Paper-based system for ion transfer across the liquid-liquid interface.

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ABSTRACT: While ion transfer studies were shown to be a promising method for fundamental electrochemistry, pharmacokinetic studies and sensing, they suffer from inherent instability of the interface formed between the organic and aqueous phases. This limits to some extent the range of solvents which can be used and confines these studies to the laboratory. We propose here the use of paper, which has revolutionized the way we think of miniaturized analytical devices during the last decade, as a perfect substrate for ion transfer studies across the liquid-liquid interface. We describe the design of a simple three-phase electrode paper-based setup for redox-driven transfer of anions from aqueous to organic phases. Electrochemical measurements of seven different anions and concentration dependence studies are in good agreement with the results obtained with traditional setups. Additionally, we show the applicability and limitations of such setups to the analysis of anion mixtures.

INTRODUCTION

Analytical chemistry from its very beginning took advantage of the unique properties of paper as a sensor substrate. For a long time, paper served mainly as a mechanical support for pH indicators and lateral flow assays, but more recently it is enjoying an unprecedented boost in interest due to its introduction to microfluidic and MEMS (microelectromechanical system) systems. Absorbency and the ability to transport fluids solely by means of capillary action are often cited as its main advantages but also of considerable importance is its abundance and low price.

Numerous paper-based analytical devices were proposed during the last decade,[1–3] including electrochemical sensors first introduced by Henry's group in 2009.[4] However, there are, apparently, no reports on the use of paper for ion-transfer studies in two-phase systems. One reason is that the most popular fabrication method uses wax to form fluid-impenetrable barriers; the wax is generally incompatible with non-aqueous solvents. Although papers describing other than wax fabrication methods often relate to the specific needs of such devices, organic solvents are still scarcely used in paper. In addition to a large number of simple proof-of-concept demonstrations of the retention of different solvents, an organic phase was applied in the case of a water-in-oil emulsification device[5] and also in a paper ionic diode,[6] where polyethylene oxide served as electrolyte host. Ionic liquids were used to some extent to modify the paper surface or impregnate the whole paper support, as in the case of all-solid-state capacitors[7] and sensors[8].

Here we extend the use of organic solvents in paper-based devices by exploring the possibilities of two-phase systems supported by paper's polymeric structure. If two immiscible liquids (e.g. water and 1,2-dichloroethane (DCE)) are placed in contact with each other an interface is formed. When coupled to proper electrode architecture, this liquid-liquid interface allows transfer of ions from one phase to the other, driven by a redox reaction. Paper's ability to adsorb both organic and aqueous phases provides a cheap and simple support for such biphasic systems. Until now ion transfer using paper-based devices was studied only in terms of potentiometric ion-selective electrodes, which were first introduced in 2012 by Novell et al.[9] and later further developed by this group[10] and others[11,12].

Numerous experimental set-ups were used to perform electrochemical measurements at the interface between two immiscible electrolyte solutions (ITIES), including different electrode configurations (three-phase junction, thin organic film and four electrode set-ups) as well as methods of interface stabilization: unsupported interface, membrane-supported phases, gels, single and array microjunctions[13].

Although electrochemistry at a liquid-liquid interface was already successfully applied to environmental monitoring, clinical diagnosis and pharmaceutical studies for the determination of drug partition coefficients, one of the biggest drawbacks of such system is the inherent mechanical instability of the interface The instability of large (range of cm^2) unsupported interfaces led to use of membranes and successful attempts to confine the interface in microholes[13], formed in film or at the mouth of a pipette, but even with those improvements experiments must still be performed in laboratory conditions by skilled and trained staff. The ability of porous paper to support each of the phases of such a system could be a key step for turning ion-transfer studies into routine point-of-need tests.

In redox reaction driven ion transfer, we differentiate between thin film electrodes, where the working electrode (WE) is completely immersed in the organic phase[14], and a three-phase electrode (TPE), where the WE crosses the interface between the liquid phases[15].

