexyltetradecylphosphonium bis(trifluoromethylsulfonyl)amide (95%) was purchased from Sigma-Aldrich and used without further purification. The electrochemical experiments were performed using a CHI model 920C and CHI630 potentiostat (CH Instruments, Austin, TX) with a three-electrode cell inside a faraday cage. Platinum wire was used as a counter electrode, and the reference electrode was either Ag/AgCl or Ag QRE. Dynamic laser scattering (DLS) data was obtained by Zetasizer Nano ZS (Malvern, Westborough, MA). The concentration of the emulsion system was obtained electrochemically using the diffusional frequency equation given in the main text.

2.2 Electrode Fabrication

Platinum ultramicroelectrodes were prepared by laser pulling (Sutter Instruments). For each experiment, the UMEs were mechanically polished to a diameter between 1 and 3 μm, then cleaned in piranha solution by dipping the UME in piranha for ten seconds and rinsed by dipping in water. This clean and rinse process was repeated several times. The radius of the Pt UME was obtained using the steady state current in cyclic voltammetry and by an optical microscope.

2.3 Emulsion Preparation

Emulsions were made by adding 5 mL of deionized water to a vial or tube, adding 0.1 mL toluene, 400 mM ionic liquid as supporting electrolyte and stabilizer, and the analyte of interest. In the experiments with Ferrocene, TTF, and DPH, 200 mM of analyte was used. In experiments with TPrA, 1 M analyte was used [24]. The contents of this vial or tube were then ultrasonicated by a Q500 ultrasonic processor (Qsonica, Newtown, CT) with a microtip probe. In order to achieve a monodisperse droplet system, this emulsion solution was filtered at least once through a porous membrane with pore sizes of 200 nm. Porous filters, with 200 nm pores in a polyethersulfone (PES) membrane (Corning, Corning, NY/Germany). Due
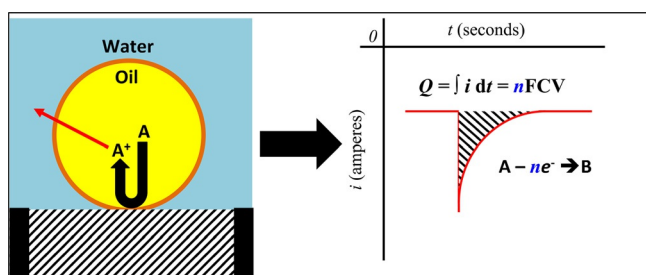

Fig. 1. Schematic representation of the collision experiment. The collision of an oil droplet on an ultramicroelectrode induces the electrolysis of the contents within the droplet, leading to a current blip on the amperometric i-t curve. The i-t curve can be integrated to get the amount of charge passed in an event, which can be directly related to either the concentration of analyte or the stoichiometric number of electrons involved in the electrochemical reaction.

to the sensitivity of emulsion droplet size to applied pressure during the filtration process care was taken to push water droplets that contain the emulsion through the syringe filter at a rate of approximately 1 drop/s.

3 Results and Discussion

In the presented experiments, the analyte of interest and the ionic liquid, trihexyltetradecylphosphonium bis(trifluoromethylsulfonyl)amide (IL-PA), were dissolved in the toluene phase. Emulsions were synthesized by mixing 5 mL nanopure water with 0.1 mL of the toluene/analyte/IL-PA solution followed by ultrasonication of the mixture. The emulsion was then filtered through a 200 nm porous filter and the electrochemical collision experiments were carried out in this filtered solution. Nanopure water, which generally contains very few ions and dissolved organic matter, is important to prevent aggregation of the emulsion droplets. For more information on the emulsion preparation, see the Experimental Section.

In order to characterize the filtered emulsion system in terms of size and dispersity, ferrocene (Fc), which undergoes a well-known one-electron oxidation to the ferrocenium cation, was used as our calibration standard. To control the size distribution, which is the controlling factor in the standard deviation of the coulometric data, the colloidal suspension was pushed through a porous filter, where the pore size was 200 nm, at least one time (see Experimental Section for more details). Figure 2 shows both results obtained with DLS and from applying Eq. 3 to the electrochemical data from 200 mM Fc in toluene droplets before and after filtration. The diameter of the electrode was between 1 and 3 micrometers. The electrode size plays an important role in the droplet collisions since the frequency that the droplets collide with the electrode scales with electrode size, in accord to Eqs. 4 and 5 below

$$f = 4CaN_AD \qquad \text{Eq.4}$$

$$D = (k_BT)(6\pi\eta r_{drop})^{-1} \qquad \text{Eq.5}$$

where f is the collision frequency, C is the concentration of the emulsion droplets, which is decreased after filtration, a is the electrode radius, N_A is Avagadro's Number, and D is the diffusion coefficient, given by the Stokes-Einstein approximation, where k_B is the Boltzmann constant, T is temperature, η is the viscosity of water, and r_{drop} is the radius of the droplet.

