Solid contact ion selective electrodes: from potentiometric application to voltammetric investigation

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Abstract

The solid contact ion selective electrodes are different from the liquid contact ion selective electrodes by replacing the inner filling solution with solid-state ion-to-electron transducers. In this thesis, two different types of ion-to-electron transducers are introduced. The first is the multi-walled carbon nanotubes modified with alkyl group for fabrication of solid contact electrodes for on-line and in-situ potentiometric detection of environmental anions (e.g., chloride, carbonate, nitrate). The second utilizes the electropolymerized poly (3-octylthiophene) for voltammetric study of ion transfer process between membrane and solution interface. By proper experimental design, the voltammetry experiment could be a useful technique for probing the ion-ionophore interactions inside the membrane. In addition to the research of solid contact ion selective electrodes, robust boundary element calculations in the computer simulations of ion exchange process for ion selective membrane are also described.
Solid Contact Ion Selective Electrodes: From Potentiometric Application to Voltammetric Investigation

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The research of solid contact ion selective electrodes has received growing scientific attention in recent years. The solid contact configuration offers several advantages with respect to liquid contact ion selective electrodes, such as their simplified miniaturization, facilitated portability, eased integration into wearable readout electronics, and their robustness to high water pressure. These advantages cater to the ongoing demand for on-line and in-situ environmental monitoring, and the increasing desire for continuous point of care tests in personal health management for the current digital era.

Even though many kinds of solid contact ion selective electrodes have been invented so far, few of them are comprehensively tested with environmental samples, especially for anion detection. Focused research on the development of an easily fabricated and generally applicable solid contact ion selective electrodes for ubiquitous anion detection (e.g., chloride, nitrite, nitrate, phosphate etc.), is a worthy endeavor. In addition, a new sensing strategy (e.g., voltammetry) backed with robust theoretical knowledge could broaden the application aspect of solid contact ion selective electrodes for tasks hardly achievable using potentiometric measurements.

The main work of this thesis has been focused on the construction of solid contact ion selective electrodes, with thick or thin layer polymeric membranes on a custom made transducing layer fabricated from multi-walled carbon nanotubes or poly(3-octylthiophenene), for potentiometric and voltammetric applications, both experimentally and theoretically. The thesis is divided into six chapters.

Chapter 1 provides a basic introduction to ion selective electrodes, including the chemical reagents to be used, the potentiometric response mechanism, the selectivity coefficient of ion selective electrodes, and the complex formation constants for ion-ionophore interactions. Moreover, the cutting-edge materials for transducing elements for fabrication of solid contact ion selective electrodes are shortly reviewed, followed by an overview of the principles of cyclic voltammetry, electrochemical impedance spectroscopy, and computer simulations that are implicated in the characterization of the electrodes.

Chapter 2 explores the application of a universal approach to the design of potentiometric solid contact electrodes for anions in environmental analysis, based on the octadecylamine (ODA) group modified lipophilic multi-walled carbon nanotubes as an inner solid contact. The versatile performances of the electrodes are tested and verified with river samples containing anions such as carbonate, nitrate, nitrite and dihydrogen phosphate.
Chapter 3 provides a comprehensive voltammetric study of thin layer solid contact silver ion selective electrodes to elucidate the effect of scan rates, sample concentrations and rotation speeds on their electrochemical behavior. The experimental evidence is confirmed and predicted by numerical simulations.

Chapter 4 focuses primarily on the theoretical aspects of the voltammetric study introduced in chapter 3. The analysis is accomplished by a semi-empirical approach, giving a clear identification of two voltammetric regimes, diffusion and equilibrium, under different sample concentrations.

Chapter 5 focuses on deciphering the dynamics behind the ion-ionophore complexation inside the membrane. A pure ion transfer potential as a function of varying ion exchanger concentration in a thin layer polymeric membrane is obtained by the sequential scanning of this membrane in samples containing the ion of interest and a reference ion, tetrabutylammonium (TBA\(^+\)). The fitting of the function gives direct information on complex stoichiometry, complex formation constants, and selectivity coefficients for various membrane compositions.

Chapter 6 examines the possible pitfalls in boundary element calculations in simulations for ion selective membranes. By introducing a thin layer concept of the space element, a more robust novel formula for boundary elements is presented and validated in numerous carefully selected conditions.
Resumé

La recherche sur les électrodes à contact solides, sélectives pour les ions, a fait l’objet d’une attention scientifique croissante ces dernières années. La configuration des contacts solides offre plusieurs avantages par rapport aux électrodes à contact liquides, fortement du à leur facilité de miniaturisation, leur portabilité, leur intégration facilité dans les instruments de mesure, ainsi que leur robustesse à la pression élevée de l’eau. Ces avantages répondent à la demande de surveillance constante pour les études environnementale en ligne et in situ, et à la demande croissante par la génération numérique actuelle d’analyses continus délocalisée pour la gestion personnelle de la santé.

Bien que de nombreux types d’électrodes à contact solides aient été inventés à ce jour, peu d’entre eux sont testés de manière exhaustive avec des échantillons environnementaux, en particulier pour la détection des anions. Des recherches ciblées sur le développement de ces électrode, pour faciliter leur fabrication et leur applicabilité général, et pour la détection d’ions omniprésents (par exemple chlorure, nitrure, nitrate, phosphate, etc.), constituent un effort louable. De plus, une nouvelle stratégie de détection (par exemple, la voltamétrie), soutenue par des connaissances théoriques robustes, pourrait élargir l’aspect d’application des électrodes à contact solide sélectives d’ions pour des tâches difficilement réalisables en utilisant des mesures potentiométriques.

Les travaux principaux de cette thèse ont porté sur la construction d’électrodes à contact solides sélectives pour les ions, avec des membranes polymères épaisse ou minces sur une couche de transduction fabriquée à partir de nanotubes de carbone à parois multiples ou de poly (3-octyl-thiophénène), pour des applications potentiométriques et voltamétriques, à la fois expérimentalement et théoriquement. La thèse est divisée en six chapitres.

Le chapitre 1 fournit une introduction de base aux électrodes sélectives d’ions, y compris les réactifs chimiques à utiliser, le mécanisme de réponse potentiométrique, le coefficient de sélectivité des électrodes sélectives d’ions et les constantes de formation complexes pour les interactions ion-ionophore. En outre, les matériaux de pointe pour les éléments de transduction destinés à la fabrication d’électrodes sélectives à ions solides de contact sont brièvement examinés, suivi par un aperçu des principes de la voltamétrie cyclique, la spectroscopie d’impédance électrochimique et les simulations informatiques impliquées dans la caractérisation des électrodes.

Le chapitre 2 explore l'application d'une approche universelle à la conception d'électrodes potentiométriques à contact solide pour les anions en analyse environnementale, basée sur des nanotubes de carbone lipophiles modifiés par l’octadécylamine (ODA) comme contact interne
solide. Les performances polyvalentes des électrodes sont testées et vérifiées avec des échantillons de rivière contenant des anions tels que le carbonate, le nitrate, le nitrite et le dihydrogénophosphate.

Le chapitre 3 présente une étude voltamétrique complète d'électrodes sélectives d'ions à contact solide composé d'une couche mince d'argent, pour éclaircir l'effet de la vitesse de balayage, des concentrations d'échantillons et des vitesses de rotation sur leur comportement électrochimique. Les preuves expérimentales sont confirmées et prédites par des simulations numériques.

Le chapitre 4 porte principalement sur les aspects théoriques de l'étude voltamétrique introduite au chapitre 3. L'analyse est réalisée par une approche semi-empirique, permettant d'identifier clairement deux régimes voltamétriques, la diffusion et l'équilibre, sous différentes concentrations d'échantillon.