In the former system, the WE is completely covered by the organic phase and must contain a supporting electrolyte to provide sufficient conductivity. This system is quite similar to ion selective electrodes, where a redox polymer is used as a solid contact for electron transfer.[16] In the case of TPEs, the electrode reaction can start at the three phase junction between the liquid phases and the electrode and then propagate deeper. Thus, there is no need for supporting electrolyte in the organic phase. A thermodynamic model for relating the voltammetric peak potential to the transfer energies and concentration of different anions was developed by Scholz and co-workers[17–19]. This Nernst-like equation for droplet based TPEs was also shown to be valid for redox reaction driven ion transfer in microfluidic TPE systems[20]. Here we investigate the performance of a simple paper-based TPE and show that this model is valid and allows this easy-to-handle system to be utilized to determine the Gibbs transfer energy of anions.

EXPERIMENTAL

Chemicals and materials. Decamethylferrocene (DMFc) (97%, Sigma-Aldrich), N-octyl-2-pyrrolidone (NOP) (98%, Santa Cruz Biotechnology), inorganic salts of analytical grade: KPF_6 (99%, ABCR), $KClO_4$ (pure p.a. International Enzymes Limited), NaSCN (pure p.a., Fluka), KNO_3 (99%, POCh), KBr (pure p.a., POCh), KCl (>99.99%, Sigma-Aldrich), NaF (pure p.a., POCh), K_2SO_4 (pure p.a., ChemPur) were used as received. Water was filtered and demineralized with ELIX system (Milipore). Whatman® nº1 cellulose chromatography paper was purchased from Sigma-Aldrich.

Electrochemical measurements. Cyclic voltammetry (CV) and differential pulse voltammetry (DPV) were performed with an Autolab potentiostat (Metrohm Autolab B.V., Netherlands) controlled by the NOVA software (version 2.1.2). Parameters for DPV were as follows: step potential 0.005 V, modulation amplitude 0.025 V, modulation time 0.05 s, interval time 0.5 s and scan rate 0.01 V/s. All measurements were performed in a three-electrode system with a silver-silver chloride electrode (Ag|AgCl|saturated KCl) as a reference electrode, platinum mesh (Goodfellow) as a counter electrode and gold mesh (Goodfellow) as a working electrode. All measurements were carried out at room temperature.

The architecture of the device is presented in Fig. 1. The working and counter electrodes were attached to separate glass slides using glass cloth insulating electrical tape (3M) to prevent their displacement during the experiment. The paper (1.5 cm x 2.5 cm) soaked in the organic phase (NOP) was placed underneath the gold grid. Another paper of the same size steeped in the aqueous solution was put on the top of the working electrode together with the platinum mesh. The reference electrode was placed above the setup in a way that ensured contact with the paper containing the aqueous phase.

RESULTS AND DISCUSSION

Effect of anion hydrophilicity. Systems in which three phase junctions are formed can be used for investigation of ion transfer driven by electrochemical reaction. Oxidation of a redox probe in the organic phase results in an excess of positive charge, so to maintain charge neutrality, anions (X^-) from the aqueous electrolyte are transferred to the organic solution.

$$DMFc_{org} + X^-_{aq} \rightleftarrows DMFc^+_{org} + X^-_{org} + e- \qquad (1)$$

The transfer potential of this process depends on the nature of aqueous anions and corresponds to the following order: $PF_6^- < ClO_4^- < SCN^- < NO_3^- < Br^- < Cl^- \approx F^-$. Transport of hydrophobic anions is preferred in comparison to hydrophilic ones, resulting in peaks at less positive potentials. This effect can be seen on DPV curves measured in our paper-based system for seven different anions (Fig. 2).
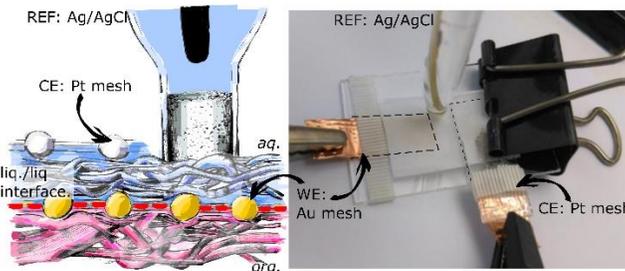
Fig. 1 Design of the system: A –schematic representation of the cross-section with the three-phase junction formed by the solutions in the papers and the Au mesh. WE –working electrode, REF –reference electrode, CE –counter electrode. B –picture of the assembled device.