In each of the filtered experiments, the polydispersity index given by DLS was less than 0.1, and the standard deviation of the DLS size distribution and calculated electrochemical size distribution data agreed well (See Tables S1 and Figure S1 in Supporting Information). Figure 2 also displays the usual i-t response for the collision experiments before and after filtration on a platinum ultramicroelectrode. The measurements required a high level of sensitivity. It should be noted that there are infrequent current spikes in the cathodic direction from environmental sources, such as a slight disturbance of the Faraday cage. As evidenced in the data shown, the filtration technique reduces the size distribution (a spread of 1100 nm before filtration versus a spread of 300 nm after filtration), which increases the confidence in the droplet size. The data also show a slow deactivation of the electrode surface, which is likely from the accumulation of toluene droplets on the electrode or other non-specifically adsorbed species that can effectively decrease the area of the electrode. The events generally lasted between 100 and 500 milliseconds. Generally, bulk electrolysis curves resemble an increase in current followed by an exponential decay, which depends on the mass transfer coefficient, the area of the electrode, and the volume of the electrochemical cell. In our model with the collisions of oil droplets on UMEs, a small hole is created when a droplet collides with the electrode surface, and the electrochemistry occurs at this contact area. Because this contact area could change over time, the overall shape of many events is not the current spike accompanied by an exponential decay; rather, the events vary in shape and duration. As observed in the electrochemical sizing experiments, most of the events correspond to droplets of 100 ± 20 nm in size, which agrees well with DLS and is shown in Figure 2. Also, several bulk electrolysis experiments can be achieved over the course of one collision experiment, increasing the confidence level of the measurement. The collision experiment with ferrocene as the analyte of interest yields insight into the dispersity of the droplet system after filtration. The size distribution of the emulsion system can be calibrated with ferrocene as a well-known, one-electron standard. Alternatively, DLS measurements can be made preceding the electrochemical collision experiments as a different means of measuring the mean droplet diameter when switching from one analyte to the next. While it is true that averaging over multiple events is necessary to attain reliable statistics, the electrochemical collision methodology allows for many collisions to occur in less time than normal bulk coulometric analyses. The method also allows for coulometric analysis in low-dielectric constant media.

Because the dimensions of the droplet are on the order of 100 nm, the volume of each droplet is about 500 zL. Due to this small volume, the droplet collisions provide a large A/V ratio for quick controlled potential electrolysis in accord to the high electrolysis time constant, p. We used the resulting DLS average size to calculate the volume of each droplet colliding with the electrode. Using Faraday's Law, Eq. 2 becomes

