Controlled Uptake and Release of Therapeutic Drug Anions: A Combined EQCM and Probe Beam Deflection Study

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An electroactive film undergoing redox switching satisfies the electroneutrality constraint by the transfer of counter ion and/or co-ion across the film/solution interface. The prospect of exploiting this for the controlled uptake/release of cation or anions for therapeutic applications was qualitatively highlighted by studies of redox-driven transfers of charged organic species across the electroactive polymer film/solution interface [1, 2, 3, 4]. To develop this for practical application requires a quantitative understanding of the various thermodynamic and kinetic factors that control ion transfer.

Our goal is to understand the competition between the opposing anion and cation transfers for redox switching of a polypyrrole film exposed to a selection of electrolytes containing drug and co-ions of disparate size. We explore the idea that the most mobile ion initially dominates the ion transfer process (kinetic control of the mechanism for maintaining electroneutrality at short time scales) and then determine the time scale on which equilibrium is achieved (thermodynamic control of the mechanism for maintaining electroneutrality at long time scales). Typical drug anions employed were salicylate and ampicillin, which are significantly larger than the sodium co-ions.

The EQCM and probe beam deflection (PBD) techniques [5, 6] are ideally suited to studying these interfacial ion transfers (and the associated solvent transfer). Due to their complementary analytical strengths, the combined EQCM-PBD technique (providing simultaneously recorded Q, ΔM and θ responses) enables the extraction of individual anion, cation and solvent fluxes into/out of an electroactive surface film [7]. Here we exploit the capability to achieve this in a time resolved manner for any selected electrochemical control function.

We present EQCM-PBD data for redox-driven ion (and solvent) transfers at polypyrrole films exposed to aqueous salicylate and ampicillin electrolytes. From these we extract time resolved fluxes and film population changes of anion, cation and solvent. This is accomplished for different electrochemical waveforms, including a linear potential sweep and both large (full conversion) and sequential small (partial conversion) potential steps. The manner in which these allow one to sample different regions of compositional space [8] is crucial to designing control functions that can deliver the active ion in a specified time profile.

For salicylate electrolytes sodium transfer transiently dominates electroneutrality within the polypyrrole film, but salicylate transfer ultimately competes effectively. This competition shows significant variation with concentration. For ampicillin electrolytes the same issues arise, but the situation is complicated by much larger solvent fluxes, to the extent that one must address the possibility of film viscoelastic effects.

Film volume constraints are critical (i) in the gravimetric regime with respect to ion dynamics and (ii) in the viscoelastic regime through *free volume* control of polymer dynamics. We have therefore used ion and solvent fluxes to estimate the overall film volume and the individual species contributions to this. Variations of these with time and film charge state reveal new insights into the relationships between ion, solvent and polymer dynamics.

Acknowledgment
HMF thanks the EPSRC for a PhD studentship.

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