To quantitatively describe the process of redox reaction coupled with anion transfer, the Nernst-like equation is used[17]:

$$E_p = E^0_{DMFc/DMFc^+} + \Delta^{NOP}_W \phi^0_{An^-} - \frac{RT}{F} ln c_{An^-}(W) + \frac{RT}{F} ln \frac{c_{DMFc}}{2}$$

(2)

where $E^0_{DMFc/DMFc^+}$ is the standard redox potential of DMFc/DMFc$^+$ couple, $\Delta^{NOP}_W \phi^0_{An^-}$ is the standard transfer potential of the transferring anion, c_{An^-} is the concentration of the anion in the aqueous solution, c_{DMFc} is the concentration of DMFc in the organic phase. One can see that the peak potential is a linear function of the standard transfer potential of the anion. This equation was derived for a three phase droplet based electrode, so to ensure that our paper device is based on the same principle, the dependence of E_p on $\Delta^{NOP}_W \phi^0_{An^-}$ was plotted (Fig. 2). For this purpose, the standard transfer potentials across the NOP|W interface determined by the L'Her method were used[20]. The very hydrophilic fluoride ion does not follow this linear trend, as explained below. The slope of the plot is 0.94±0.11, confirming that measurements of electrochemically driven ion transfer in the paper-based cell are comparable to traditional systems.

Effect of anion concentration. The concentration dependence is the second effect typically observed in ion transfer experiments. According to Eq.1 there is a linear relation between logarithm of the anion concentration and the peak potential of its transfer across the interface. For a one-electron redox reaction, the slope of the plot should be 59 mV per decade. Results obtained for KPF_6 transfer measured in the paper-based setup (Fig.3A) are in very good agreement with this theory.

However, a linear correlation is found only for hydrophobic anions. In the presence of highly hydrophilic species like Cl⁻ or F⁻, instead of anion transfer, decamethylferrocene cation is transferred from the organic to the aqueous phase. In the present system, Cl⁻ lies just on the transition between the two regimes. Then the peak potential is described by the modified Nernst-like equation[21] :

$$E = E^0_{DMFc/DMFc^+} - \Delta^W_{NOP}\phi^0_{DMFc^+} + \frac{RT}{F} ln \frac{c_{DMFc^+}(W)}{c_{DMFc}(NOP)} \quad (3)$$

where $\Delta^W_{NOP}\phi^0_{DMFc^+}$ is the standard transfer potential of $DMFc^+$ from NOP to water, $c_{DMFc^+}(W)$ and $c_{DMFc}(NOP)$ are concentrations of $DMFc^+$ in the aqueous phase and DMFc in the organic phase, respectively.
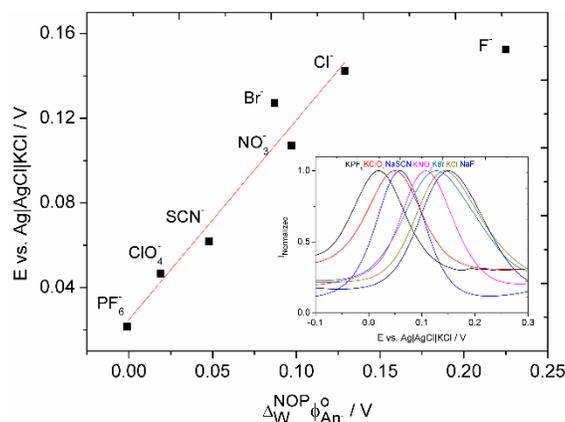