Le chapitre 5 se concentre sur le décryptage de la dynamique derrière la complexation ion-ionophore à l'intérieur de la membrane. Le balayage séquentiel de cette membrane dans des échantillons contenant l'ion d'intérêt et un ion de référence, le tétrabutylammonium (TBA), a permis d'obtenir un potentiel de transfert d'ions pur en fonction de la concentration variable de l'échangeur d'ions dans une membrane polymère en couche mince. L'ajustement de la fonction fournit des informations directes sur la stœchiométrie complexe, les constantes de formation complexes et les coefficients de sélectivité pour diverses compositions de membranes.

Le chapitre 6 examine les écueils possibles dans le calcul des éléments limités dans les simulations pour les électrodes sélectives. En introduisant un concept de couche mince de l'élément spatial, une nouvelle formule plus robuste pour les éléments limites est présentée et validée dans de nombreuses conditions soigneusement sélectionnées.
List of Publications


6. Yuan D., Nemr C., Li M., Kelly C., Mallires K., What are the emerging generation of researchers think is hot in sensors. *ACS Sens.*, **2017**, *2*, 710-711

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Chapter 1 Introduction

Inorganic ions are ubiquitous in natural waters and biological fluids. They play important roles on life activities on earth. Reasonable distribution of mineral ions in the planet water is one necessary condition for the evolution of life.\textsuperscript{1} In the ocean, chloride and other halides dominate the water salinity, whose proper value is vital for the living environment for marine biology.\textsuperscript{2} In the lakes and rivers, excessive level of nutrient ions such as nitrate, nitrite, phosphate may result in eutrophication and algal bloom, possibly causing hypoxia and large number of deaths of aquatic organisms.\textsuperscript{3} In the farming soils, toxic heavy metals including arsenic, cadmium, lead are potential to be accumulated in farmed vegetables, cereals, posing high risks of human health.\textsuperscript{4,5} In the human body, maintaining electrolyte balance is very important. For instance, blood potassium deficiency is called hypokalemia, which may bring in comorbidities such as chronic kidney disease(CKD), heart failure (HF) and diabetes mellitus (DM).\textsuperscript{6} In the animal brain, extracellular calcium concentrations associate with synaptic activity. Measuring extracellular calcium concentration \textit{in vivo} is of great value for both scientific research and medical treatments.\textsuperscript{7}

Monitoring ion concentration and distribution change in environmental samples is therefore of great value, for reviewing, foreseeing and correlating them with the biospecies activities in the ecosystem in oceans, lakes, rivers, soils, and forests and finally, for protection. After all, our life is relying on them. Nowadays, demand for convenient, fast, and continuous detection of ion concentrations such as potassium, sodium, hydrogen ion, ammonium, and calcium in the human blood, sweat, saliva, and urine is greatly increasing as they are very informational to correlate with health condition of individuals.\textsuperscript{8–11} Both the environmental and body fluid ion detections request ion sensors that could meet with required criteria such as sensitivity, selectivity, spatial and temporal resolution, response time, \textit{in-situ/ex-situ} needs, materials cost and limited power consumption.

Ion selective electrodes (ISEs) are one of the established analytical tools for ion sensing in both environmental and clinical applications due to their low energy cost, capability of on-line and \textit{in-situ} measurements and ideally no consumption of analytes during measurement.\textsuperscript{12,13} Moreover, the detection usually does not need sample preparation.\textsuperscript{14} There are several kinds of ion selective electrodes, including glass based pH electrode, precipitate based crystalline electrode and polymeric membrane based electrode. The pH electrode has the longest history and is perhaps still most widely used in research laboratory and industrial quality control. Crystalline based electrodes were later discovered and their applications are still seen today.
They are limited to only a few ions that form stable precipitations and many suffer from limited selectivity.\textsuperscript{15} Since its first introduction in the 1960s, the carrier based polymeric ion selective membrane electrode has evolved into a routine technique in many applications, including physiology, process control, and environmental analysis.\textsuperscript{16} Their versatile application is firstly accredited to the synthesis of many ionophores that could combine specifically with ions of interest,\textsuperscript{17} and secondly, the wide utilization of solid contact ion selective electrodes (SC-ISE) that overcome many drawbacks of the conventional liquid-contact electrodes.\textsuperscript{18} The research of solid contact ion selective electrodes is very active now, but facing many challenges as well, such as new materials search, potential stability, mechanism explanation, and new sensing strategy.

The work of this thesis includes the construction of solid contact polymeric ion selective electrodes for potentiometric anion detection, the explorations for SC-ISE voltammetric applications in their thin layer configuration and solvation of the theoretical problems thereof. For the potentiometric practice, the SC-ISE shares the same response mechanism as conventional liquid contact ISE. Therefore, for guidance, an introduction of the basic concept of conventional ISE is necessary, including the two-electrode device configuration, the membrane compositions, the response mechanism, selectivity coefficient, and complex formation constant. This is followed by a discussion of the transducing elements of SC-ISE, with a focus on conducting polymers that form the basis of the main part of the work. Later on, dynamic electrochemical techniques utilized for the membrane study are then detailed. Finally, brief principles of computer simulation are introduced in this chapter.

1.1 Polymeric ion selective membrane based electrodes

A polymeric ion selective membrane usually consists of a polymer matrix of high viscosity doped with several active chemical components, as listed below:

**Polymer matrix**

The polymer matrix provides mechanical stability of the membrane and serves as water immiscible phase with no chemical interaction with the sensed ions. While the most commonly used polymer matrix is poly (vinyl chloride) (PVC), other materials such as silicon rubber,\textsuperscript{19} methacrylates,\textsuperscript{20} and polyurethanes (PU)\textsuperscript{21} may be an alternative for special purposes. For instance, for the voltammetric thin layer polymer membrane, PU is advantageous to PVC in terms of avoiding lipophilic ions from leaching outside the membrane.\textsuperscript{22} Figure 1 shows the structure of high molecular weight PVC and PU.
Plasticizer

The plasticizer decreases the viscosity of the membrane matrix and ensures the mobility of membrane constituents within the membrane phase. Plasticizer should not react with other membrane components. Different plasticizers have different polarity, affecting the dielectric constant of the membrane and as a consequence, the selectivity. Two commonly used plasticizers for PVC membrane are bis (2-ethylhexyl) sebacate (DOS) and ortho-nitrophenyl octyl ether (o-NPOE). (Figure 2) Typical weight ratio of polymer:plasticizer used in ISE membranes is 1:2.

Ion exchanger or lipophilic salts

The addition of ion exchanger or lipophilic salts to the membrane is to ensure that the membrane is permeable to ions of the same charge sign as the measurable ions. This is called permselectivity or Donnan exclusion. The added non-exchangeable ions in the membrane make sure that the total concentration of measured ions in the membrane is constant, which forms the basis of Nernstian response of the ISE membrane. A Donnan exclusion failure may happen when the co-extraction of measured ions and its counterions are not negligible, and the membrane is not permselective anymore. The two frequently used cation exchanger or anion exchanger are sodium tetrakis[3,5-bis(trifluoromethyl)phenyl] borate (NaTFPB) and tridodecylmethylammonium chloride (TDMACl), respectively.
Ionophores or ion carriers

Ionophores, alternatively called ion carriers, are lipophilic compounds that selectively combine with and transport ions within the membrane. For an ionophore-free membrane, its selectivity pattern follows the hydration energy of the ions. Ionophore-based membranes, however, show very different selectivity due to different values of the complex formation constant for different ions with the same ionophore. The free energy of transfer of ions from aqueous to membrane phase and the complex formation constant between the extracted ions and the ionophore.
together dictate the membrane selectivity (*vide infra*). Ionophores may be neutral, positively charged or negatively charged. Figure 4 shows some of the ionophores used in the thesis work.