$$n = Q(FCV)^{-1} \qquad \text{Eq.6}$$

where all variables are as previously defined. Through this equation, the stoichiometric number of electrons can be determined using the electrochemical collision methodology.
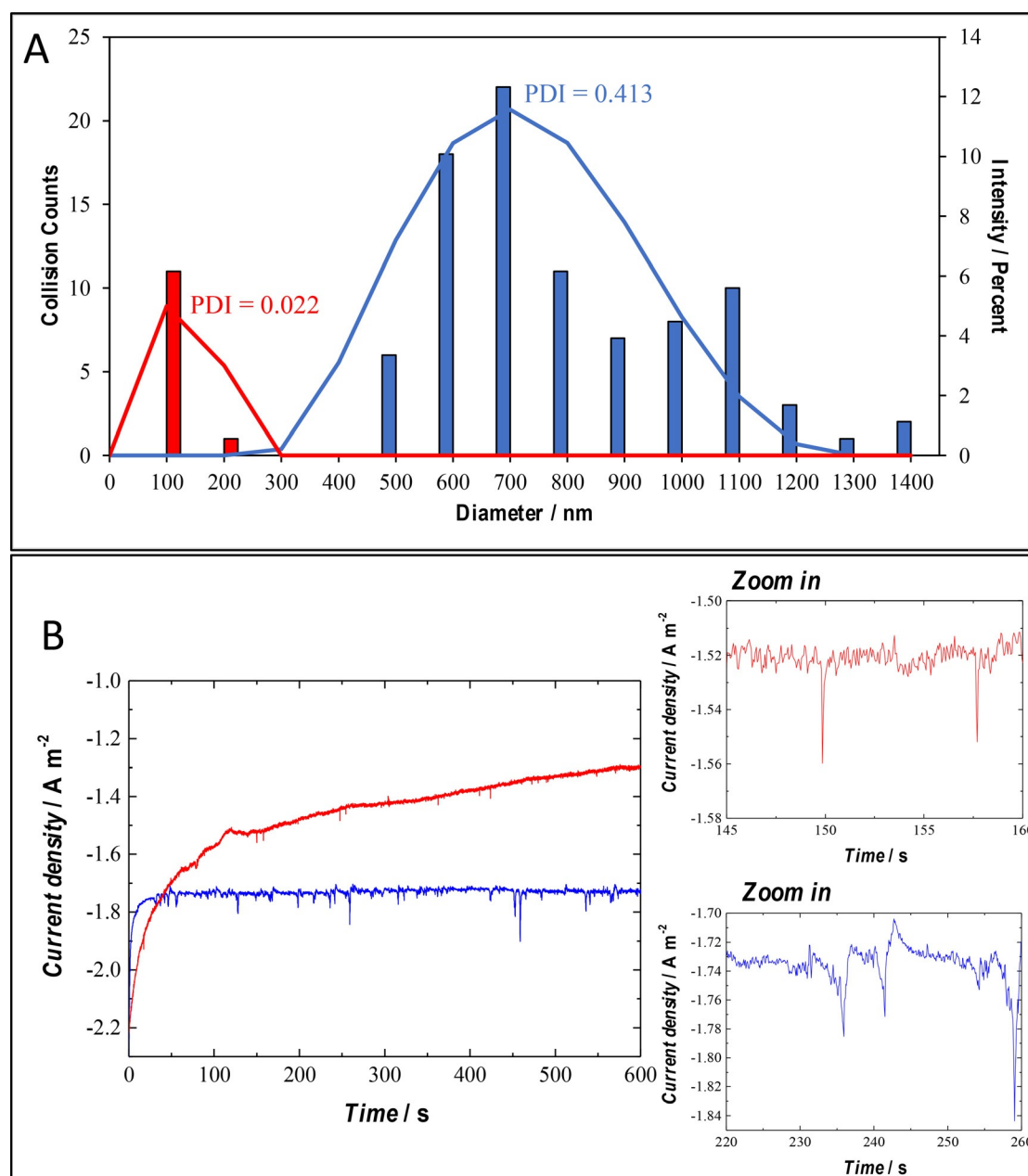
Fig. 2. A.) DLS (line trace) and electrochemical size distribution (histogram) before (blue trace) and after (red trace) filtering the emulsion solution through a filter with pore diameter of 200 nm, and B.) Usual *i*-t response for collision experiments before filtration (blue trace) and after filtration (red trace). The Pt UME was between 1 and 3 micrometers in diameter, and the droplets had 200 mM ferrocene dissolved inside. Amperometric experiments were carried out at 0.4 V against an Ag quasi-reference electrode (QRE), and the data acquisition time was 50 ms.

Table 1 gives results over several experiments calculating the number of electrons for the oxidation of ferrocene (Fc), tetrathiafulvalene (TTF), tripropylamine (TPrA), and diphenylhydrazine (DPH), and Scheme I gives the corresponding molecular structures. This variety of redox molecules offers examples of electrochemical reactions (E) coupled with chemical reactions (C) as well as multi-electron transfer reactions (EE). A more detailed summary of individual experiments is given in Table S2 in the Supporting Information. It is well known that ferrocene

Table 1. Values of *n* calculated for different experiments using various analytes at certain applied potentials (E_{appl}).

Experiment	E_{appl} (V)	*n* (electron)
Fc	0.4	0.96 ± 0.25
TTF	0.5	0.93 ± 0.19
TTF	1.0	1.90 ± 0.25
TPrA	0.9	1.89 ± 0.30
DPH	0.8	4.08 ± 0.63
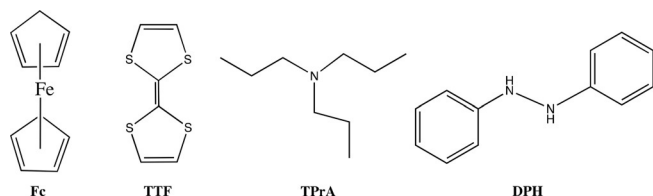
Scheme 1. Chemical structures of species investigated in this report.

will undergo a one-electron oxidation in many media; here, we show that ferrocene is oxidized at one electron in toluene to demonstrate the utility of the proposed collision technique.