Fig. 2. Correlation between the peak potential and the standard transfer potential for all studied anions. Concentration of inorganic ions 0.1 M, DMFc 0.01 M. The slope is 0.94±0.11. Inset: DPV curves measured for transfer of different aqueous electrolytes.
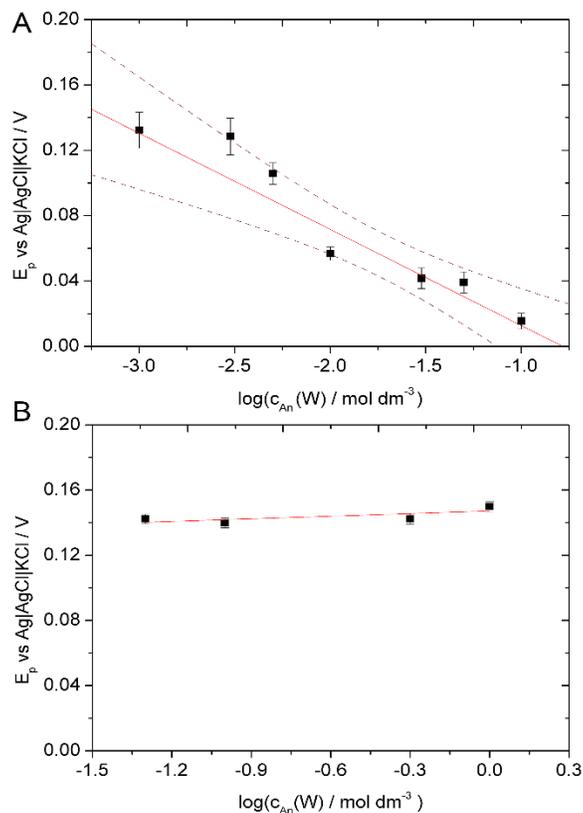
Fig. 3 Correlation between peak potential and concentration of **A.** KPF_6 and **B.** KCl in the aqueous phase. The dashed lines represent 95% confidence limits. The slope is -59±4 mV for KPF_6 and 5±3 mV for KCl.

According to Eq.3, the peak potential does not depend on any terms related to the aqueous electrolyte, which explains the lack of concentration dependency on chloride concentration (Fig.3B). The presence of the DMFc$^+$ transfer potential in Eq.2
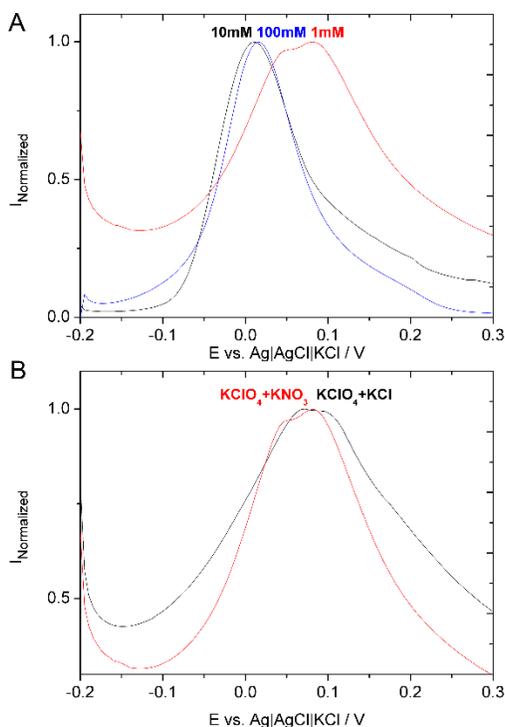
Fig. 4 A. DPV curves measured for mixture of KClO$_4$ and KNO$_3$ of different concentrations and **B.** 1 mM mixture composed of KClO$_4$, KNO$_3$ and KClO$_4$, KCl. 10 mM DMFc dissolved in NOP was used as the organic phase in both experiments.

shows that expulsion of electrogenerated cations makes a significant contribution to the overall process. This is a well- known effect[22] and its observation in this paper-based system confirms it can be an alternative device for ion transfer studies.

Mixture of anions. The promising results described in the previous sections encouraged us to investigate mixtures of anions, to determine to what extent the system can be used for the determination of ions in a sample. The main objective was to verify the possibility of simultaneous transfer of two aqueous anions across the NOP|W interface. For this purpose, aqueous solutions containing 100 mM, 10 mM or 1 mM mixture of KClO$_4$ and KNO$_3$ were studied (Fig.4A). Perchlorates and nitrates were chosen due to significant differences in their transfer potentials. Moreover, detection of those anions in water samples could be a possible application of the proposed ion transfer paper-based system.