### 1.1.1 Response mechanism

The potentiometric measuring cell (Scheme 1) consists of two electrodes, i.e., the polymeric ion selective electrode and the reference electrode. The measured potential difference (electromotive force, EMF) measured at zero current between the two electrodes is the sum of all potential differences in the cell. Considering that all other potentials are independent of the sample except the phase membrane boundary potential $\Delta \phi$ and the liquid junction potential of

![Scheme 1. Schematic representation of an ISE potentiometric measuring cell.](image)

the reference electrode $E_{\text{ref}}$, the total potential may be expressed as eq 1.1,

$$EMF = E_{\text{const}} + \Delta \phi + E_{\text{ref}}$$

1.1

where $E_{\text{const}}$ denotes other potential contributions. By using an appropriate electrolyte of high concentration (e.g., 1M KCl, or LiOAc) or by using samples with constant ionic strength, the liquid junction potential between sample and reference electrode could be regarded as constant in agreement with the Henderson equation. Therefore, the measured EMF change will rely only on the variation of phase boundary potential between the ion selective membrane and sample solution.
The phase boundary potential originates from an exchange of charged ions between two phases. For the membrane prepared as introduced above, the ISE membrane is perm-selective to only cations or anions. If the ion exchange is thermodynamically reversible, i.e., without kinetic limitations, electrochemical potential of primary ion (denoted as “I” here) should be equal to each other in two phases, described in eq 1.2.

\[
\bar{\mu}_i^{aq} = \bar{\mu}_i^{m}
\tag{1.2}
\]

where \(\bar{\mu}_i^{aq}\) is the electrochemical potential of I in the aqueous phase and \(\bar{\mu}_i^{m}\) is the electrochemical potential of I in the membrane phase. Expansion of eq 1.2 gives us

\[
\mu_i^{0,aq} + RT \ln a_i^{aq} + z_i F \phi^{aq} = \mu_i^{0,m} + RT \ln a_i^{m} + z_i F \phi^{m}
\tag{1.3}
\]

where \(\mu_i^{0,aq}\), \(\mu_i^{0,m}\) are the standard chemical potential of I in aqueous phase and membrane phase, respectively; \(\phi^{aq}\) and \(\phi^{m}\) are the electrical potential for aqueous and membrane interface; \(z_i\) is the charge number of ion I; R, T, and F have their usual meanings. By rearranging eq 1.3, we have

\[
\Delta \phi = \phi^{m} - \phi^{aq} = \frac{\mu_i^{0,aq} - \mu_i^{0,m}}{z_i F} + \frac{RT}{z_i F} \ln \frac{a_i^{aq}}{a_i^{m}}
\tag{1.4}
\]

This equation is known as the phase boundary potential equation and correlates directly the interfacial potential with ion activity. Note that \(a_i^{aq}\), \(a_i^{m}\) denote the interfacial activities of ions I at the aqueous and membrane interface, and are not necessarily equal to the bulk activities in each phase. Eq 1.4 is also used for simulating and predicting potential variations by the diffusion layer model\textsuperscript{25} where ion exchange is thermodynamic and diffusion from/to bulk phase also plays an important role. If the ion exchange process is not totally reversible, other equations should be used to describe the phase boundary potential, such as the widely used Butler-Volmer equation,\textsuperscript{26} which is not within the scope of the thesis work and thus intentionally not discussed here.

For ion-selective polymers, it is ideally possible to keep the ion activity in the whole organic phase constant, in which case eq 1.4 reduces to the well-known Nernst equation,

\[
E_i = \Delta \phi = E_i^{0} + \frac{RT}{z_i F} \ln a_i^{aq}
\tag{1.5}
\]

with
\[ E_i^0 = \frac{\mu_{i,a}^{0} - \mu_{j,m}^{0}}{z_j F} + \frac{RT}{z_j F} \ln \frac{1}{a_j^m} \]  

Eq 1.5 forms the basis of the response mechanism of ion selective electrodes where the potential changes only as a function of the sample activity. For example, at room temperature (25°C), one order of magnitude of ion activity (concentration) change may result in a 59.2 mV of EMF potential change for monovalent ions and 29.6 mV EMF potential difference for divalent ions. Eq 1.5 is an idealized formalism for considering only primary ion present. In real samples containing interfering ions, the selectivity of ion selective membranes should be taken into account, and the more relevant Nikolsky-Eisenman equation is preferred,

\[ E_i = E_i^0 + \frac{RT}{z_j F} \ln\left(a_{i,a}^{0} + \sum_{j \neq i} K_{i,j}^{pot} a_j^{z_j/z_i}\right) \]

where \( K_{i,j}^{pot} \) is called selectivity coefficient of ion I to J, and \( a_j \) is the activity of interfering ion J. \( K_{i,j}^{pot} \) is effectively a weighting factor for J on the effect of the measured potential which helps to bracket potential influence from interfering ions. It is defined as follows.

### 1.1.2 Selectivity coefficient of ion selective electrodes

The selectivity coefficient is one of the main characteristics of an ISE and determines the electrode’s sensitivity to the primary ion I in the presence of interfering ion J. The selectivity coefficient can be defined from the response function of primary and interfering ions. The membrane responds to the interfering ions J, following the same pattern as primary ions,

\[ E_j = E_j^0 + \frac{s}{z_j} \log a_{j,a}^{q} \]

with

\[ s = \frac{2.303RT}{F} \]

\[ E_j^0 = \frac{\mu_{j,a}^{0} - \mu_{j,m}^{0}}{z_j F} + \frac{RT}{z_j F} \ln \frac{1}{a_j^m} \]

In a similar way, eq 1.5 may be rewritten as eq 1.11,

\[ E_j = E_j^0 + \frac{s}{z_j} \log a_{j,a}^{q} \]

The selectivity coefficient is defined as:
\[ \log K^\text{pot}_{i,j} = z_j (E_j^0 - E_i^0) / s \]

This allows us to rewrite the Nernstian response to J as a function of \( E_i^0 \) described in eq 1.13,

\[ E_j = E_j^0 + \frac{s}{z_j} \log K^\text{pot}_{i,j} a_j^{z_j} \]

By substituting eq 1.6 and eq 1.10 in eq 1.12, one obtains another expression for the selectivity coefficient,

\[ \log K^\text{pot}_{i,j} = \frac{z_j}{s} (\Delta_m \phi_i^0 - \Delta_m \phi_j^0) + \log \left( \frac{a_j^m}{a_j^m} \right)^{z_j^{z_j}} \]

where \( \Delta_m \phi_i^0 \) and \( \Delta_m \phi_j^0 \) are the standard electrode potentials that incorporate the standard chemical potential difference of ions I and J.

\[ \Delta_m \phi_i^0 = \frac{\mu_i^{0,\text{aq}} - \mu_i^{0,m}}{z_i F} \]

\[ \Delta_m \phi_j^0 = \frac{\mu_j^{0,\text{aq}} - \mu_j^{0,m}}{z_j F} \]

It is now obvious that the selectivity coefficient is determined by two factors, as shown in the two terms on the right side of eq 1.14. The first term relates with the standard potential difference for primary ion and interfering ion, which is governed by solvation energy differences of ion I and J in the respective phases. This term corresponds to the Hofmeister selectivity sequence. Changing the membrane matrix composition may result in a selectivity sequence that deviates from that of the Hofmeister series. The second term points out that membrane selectivity could be operationally optimized by adjusting the ion activities \( a_j^m \) and \( a_j^m \). This is achieved by doping the membrane with the ionophore that interacts strongly with primary ions but weakly with the interfering ions. A lower value of selectivity coefficient means a better discrimination toward interfering ions for the ion selective membrane.