To investigate multi-electron oxidation reactions, we used TTF as a model system. Figure 3 displays a linear sweep voltammogram of TTF in toluene with 400 mM IL-PA as the supporting electrolyte. TTF undergoes two sequential one-electron oxidation steps that are separated by about 500 mV; therefore, by controlling the potential bias for the collision experiments, the number of electrons transferred can be controlled. In a regular bulk coulometry experiment, biasing the potential at 0.5 V versus Ag quasi-reference electrode (QRE) is expected to yield an electron stoichiometry of one, whereas a potential bias at 1 V would give an electron stoichiometry of 2. Table 1 gives results from several experiments at different applied potentials for 200 mM TTF in toluene droplets. As evidenced by the results, changing the potential between 0.5 V and 1 V changed the stoichiometry of electrons, as expected from our previous results with Fc. Like Fc, the electro-oxidation of TTF in toluene has not been explored in the literature. Figure 4 shows representative amperometric i-t curves for the collision experiments of toluene droplets containing TTF at 0.5 V (TTF1) and 1 V (TTF2) on a 2 μm Pt UME. Because the overall current is essentially the same in both experi-

ments, background water oxidation on the Pt UME is not occurring at 1 V.

Tertiary aliphatic amines in aqueous solutions are known to undergo a two-electron oxidation [17]. However, in the absence of water, oxidation is a one-electron step [18]. The difference in electron numbers allows us to utilize the proposed technique to explore whether or not the electrolysis occurs at the three-phase boundary (toluene|water|platinum). Table 1 gives a summary of experiments for TPrA, and Figure 4 gives representative amperometric i-t curves for the collision experiments. The solubility of TPrA in water is about 6 mM, which undoubtedly contributes to the wave-like behavior seen in amperometry for TPrA and likely increases the standard error in the coulometric analysis. Our results indicate that TPrA undergoes a two-electron oxidation. We propose that TPrA is more capable of interacting with the three-phase boundary (toluene|water|platinum) because of its ability to solvate in water. Due to this interaction, the oxidation product of TPrA can react with water in a dealkylation reaction [19], producing ketone or aldehyde and a secondary amine[18], which will then be oxidized at a slightly more positive potential, resulting in a 2 electron stoichiometry. Our results, coupled with what is already known in the literature about TPrA electrochemistry, imply that the three-phase boundary is important in electrolysis considerations in droplet systems and warrants further investigation.

We furthered the technique by studying the number of electrons involved in the oxidation of DPH in the emulsion droplet system. DPH is limitedly soluble in water at about 1 mM. Generally, the oxidation of hydrazine is dependent on the reaction media; therefore, coulometric *n* values of 1, 2, and 4 have been reported for dimethylsulfoxide, acetonitrile [21], and aqueous [22] solvents, respectively. Furthermore, Michlmayr and Sawyer[20] demonstrated that the reaction of 1,1- and 1,2-dimethylhydrazine undergoes a four-electron process in dimethylsulfoxide containing 20 % water, which emphasizes the importance of water in the complete oxidation of hydrazine [23]. Representative current blips are given in Figure 4 for the oxidation of DPH in a toluene droplet. Our results indicate that the oxidation of DPH undergoes a 4-electron transfer reaction, implying that water may be involved in the overall oxidation of DPH.