Fig. 4A shows DPV curves obtained for different anion concentrations present in the aqueous phase. For 100 mM and 10 mM mixtures, only one peak is visible in the position corresponding to the transfer of perchlorate ions. When the concentration of both counterions was decreased to 1 mM (i.e. much lowerr than that of the redox probe) two peaks appeared, however both were shifted to more positive potentials. Fig 4B shows comparisons of two different anion mixtures at low concentrations, both showing double-peaks. This indicates that the possibility of double ion transfer is probably determined by the concentration ratio of anions and the redox probe. This is a reasonable result, since if the redox probe is depleted at the three-phase boundary by the first ion transfer, there is no probe left at the junction that can be oxidized to drive transfer of the second ion. This effect is exacerbated in our setup due to the high viscosity of the NOP used as the organic phase, which slows diffusion of the redox probe to the reaction zone. If the ion concentration is kept in a much lower regime than the DMFc concentration, transfer of two anions might be possible. This explanation is backed by a very simplistic computer simulation performed in COMSOL, illustrated in Fig. 5.

Here, the reaction in eq. 1 is simulated as a simple heterogeneous reaction at the interface between the two liquids in 2D, where the rate of the (forward) reaction is proportional to the concentrations of the redox probe and the ion on either side of the interface, such that

$$k_f = k_0 \left[DMFc_{org,interface} \right] \left[X^-_{aq,interface} \right] \quad (4)$$

where k_0 has a Butler-Volmer like exponential potential dependence. The system contains two anions, An1 and An2, with transfer potential 0 V and 0.2 V, respectively. The simulations were performed for different ion concentrations. This is obviously not a complete model, and does not capture the details of more sophisticated models[23,24], but it does show how the redox probe is depleted at the interface for high anion concentration, resulting in only one peak, while at low concentration, two peaks are visible. A similar result was shown by Zanotto et al. [25] for ion transfer in a film electrode. However, at very low concentrations of the transferring ion(s), eq. 2 might no longer be applicable[26], and this limits the scope for using the TPE for ion determination at such low concentrations.
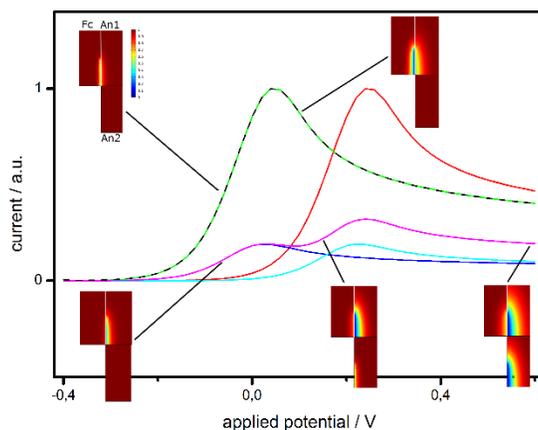
Fig. 5 Simulation of linear sweep voltammograms for systems in which the aqueous phase contains two anions (An1 and An2). The curves show the results of different initial concentrations of An1 and An2, $c_{0,An1}$ and $c_{0,An2}$: black - $c_{0,An1}=c_{0,DMFc}$, $c_{0,An2}=0$; red - $c_{0,An2}=c_{0,DMFc}$, $c_{0,An1}=0$; green (identical to black) - $c_{0,An1}=c_{0,An2}=c_{0,DMFc}$; blue - $c_{0,An1}=0.1\times c_{0,DMFc}$, $c_{0,An2}=0$; teal - $c_{0,An2}=0.1\times c_{0,DMFc}$, $c_{0,An1}=0$; magenta - $c_{0,An1}=c_{0,An2}=0.1\times c_{0,DMFc}$. The insets show the concentrations of the redox probe in the organic solution on the left, and the anions (An1 and An2 shown separately) in the aqueous solution on the right at different points during the scan. The map for An2 has been displaced vertically for clarity.