### 1.1.3 Correlation between selectivity coefficient and complex formation constant

For simplicity, a cation that forms strong 1:1 complexes with an electrically neutral ionophore is chosen as a model case. If only a monovalent ion J is extracted into the membrane and forms complexes of the type JL and the ion-exchanger is a monovalent anion, the charge balance holds for the pairs of ion,

\[ c_m^{m} = c_m^{m} \]
where \( c_{JL}^m \) is the concentration of complexed ion and \( c_{Rc}^m \) is the concentration of cation exchanger inside the membrane. Free membrane ions J exist and there is a complexation equilibrium between the free ion, the complexed one, and the ionophore,

\[
c_{JL}^m = c_J^m \beta_{HL} c_{L}^m
\]  

where \( c_J^m \) denotes the concentration of free ion J inside the membrane, and \( \beta_{HL} \) is the complex formation constant. Primary ion I could replace J in eq 1.17 and eq 1.18, and thus repetition is omitted here. If ion pairing is neglected and ion activity coefficient inside membrane is considered as one, by inserting eq 1.17 and 1.18 into eq 1.14, we get the desired equation,

\[
\log K^\text{pot}_{i,J} = \frac{z_i}{s} (\Delta_{a}^m \phi_j^0 - \Delta_{a}^m \phi_I^0) + \log \frac{\beta_{HL}}{\beta_{HL}}
\]  

1.19

The selectivity coefficient thereby depends on two key factors. The first factor is already depicted above. The second factor incorporates now the complex formation constants for each ion in the membrane. Eq 1.19 reflects that the higher value of \( \beta_{HL} \) compared with \( \beta_{HL} \), the better the selectivity coefficient. This trend should also apply to multivalent ions and other stoichiometry complexes, though eq 1.19 is derived based on monovalent cation and 1:1 complexes.

Since complex formation constant determines the selectivity performance of the ion selective membrane, it is necessary to determine their values for investigated ionophores for the ions of interest. There are several methods for determining complex formation constants including the three main approaches: the reference ionophore method, the segmented sandwich membrane method and the reference ion method. The reference ionophore method uses an ionophore (e.g., chromoionophore) that does not chemically interact with the ion for which the ionophore is selective, and the determination of the selectivity coefficient of membranes with and without ionophore of interest result in apparent complex formation constants. The sandwich method measures the EMF potential for a single blank membrane without ionophore and a fused double layer membrane with one layer containing ionophore and another layer using the same blank. The resultant potential difference determines the complex formation constant. The reference ion method uses a chemically inert reference ion, such as tetraethylammonium for cation ionophore and perchlorate for anion ionophore. With the reference ion method, the selectivity coefficients for investigated ion relative to the reference ion are firstly determined for two membranes with only one containing the ionophore but otherwise of the same composition. The complex formation constant is calculated from the two different selectivity coefficients.
Chapter 5 describes a new method which utilizes a solid contact thin layer ion selective membrane. Compared to the above three methods that are limited to only one given membrane composition (i.e. the unchanging molar ratio of ionophore and ion exchanger), voltammetric scans of a single thin layer membrane may give information not only about complex formation constants but also the selectivity coefficient for varying membrane compositions.

1.2 Solid-contact ion selective electrodes

In contrast to conventional ion selective electrodes, the solid-contact ion selective electrodes (SC-ISE) are devices where the internal electrolyte and the internal reference element are replaced by a solid ion-to-electron transducer and a conducting substrate. The merits of the SC-ISE include ease of miniaturization, the ability to use them at arbitrary orientation, and a higher tolerance to increased temperature and pressure. While the conducting substrate could be of various materials and shapes, such as conventional macro-glassy carbon electrode/gold electrode, platinum wire electrode, screen printed disposable electrode and inkjet printed paper-based electrode, the ion-to-electron transducers play a dominant role in the performance of the SC-ISE. A good ion-to-electron transducer should be sufficiently lipophilic, either with high charge transfer capacitance or composed of a reversible, well-defined redox couple.

The basic concept for utilizing molecular redox couples is that principally they could define the underlying electron transfer potential according to the Nernst equation shown below.

$$E = E_0 + \frac{RT}{nF} \ln \frac{a_{\text{ox}}}{a_{\text{red}}} \quad \text{1.20}$$

where $a_{\text{ox}}$ and $a_{\text{red}}$ is the activity of oxidized form and reduced form of the redox couple. In order to keep the potential constant, the activity (or concentration) of oxidized and reduced form of the redox couple should be kept invariable. Poly (vinyl-ferrocene) was earlier used as a solid contact for a K$^+$ ISE. Long-term measurements over 20d in which the potential was determined repeatedly in a 0.1 M KNO$_3$ showed a peak to peak deviation only of about 14mV, slightly larger than 10 mV of the conventional liquid contact K$^+$ ISE. A fullerene lipophilic redox active self-assembled monolayer (SAM) was also introduced as a solid contact. This SAM, however, exhibits a relatively low redox capacity. The Bühlmann group came up with Co(II)/Co(III) complex as redox buffer, either doping it directly in the same PVC ISE membrane or putting it together with colloid imprinted mesoporous carbon materials as an underlying solid contact layer. This complex holds good promise for calibration-free ion selective electrodes and shows very small interelectrode potential variability. Some other
molecules such as tetracyanoquinodimethane (TCNQ),\textsuperscript{43} prussian blue analogues,\textsuperscript{44} and cationic Helicenes\textsuperscript{45} were also investigated. One drawback of using redox couples is that it requires an adjustment of redox couple in a defined ratio, ideally with half of the material present in either an oxidized or a reduced state, which may not be easily achieved at preparation nor maintained during a longer shelf time.

Another strategy for the solid-contact transducing layer is using lipophilic high capacitance materials. The materials do not have defined redox potential but are resistant to a potential change upon faradaic perturbation. As shown in eq 1.21, where \( C \) denotes as the capacitance of the underlying layer, \( \Delta q \) means the perturbing charge passing at the electrode surface and \( \Delta E \) is the potential change. A higher capacitance induce a smaller \( \Delta E \) for a given charge perturbation \( \Delta q \).

\[
\Delta E = \Delta q / C
\]

Conducting polymers (CP) appear to be promising candidates for the construction of SC-ISEs with improved stability due to their high capacitance property, ease of preparation, and stable electrochemical behavior.\textsuperscript{18} The most popular CPs used so far for SC-ISEs are poly(pyrrole) (PPy), poly(ethylenedioxythiophene) (PEDOT), poly(3-octylthiophene) (POT), and polyaniline (PANI). Figure 5 presents the molecular structure of some CPs. These polymers are predominantly p-doped instead of n-doped for transducing. The n-doped forms of CPs exhibit a much lower specific capacitance than p-doped forms of the same CPs. In addition, n-doped CPs are not stable and more easily to react with ambient O\textsubscript{2}. The fabrication of p-doped CP transducing layer could be either by coating the electrode surface with CP particle cocktails or by electropolymerization. Normally, electropolymerization gives more uniform layers but can only be applicable on conducting substrate, not on a non-conducting substrate such as papers. CP is also advantageous to most redox molecules for a voltammetric study of ISE. The experiments within CP as redox buffer shows better reversibility, repeatability, and

![Figure 5. Molecular structure of PEDOT, POT and PPy](image-url)
In this thesis, POT is chosen as inner transducers for fabricating solid contact thin layer ISE (Chapter 3, 4, 5). The concept of thin layer ISE will be detailed in corresponding chapters and thus not necessarily carefully discussed here. Briefly, a thin layer ISE has membrane thickness only of several hundred nanometers to several micrometers, much thinner than conventional ISE with thickness of hundreds of micrometers. Thin layer voltammetry shows a different scan rate dependency characteristic than bulk sample voltammetry, which will be discussed in the coming section.