4 Conclusions

In the present work, we have applied the discrete collisions of zeptoliter droplets on ultramicroelectrodes to millisecond coulometry. Each discrete collision, lasting less than 500 milliseconds, serves as one coulometry experiment. While the mass transfer of droplets to the electrode surface limits the technique, inducing migration or convection as other modes of mass transfer could decrease the experimental time. The fast coulometry allows for bulk electrolysis studies in low dielectric media. From this work, other types of droplet systems can be envis-
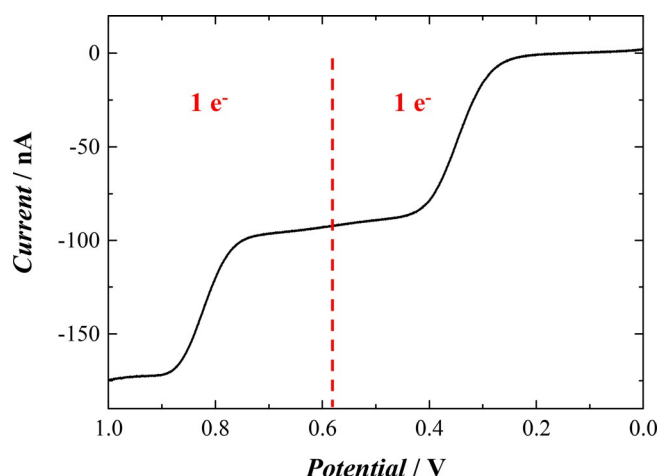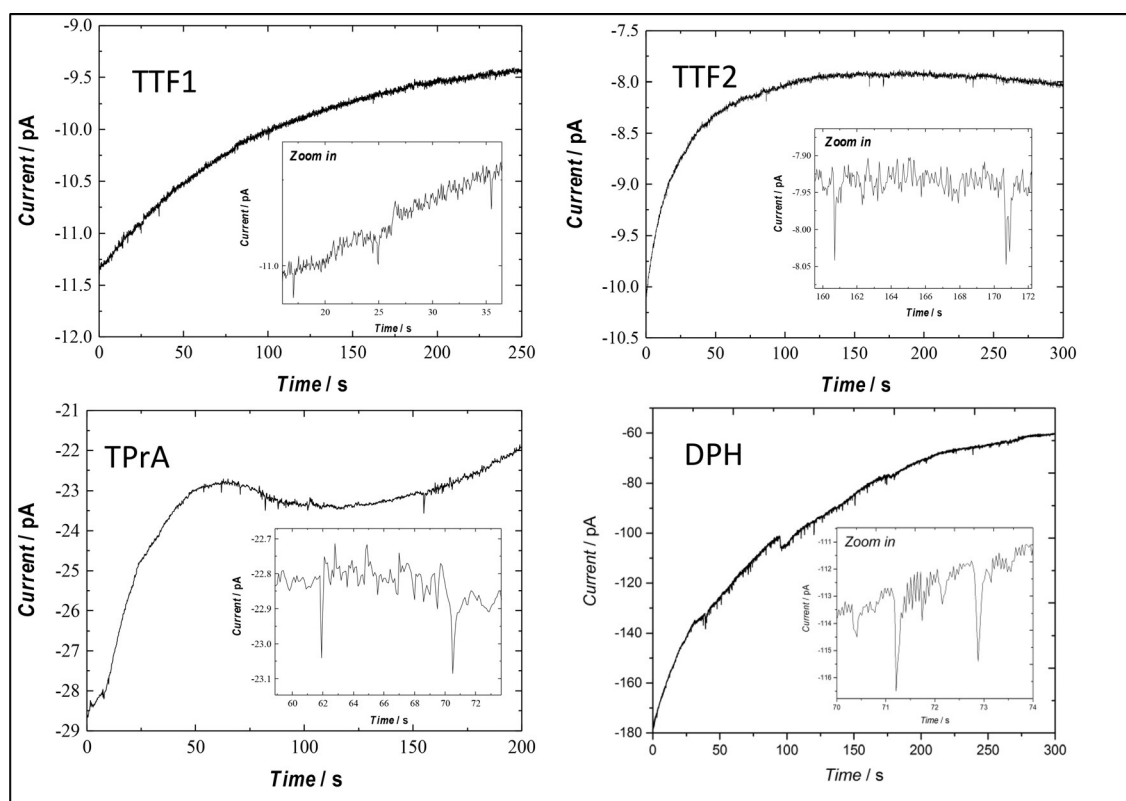

Fig. 3. Linear scan voltammogram on the oxidation of TTF in toluene against a Ag quasi-reference electrode on a 25 μm Pt ultramicroelectrode working electrode using 400 mM IL-PA as the supporting electrolyte. The scan rate was 50 mVs^{-1}.

Fig. 4. Representative i-t curves for filtered toluene emulsion droplet systems for each oxidation of TTF1 and TTF2 at 0.5 and 1 V, respectively, and the oxidation of TPrA and DPH. Each experiment was completed on an electrode with a diameter of 1–3 μm. The applied potentials are given in Table 1.

aged:, e.g. dichloroethane as the dispersed phase in water, or water as a dispersed phase in an organic solvent (inverse emulsion). These separate systems would expand the versatility of the technique, allowing for the ultrafast evaluation of electron stoichiometry and possible mechanistic details using relatively monodisperse zeptoliter droplet collisions on ultramicroelectrodes. Furthermore, it would also be possible to use the collisions as an analytical technique to gain information on the concentration of a redox molecule of interest in an oil droplet if the number of electrons and the volume of the droplet are known to high degrees of precision.

Supporting Information

Tables of calculated n values, raw charge data, and DLS data are available in the supplementary information.

Acknowledgements

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