CONCLUSIONS

We have shown that a simple paper-based three-phase electrode device can be successfully applied for ion transfer studies. To the best of our knowledge this is the first time that anion transfer across the liquid-liquid interface has been measured in a paper-based system. Two effects typical for ion transfer experiments were observed: shift of the peak potential to more positive values with an increase of the hydrophilicity of the anion; and the dependence of the peak potential on the anion concentration. All results are in very good agreement with literature data for ion transfer in traditional, droplet-based three-phase electrode setups. Experiments performed using a mixture of anions showed that simultaneous transfer of two anions is possible, however the concentration ratio between the redox probe and the anion must be controlled. Based on experiments and simulations, two peaks can appear only when the concentration of DMFc is at least several times higher than the concentration of the aqueous electrolyte. Our results help to understand the basis of the double transfer mechanism, however to fully explain this process more detailed analysis is needed.

Successful investigation of anion transfer in a paper-based liquid-liquid system shows that paper devices are a very promising alternative for the traditional three-phase electrode setup. The unique properties of paper makes it an ideal support both for aqueous and organic solvents. The possibility to create a stable interface may enable ion transfer experiments to be performed with solvents that were never used before because of the mechanical instability of the unsupported interface.

AUTHOR INFORMATION

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REFERENCES

(1)   Santhiago, M.; Nery, E. W.; Santos, G. P.; Kubota, L. T. *Bioanalysis* **2014**, *6* (1), 89–106.
(2)   Nery, E. W.; Kubota, L. T. *Anal. Bioanal. Chem.* **2013**, *405* (24), 7573–7595.
(3)   Yang, Y.; Noviana, E.; Nguyen, M. P.; Geiss, B. J.; Dandy, D. S.; Henry, C. S. *Anal. Chem.* **2017**, *89* (1), 71–91.
(4)   Dungchai, W.; Chailapakul, O.; Henry, C. S. *Anal. Chem.* **2009**, *81* (14), 5821–5826.
(5)   Li, C.; Boban, M.; Tuteja, A. *Lab Chip* **2017**, *17* (8), 1436–1441.
(6)   Zhao, R.; Zhang, X.; Xu, J.; Yang, Y.; He, G. *RSC Adv.* **2013**, *3* (45), 23178.
(7)   Rath, T.; Kundu, P. P. *RSC Adv.* **2015**, *5* (34), 26666–26674.
(8)   Toniolo, R.; Dossi, N.; Svigely, R.; Susmel, S.; Casella, I. G.; Bontempelli, G. *Electroanalysis* **2014**, *26* (9), 1966–1974.
(9)   Novell, M.; Parrilla, M.; Crespo, G. a.; Rius, F. X.; Andrade, F. J. *Anal. Chem.* **2012**, *84* (11), 4695–4702.
(10)   Novell, M.; Guinovart, T.; Blondeau, P.; Rius, F. X.; Andrade, F. J. *Lab Chip* **2014**, *14* (7), 1308–1314.
(11)   Hu, J.; Stein, A.; Bühlmann, P. *Angew. Chemie - Int. Ed.* **2016**, *55* (26), 7544–7547.
(12)   Ruecha, N.; Chailapakul, O.; Suzuki, K.; Citterio, D. *Anal. Chem.* **2017**, *89* (19), 10608–10616.
(13)   Herzog, G. *Analyst* **2015**, *140* (12), 3888–3896.
(14)   Quentel, F.; Mirčeski, V.; L'Her, M. *Anal. Chem.* **2005**, *77* (7), 1940–1949.
(15)   Donten, M.; Stojek, Z.; Scholz, F. *Electrochem. commun.* **2002**, *4* (4), 324–329.
(16)   Bobacka, J.; Ivaska, A.; Lewenstam, A. *Chem. Rev.* **2008**, *108* (2), 329–351.
(17)   Scholz, F.; Komorsky-Lovrić, Š.; Lovrić, M. *Electrochem. commun.* **2000**, *2* (2), 112–118.
(18)   Gulaboski, R.; Mirčeski, V.; Scholz, F. *Electrochem. commun.* **2002**, *4* (4), 277–283.
(19)   Scholz, F.; Gulaboski, R.; Caban, K. *Electrochem. commun.* **2003**, *5* (11), 929–934.