Conducting polymers are intrinsically similar to semiconductors. To maintain electroneutrality, the charging and discharging of CPs are accompanied by counterion diffusing into the film or out of the polymer, respectively. The current for an ideal reversible electron transfer CV of CPs is described by eq 1.22,

\[ i = \frac{n^2F^2A\Gamma_v\exp\theta}{RT(1+\exp\theta)^2} \]

where \( \theta = (nF/RT)(E-E^0) \) and \( \Gamma_v = \Gamma_0 + \Gamma_R \) correspond to the total surface covered with reduced and oxidized states. In principle, eq 1.22 is only valid for monomolecular layers. For a larger increase of membrane thickness, diffusion should be considered and the voltammetric response is not mirror symmetrical anymore. It was also stated that the charging process of CPs is a sequence of discrete but overlapping redox steps. However, to precisely mathematically quantify the redox process is difficult. A pseudo-Nernst formula is used to describe the electrochemical properties of POT in this thesis for thin layer ion transfer simulation. The simulation results still agree with experimental data (chapter 3), since POT only acts a reversible electron reservoir in that process. With either method, underlying POT oxidized charge-potential function is experimentally extracted by assuming a reversible ion transfer for the reference ion, tetrabutylammonium (TBA\(^+\)). This provides a new method for studying ion-ionophore complexation inside the membrane (chapter 5).

CPs, however, still have some drawbacks, which possibly will limit their practical potentiometric applications. CPs are sensitive to light and there is evidence of water layer formation at the interface between solid contact and ISE membrane, a major cause of potential shift. To overcome these limits, a new class of nanostructured materials has emerged for solid contact electrodes, including carbon nanotubes,\(^{49}\) graphenes,\(^{50}\) crystalline C60\(^{40}\), and gold nanoparticles.\(^{51}\) These materials are preferred for long-term environmental \textit{in situ} monitoring because they are insensitive to light, highly lipophilic and are of high capacitance.\(^{32}\) For this motivation, one step modification of lipophilic multi-walled carbon nanotubes (f-MWCNTs) is achieved in the work (Chapter 2) and a simple fabrication of SC-ISE allows the sensors
prepared in batch by non-specialists. These electrodes are applicable for different anions and are proved promising for environmental anion detection that could not be obtained by using CPs as inner transducers.

1.3 Dynamic electrochemical techniques

The two dynamic electrochemical techniques used in the frame of this research are cyclic voltammetry and electrochemical impedance spectroscopy.

1.3.1 Cyclic voltammetry

Cyclic voltammetry (CV) is one of the most popular potential sweeps and has proven very powerful in obtaining information about fairly complicated electrode reactions. It is typically applied to study the kinetics of electrochemical reactions, to probe active redox species in solution and to investigate ion transfer at liquid-liquid interface. In the linear CV technique, the potential is linearly scanned from a starting potential ($E_0$) to a turning potential ($E_\lambda$) and then reversed back to the original value within the same scan rates (Scheme 2a). The current recorded as a function of applied potential is called a cyclic voltammogram (Scheme 2b).

![Scheme 2. (a) Linear cyclic potential sweep. (b) Resulting cyclic voltammogram. O denotes the oxidized form and R denotes the reduced form.](image)

A small A/V condition means that the electrode surface, $A$, is sufficiently small and the solution volume, $V$, is sufficiently large so that chemical reaction at electrode surface does not alter the concentrations of electroactive species in the bulk solution. This small A/V condition is ubiquitous in routine experiments. The electrochemical reaction at electrode surface could be reversible, irreversible or quasi-reversible, depending on the heterogeneous electron transfer rate at electrode-solution interface. A reversible cyclic voltammogram under small A/V
condition can be mathematically predicted. Let’s consider the reaction \( O + ne \rightleftharpoons R \). The boundary equation at the interface is following the Nernst equation,

\[
\frac{c_o(0,t)}{c_R(0,t)} = f(t) = \exp \left[ \frac{nF}{RT}(E_t - vt - E^{0'}) \right] \tag{1.23}
\]

where \( c_o(0,t) \) and \( c_R(0,t) \) are the aqueous interfacial concentration for O and R, respectively. Together with other diffusional equations and boundary conditions (omitted here), the current–potential function could be in principle achieved. After Laplace transformation, the final dimensionless integral that needs to be numerically solved is

\[
\int_0^{\sigma_t} \frac{\chi(z)dz}{\sigma t - z^{1/2}} = \frac{1}{1 + \xi \theta S(\sigma t)} \tag{1.24}
\]

with \( S(t) = e^{-\sigma t} \), \( \theta = \exp \left[ \frac{nF}{RT}(E_t - vt - E^{0'}) \right] \), \( \sigma = \frac{nF}{RT} \), \( \xi = (D_o / D_R)^{1/2} \) and

\[
\chi(z) = \frac{i(\sigma t)}{nFAC_o(\pi D_o \sigma)^{1/2}}.
\]

Figure 6 shows the calculated dimensionless form of current as function of potential.\(^{23}\) It is obvious that the peak is not symmetric. The peak occurs after the total depletion of O at surface and expansion of the diffusion layer. Based on the numerical formalism above, the peak current function is obtained,\(^{23}\)

\[
i_p = 0.4463 \left( \frac{F^3}{RT} \right)^{1/2} n^{3/2} AD_o^{1/2} c_o^{1/2} \tag{1.25}
\]

Noteworthily, eq 1.25 indicates that peak current is linear with square root of scan rate and concentration. This is an important sign of a diffusion controlled process in cyclic voltammetry.

If the small A/V condition no longer holds, such as for voltammetric experiments in a thin layer chamber where the bulk sample is altered or even exhausted, the CV function changes. For example, Scheme 3 represents a twin-electrode configuration where the sample cell is enough thin that all the species concentrations are uniform and mass transport is neglected during CV scans. A reversible CV function for this twin-electrode thin layer cell is calculated as\(^{23}\)

\[
i = n^2 F^2 v C_o^* \frac{\exp \left[ \frac{nF}{RT}(E - E^{0'}) \right]}{1 + \exp \left[ \frac{nF}{RT}(E - E^{0'}) \right]^2} \tag{1.26}
\]

with the peak current centered at \( E = E^{0'} \),
where $V$ is the volume of the thin layer cell and $E^0$ is the formal potential; the other parameters have their usual significant meanings. The peak current now is proportional to scan rate instead of square root of scan rate, and the voltammogram is symmetric at peak position.

Figure 6. Linear potential sweep voltammogram in terms of dimensionless current function. Values on the potential axis are for 25 °C.

Scheme 3. Diagram of a twin-electrode thin layer cell with a cell volume of $V$. The concentration of species O and R can be considered uniform in this cell during CV scans.

Note that the formulas derived above are only applicable for reversible CVs. For a non-reversible electrochemical system, mathematical treatments become more complex and sometimes it is impossible to obtain the pure solution of differential equations. In that case,
digital simulation serves a strong tool for fitting and prediction, which will be briefed in the next section.

### 1.3.2 Electrochemical impedance spectroscopy

Electrochemical impedance spectroscopy (EIS) is another frequently used technique in an electrochemical system for evaluation of heterogeneous charge-transfer parameters and for studies of the double-layer structure. It has been widely used for applications such as electrochemical sensing, characterization of fuel batteries and solar cells and corrosion processes.

In contrast to CV technique with large potential perturbations on the systems, for EIS one only applies a small sinusoidal potential around the open circuit potential at varying frequency. The excitation signal as a function of time, is as follows:

\[
E = E_0 \sin(\omega t)
\]

where \(E\) is the potential at time \(t\), \(E_0\) is the amplitude and \(\omega\) is the radio frequency. The resulting current response for a complex cell is also a sinusoidal signal with normally a phase shift (\(\phi\)) to excited potential,

\[
I = I_0 \sin(\omega t + \phi)
\]

The resistance of the system to the current flow could now be defined as impedance as it is frequency dependent,

\[
Z(\omega) = \frac{E}{I} = \frac{Z_0}{\sin(\omega t)} \frac{\sin(\omega t)}{\sin(\omega t + \phi)}
\]

where \(Z_0\) is the amplitude of the resulting impedance. Eq 1.30 indicates that the impedance may be represented as a vector, with in phase components on the x-axis and out of phase components on the y-axis. By introducing complex numbers, the impedance is transformed to a ratio of two relationships as follows:

\[
Z(\omega) = Z_0 (\cos \phi + j \sin \phi)
\]

where the first term in the right bracket denotes real part while the second term denotes imaginary part, \(j\) is the imaginary number.

A Randles cell, composed of an RC element (in parallel) and a resistor in series, representing a solution resistance, a double layer capacitor and charge transfer resistance, is a typical idealized equivalent circuit for many electrochemical systems, as illustrated in Figure 7.
impedance of the Randles cell can be predicted theoretically, with its real part component and imaginary part component calculated as

\[ Z_{re} = 1 + \frac{R_2}{1 + \omega^2 R_2^2 C_2^2} \]

\[ Z_{im} = \frac{R_2^2}{1 + \omega^2 R_2^2 C_2^2} \]

Both of the real part and imaginary part are frequency dependent. In Nyquist plot, \( Z_{im} \) is plotted as a function of \( Z_{re} \), without showing any frequency information. The plot is represented as a semi-circle in a complex plane (Figure 8), giving explicit information about the resistance of the system.

**Figure 7.** Equivalent circuit for a simple electrochemical cell, consisting of an RC element in parallel and a resistor placed in series

**Figure 8.** Nyquist Plot: real and imaginary components of the impedance vector. \(|Z|\) denotes the absolute value of impedance vector.
1.4 Computer simulation

In electrochemistry, the importance of diffusion can never be overemphasized as an electrochemical process is always affected or even governed completely by mass transport. The function to describe mass transport is usually a set of coupled partial differential equations (PDEs), with some boundary conditions if necessary. However, most of the equations are not solvable algebraically in complicated systems, yet one still wants answers. Fortunately, computer simulation, also called numerical simulation, provides an alternative or perhaps the only way to get numerical solutions of the quested PDEs. In a computer simulation, space is divided into small discrete finite volume elements where the concentrations of all substances in one element are regarded as uniform, but vary from one element to the other. In the meantime, time is discretized into many small separate steps as well. The underlying philosophy of numerical simulation is to calculate next-time-step substance concentrations in all elements from previous-time-step substance concentrations. The calculation is then repeated one by one until the whole evolution ends.

The simplest calculation is the explicit finite difference method that utilizes the same space and time element distance. It is valuable in developing an intuitive insight in important process in an electrochemical system. Fick’s first diffusion law is the most favorable way to describe interactions between elements,

\[ J(x,t) = -D \frac{\partial c(x,t)}{\partial x} \]  \hspace{1cm} (1.34)

where D denotes diffusion coefficient in a homogenous phase (water, membrane etc.). Recall one mathematical definition of eq 1.34, we have

\[ J(x,t) = \lim_{\Delta x \to \infty} -D \frac{(c(x+\Delta x,t) - c(x,t))}{\Delta x} \]

If \( \Delta x \) is chosen small enough in finite difference method, one can take an approximation that

\[ J(x,t) = -D \frac{(c(x+\Delta x,t) - c(x,t))}{\Delta x} \]  \hspace{1cm} (1.35)

If \( \Delta x \) is chosen small enough in finite difference method, one can take an approximation that

\[ J(x,t) = -D \frac{(c(x+\Delta x/2,t) - c(x-\Delta x/2,t))}{\Delta x} \]  \hspace{1cm} (1.36)

or

\[ J(x,t) = -D \frac{(c(x+\Delta x,t) - c(x-\Delta x,t))}{\Delta x} \]  \hspace{1cm} (1.37)

Now we introduce the law of mass conservation:

\[ \frac{\partial c(x,t)}{\partial t} = \frac{\partial J(x,t)}{\partial x} \]  \hspace{1cm} (1.38)
By the finite difference method, it is discretized into

\[
\frac{c(x,t + \Delta t) - c(x,t)}{\Delta t} = \frac{J(x + \Delta x / 2,t) - J(x - \Delta x / 2,t)}{\Delta x}
\]

1.39

Using eq 1.37 to replace the flux in eq 1.39, one gets

\[
c(x,t + \Delta t) = c(x,t) + \frac{D \Delta t}{\Delta x^2} \left( c \left( x + \Delta x, t \right) - 2c \left( x, t \right) + c \left( x - \Delta x, t \right) \right)
\]

1.40

where \( \Delta x \) is now the discretized space distance and \( \Delta t \) is time increment in the simulation; \( \frac{D \Delta t}{\Delta x^2} \) is called the model diffusion coefficient. The value of \( \Delta x \) and \( \Delta t \) should be carefully chosen to ensure that the value of \( \frac{D \Delta t}{\Delta x^2} \) is less than 0.5. If \( \frac{D \Delta t}{\Delta x^2} \) is more than 0.5, the total simulation will crash with oscillating results.\(^{24}\) Generally, the less value of \( \Delta x \) and \( \Delta t \) is chosen, the more accurate the simulation results will be. Eq 1.40 is the explicit formula used to calculate the bulk elements except for the boundary elements. The boundary elements calculation depends on the underlying electrochemistry. For a chemically inert boundary element, usually the last boundary element is described by a reflection of the concentration gradient.\(^{56}\)

\[
c(x_m,t + \Delta t) = c(x_m,t) + \frac{2D \Delta t}{\Delta x^2} \left( c \left( x_m - \Delta x, t \right) - c \left( x_m, t \right) \right)
\]

1.41

where \( x_m \) denotes the last element. For a chemically reactive boundary element, usually the first boundary element, the calculation should combine the diffusion process and electrochemical reaction process. The electrochemical reaction could be a redox reaction at metal electrode surface, ion exchange at membrane/solution interface, adsorption or desorption, accumulation or stripping, either reversible or irreversible. The correct calculation of the first element determines the quality and accuracy of the simulation results.

Above, the concept of space element was introduced as a small finite volume where the substance concentration is regarded as uniform in one element. This method is called “box” method, which was probably first utilized by Feldberg in 1964.\(^{55}\) Another method is called “point” method where sample concentration is placed along the x-axis at a number of points (Scheme 4a). The “point” method is sometimes favored because it is easier to arrive at a discrete form of PDEs, especially when the differential equation is complicated.\(^{55}\) However, the “box” method has a more physical meaning of elements towards electrode systems. For instance, the first element in a “box” method relates to a finite small volume near electrode surface (Scheme 4b) while in a “point” method only represents an abstract point on the
electrode surface. This box definition is more advantageous in differentiating the influence of diffusion and electrode flux on the first element. Based on this, chapter 6 serves a work in explanation of how to properly treat boundary elements for a reversible ion exchange in ion selective membranes, which seems to have been perplexing for a decade in that field.

Scheme 4. (a) Point method: the discretized element is represented as a solid black point. The distance between points is $\Delta x$. (b) Box method: the discretized space element is regarded as a small volume box. The thickness of the box is $\Delta x$. Time increment for both point method and box method is $\Delta t$.