(20) Kaluza, D.; Adamiak, W.; Opallo, M.; Jonsson-Niedziolka, M. *Electrochim. Acta* **2014**, *132*, 158–164.
(21) Scholz, F.; Schröder, U.; Gulaboski, R.; Doménech-Carbó, A. *Electrochemistry of Immobilized Particles and Droplets*, 2nd ed.; Springer International Publishing: Cham, 2015.
(22) Adamiak, W.; Opallo, M. *J. Electroanal. Chem.* **2010**, *643*, 82–88.
(23) Myland, J. C.; Oldham, K. B. *J. Electroanal. Chem.* **2002**, *530* (1–2), 1–9.
(24) Lovrić, M.; Scholz, F. *J. Electroanal. Chem.* **2003**, *540*, 89–96.
(25) Zanotto, F. M.; Fernández, R. A.; Dassie, S. A. *J. Electroanal. Chem.* **2017**, *784*, 25–32.
(26) Komorsky-Lovrić, Š.; Lovrić, M.; Scholz, F. *Collect. Czechoslov. Chem. Commun.* **2001**, *66* (3), 434–444.
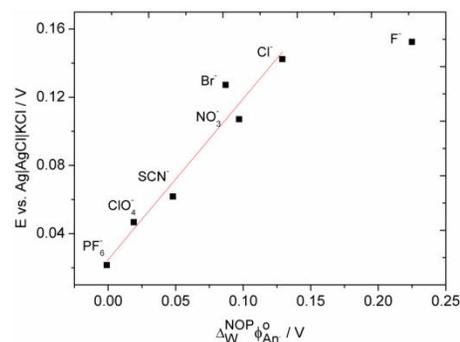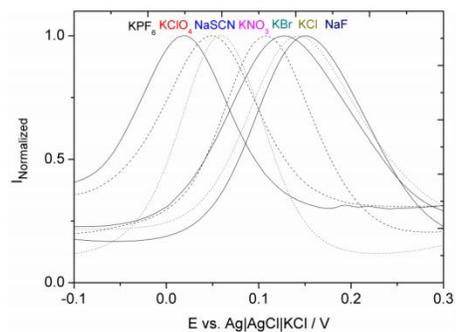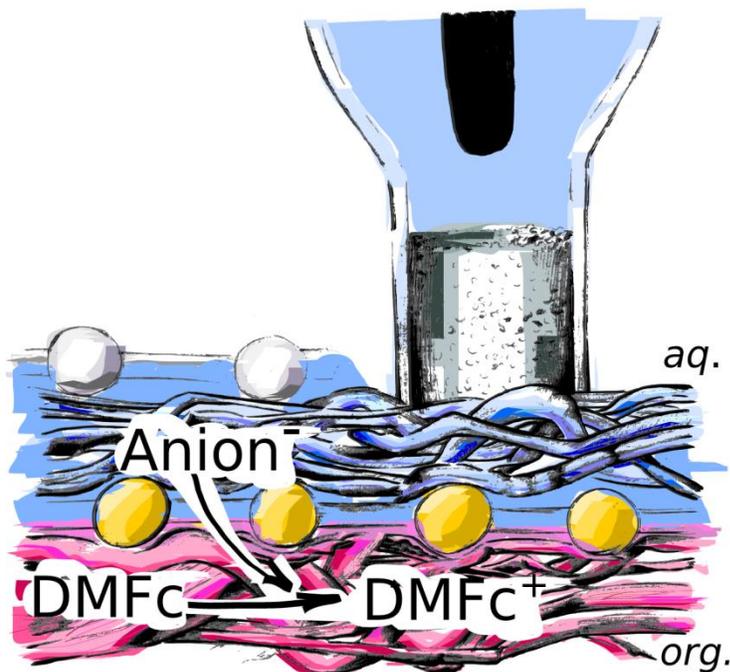
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