Note that Fick’s first law only takes diffusion process into account, but in real cases, migration and convection may not be neglected. Eq 1.42 is the Nernst-Planck equation in one-dimensional form that considers migration and convection,

$$J_j(x,t) = -D_j \frac{\partial c_j(x,t)}{\partial x} - z_j D_j c_j(x,t) \frac{F}{RT} E(x,t) + c_j(x,t) v$$  \hspace{1cm} (1.42)

where $E(x,t)$ is the electrical field, and $v$ is the linear velocity; subscript $j$ denotes general ion $j$; other terms are established. For the solvation of eq 1.42, the Poisson equation is used to relate $J_j(x,t), c_j(x,t)$, and $E(x,t)$,

$$I(t) = F \sum_j z_j J_j(x,t) + \varepsilon \frac{\partial E(x,t)}{\partial t}$$  \hspace{1cm} (1.43)

where $I(t)$ means the total current density and $\varepsilon$ is the dielectric permittivity. The simulation for ion selective membrane using the Nernst-Planck and Poisson equations within non-equilibrium boundary condition is called NPP model while diffusion layer model (DLM) only utilizes Fick’s diffusion laws and assumes a local equilibrium. NPP model is more comprehensive than DLM model, yet more complex and sometimes time-consuming. In some experiments where homogeneous chemical reactions exist, such as the protonation and deprotonation of carbonate with protons, the relevant term should add to mass conservation law.
\[ \frac{\partial c(x,t)}{\partial t} = - \frac{\partial J(x,t)}{\partial x} + f(c) \]

where \( f(c) \) is the unspecified homogeneous term representing all the chemical reactions that lead to the concentration change. The simulation now refers to the discretization of eq 1.44.

1.5 References

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Chapter 2 All-Solid-State Potentiometric Sensors with a Multi-Walled Carbon Nanotube Inner Transducing Layer for Anion Detection in Environmental Samples

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Abstract

While ion to electron transducing layers for the fabrication of potentiometric membrane electrodes for the detection of cations have been well established, similar progress for the sensing of anions has not yet been realized. We report for this reason on a novel approach to the development of all-solid-state anion selective electrodes using lipophilic multi-walled carbon nanotubes (f-MWCNTs) as inner ion to electron transducing layer. This material can be solvent cast, as it conveniently dissolves in tetrahydrofuran (THF), an important advantage to develop uniform films without the need of using surfactants that might deteriorate the performance of the electrode. Solid contact sensors for carbonate, nitrate, nitrite and dihydrogen phosphate are fabricated and characterized, and all exhibit comparable analytical characteristics to the inner liquid electrodes. For example, the carbonate sensor exhibits a Nernstian slope of 27.2 ± 0.8 mV.dec⁻¹, a LOD = 2.3µM, a response time of 1 s, a linear range of four logarithmic units and a medium-term stability of 0.04 mV.h⁻¹ is obtained in a pH 8.6 buffered solution. Water layer test, reversibility, and selectivity for chloride, nitrate and hydroxide are also reported. The excellent properties of f-MWCNTs as a transducer are contrasted to the deficient performance of poly(3-octyl-thiophene) (POT) for carbonate detection. This is evidenced both with a significant drift in the potentiometric measures and as well as a pronounced sensitiveness to light (either sunlight or artificial light). This latter aspect may compromise its potential for environmental in-situ measurements (night/day cycles). The concentration of carbonate is determined in a river sample (Arve river, Geneva) and compared to a reference method (automatic titrator with potentiometric pH detection). The results suggest that nanostructured materials such as f-MWCNTs are an attractive platform as a general ion-to-electron transducer for anion-selective electrodes.
2.1 Introduction

Solid contact ion-to-electron transducers have been established mainly for cation-selective potentiometric sensors and contributed to the establishment of reliable sensing platforms that involve simpler manufacturing and improved mechanical and chemical robustness. The very first solid contact ion-selective electrode was constructed using polypyrrole (PPy) as an ion-to-electron transducer. While reliable determination of sodium had been confirmed, the most important advantage over the coated wire electrode (CWE) was the stability of the sensor signal, from tens of mV to just a few mV per hour. This particular field has subsequently experienced rapid growth, which was mainly based on the three conducting materials poly(3-octylthiophene) (POT), poly(3,4-ethylene-dioxythiophene)(PEDOT) and polypyrrole (PPy).

While dozens of reports have appeared in the literature for cation detection (potassium, proton, calcium, copper, lead, see reference), so far very few papers were dedicated to the detection of anions using all solid state potentiometric sensing devices.

As a model system chloride was repeatedly measured with films formed by POT doped with tridodecylmethlyammonium chloride (RCl). A Nernstian response was obtained as a function of chloride concentration, suggesting that the doped POT film functions as an electrode of the second kind. In a similar approach either PEDOT or PPy were utilized for detecting chloride and nitrate, respectively. These systems did not involve an overlaid ion-selective membrane and therefore exhibited only limited selectivity.

An ion-selective membrane deposited over a doped conducting polymer should result in a more attractive sensing behavior. One report for the detection of chloride involved a very high concentration of quaternary ammonium in the membrane phase (around 30-40 w/w), making the ion transduction mechanism somewhat unclear. Furthermore, the long term stability was far worse than for cation-selective sensors based on POT. Carbonate was determined using a POT layer backside contacted with a Ag/AgCl film, but the use of two seemingly competing transducers, one overlaid on the other, was not mechanistically justified. Moreover, the selectivity over chloride was found to diminish by three logarithmic units when the electrode configuration was altered from an inner liquid solution to a solid contact. Both nitrate and chloride were also explored using ion-exchanger membranes backside contacted with POT or PPy but they resulted in a poor stability over time.

While few investigations considered using POT as an inner layer for hydrophilic anion detection, no fundamental explanation for its use was given. Indeed, the ion transduction mechanism of a conducting polymer model system was not clarified until recent evidence
acquired from synchrotron experiments using X-ray photoelectron spectroscopy (XPS) and near edge X-ray absorption fine structure (NEXAFS) on cation-selective membranes. Those results suggest that solvent cast poly(3-octylthiophene) may spontaneously form a mixed surface/bulk oxidation state (POT/POT\textsuperscript{+}), which may explain the high potential stability of the resulting ion-selective electrode.\textsuperscript{26} Accordingly, the cation exchanger sites (TFPB\textsuperscript{−}) at the inner interface must compensate the positive charge of oxidized POT, and thus, at zero-current measurements, the concentration ratio (POT/POT\textsuperscript{+}) should remain constant. As the surface oxidation of POT is accompanied by an expulsion of a hydrophilic cation from the membrane, this processes is expected to be spontaneous for cation-selective sensors. Indeed, POT-based solid contact electrodes were put forward as a general approach for the detection of silver, lead, potassium and calcium at nM levels.\textsuperscript{27}

The suggested mechanism may not be applicable with an overlaid anion-selective membrane since POT surface oxidation may be energetically unfavorable when coupled to the extraction of a hydrophilic anion into the membrane.

One may conclude that there is a strong unmet need for a general procedure for preparing solid contact anion-selective electrodes. The few papers available in the literature and discussed above involved just a single analyte (typically chloride), used a range of different electrochemical procedures and protocols, and are of limited utility for the design of new anion-selective electrodes.

As a point in case, solid state carbonate electrodes are required to record reliable carbonate profiles as a function of depth in a range of ecosystems (seawater, rivers and lakes) to obtain information on alkalinity, pH and bioavailability by limnologists.\textsuperscript{28} Advances in carbonate ionophore synthesis have been significant, making it today possible to discriminate most interfering ions in environmental samples (chloride and sulfate).\textsuperscript{29-32}

A new generation of solid contact electrodes has recently emerged based on the use of nanostructured materials such as carbon nanotubes\textsuperscript{33}, graphene,\textsuperscript{34} three-dimensionally ordered macroporous carbon,\textsuperscript{35} or gold nanoparticles.\textsuperscript{36} These may be preferred because they rely on a capacitive mechanism, which makes them a more general transducer at zero current measurements,\textsuperscript{33,37} and because they are insensitive to changes in light illumination (day/night cycles), which is a crucial characteristics for environmental in-situ measurements.\textsuperscript{38}

We report here on what appears to be a general approach to the design of potentiometric solid contact electrodes for anions in environmental analysis, with carbonate, nitrate, nitrite and dihydrogen phosphate as examples, based on functionalized lipophilic carbon nanotubes. The obtained results enhance the use of nanostructured materials as ubiquitous ion-to-electron
transducers (indistinctive towards the charge and nature of the ion) as was earlier exhibited for a wide range of cations.\textsuperscript{35,39-44} A simple fabrication allows the preparation of these sensors by a non-specialist. The developed all-solid-state anion sensors were fully characterized and tested in river samples. As a consequence of the excellent analytical performance, we believe that this technology may become promising for the design of \textit{in-situ} anion sensing probes.

2.2 Experimental section

2.2.1 Materials

Muti-walled carbon nanotubes (MWCNT), Thionyl chloride (SOCl\textsubscript{2}), octadecylamine (ODA), bis(2-ethylhexyl) sebacate (DOS), sulphuric acid (97%), nitric acid (65%), Poly(vinyl-chloride) (PVC, high molecular weight), bis(2-ethylhexyl) adipate (DOA), N,N-dioctyl-3α,12α-bis(4-trifluoroacetylbenzoyloxy)-5β-cholan-24-amide (carbonate ionophore VII), nitrite ionophore (IV), TDMAN (tridodecylmethylammonium nitrate), tridodecylmethylammonium chloride (TDMACl), tetradodecylammonium chloride (TDDA), Poly(3-octylthiophene-2,5-diyl) regioregular, tetrahydrofuran (THF) were purchased from Sigma-Aldrich (analytical grade). Synthesis of uranyl salophene III was performed according to Wroblewski et al.\textsuperscript{45} Synthesis of lipophilic multi-walled-carbon nanotubes was performed by following the Blondeau et al. procedure\textsuperscript{46} with some modifications (see Supporting information).

2.2.2 ISE membranes

A mixture of ionophore, ion exchanger, plasticizer and PVC were used to prepare the cocktail for each analyte (Supporting Information for membrane composition).

2.2.3 Electrochemical equipment

A Metrohm 827 pH meter, a double-junction Ag/AgCl/3 M KCl/1 M LiOAc reference electrode, glassy carbon electrode with a diameter of 3.00 ± 0.05 mm, a platinum-working rod (3.2 cm\textsuperscript{2} surface area), electrode bodies (Oesch Sensor Technology), a high impedance input 16-channel EMF monitor, a 765-automatic Dosimat (Metrohm Autolab, Utrecht) and an Autolab PGSTAT101 Metrohm Autolab were used (see supporting information for more details).

2.3 Results and discussion

The aim of this work was to establish a reliable and robust potentiometric carbonate solid contact electrode based on functionalized carbon nanotubes, which is suggested to serve as a general materials platform for the design of \textit{in-situ} environmental anion sensors. Figure 1
schematically illustrates the fabrication protocol of the solid contact electrodes. To avoid any unnecessary exposure of the transducer to the solution, a two-layer configuration was selected. The first layer consists of functionalized multi-walled carbon nanotubes (f-MWCNTs). Owing to the lipophilic nature of f-MWCNTs, a homogenous and concentrated solution can be prepared in organic solvents such as THF. The use of lipophilic carbon nanotubes (specifically SWCNTs) is an elegant concept recently introduced by Blondeau et al. Unfortunately, key advantages of using this approach have not been clearly described. Ease of preparation, avoiding of water-soluble surfactants and minimization of any source of water must influence the sensor quality. A custom-made mask made out of silicon rubber is used to only cover the conductive glassy carbon surface and to spatially delimit the f-MWCNTs layer. This mask is later removed so that the polymer membrane can be deposited onto the entire electrode surface. The suitable adherence of the membrane to the PEEK body ensures a tight seal that prevents water penetration.

To mimic environmental conditions, a calibration curve was carried out by adding a successive aliquots of 0.1 M NaHCO₃ to 100-mL of a buffered solution at pH=8.6 (0.1M Tris-H₂SO₄). The carbonate concentration (strictly activity) was calculated at this pH using the mass balance and the acidity constants (pK₁=6.3 and pK₂=10.3). Because recording the calibration curve was performed within 30 min, the amount of atmospheric CO₂ continuously dissolving in solution was not considered for calculation.

While the pH changes were insignificant upon each NaHCO₃ addition (high buffer capacity), an independent pH probe was used to monitor any eventual pH variation. The analytical characteristics are shown in Figure 2. A lower detection limit of 2.3 µM, an upper limit of detection of 1 mM and a linear range of 4 logarithmic units are observed (Inset of Figure 2). The potentiometric time trace suggests a rapid kinetic reaction between the ionophore and
carbonate, which is in contrast to many other anion-selective membranes containing porphyrins, salophens, etc. as carriers.\textsuperscript{48,49} In fact, the response time according to IUPAC (\(\Delta E/\Delta t \sim 0.2\text{mV.min}^{-1}\)) is about 1-s.\textsuperscript{50}

Considering the possibility of extending this approach to more anions, Figure 3 shows a calibration curves for nitrate (slope \(-57.7\text{ mV dec}^{-1}\)), nitrite (\(-55.5\text{ mV dec}^{-1}\)) and dihydrogen phosphate (\(-56.0\text{ mV dec}^{-1}\)). Potentiometric time traces are displayed in Figure S1 and Table S1 summarizes the analytical performance of these three sensors.

![POTENTIOGRAPHIC TIME TRACE](image)

**Figure 2.** Analytical performance of the proposed electrode. Potentiometric time trace obtained by adding successive additions of carbonate to 0.1M Tris-\(\text{H}_2\text{SO}_4\) buffer (pH=8.6). Inset: A triplicate of the calibration curve (RSD=1.5%) as a function of the carbonate activity (slope=27.2 ± 0.8 mV.dec\(^{-1}\), LOD=2.3µM).

While the obtained analytical characteristics are comparable to those of the corresponding inner liquid configuration,\textsuperscript{29,45,49} the quality of the transducer must be reflected in the potential stability of the sensor. Generally, in the absence of strong interfering ions and in a reasonable concentration range, a Nernstian response is expected, independently of the selected transducer. As an example, two electrodes were fabricated here using both POT and f-MWCNTs as transducers (see experimental section for details). Both electrodes were comparable in terms of slope, limit of detection, response time and linear range. However, a simple stability experiment over one hour revealed important fluctuations of the recorded potential for the POT electrode, while the response of the f-MWCNTs electrode remained stable (Figure 4a).
Figure 3. Calibration curves for nitrate, nitrite and dihydrogen phosphate. 1 mM sodium chloride as background for nitrate and nitrite detection. 10 mM MES buffer (pH 4.5) + 1 mM sodium chloride as background for dihydrogen phosphate detection.

Furthermore, large potential variations were observed for the POT electrode upon changes in light illumination. Figure 4b illustrates the natural day/night cycle by intermittent LED illumination (20 W). While the f-MWCNTs electrode did not exhibit any significant change in the potentiometric signal the POT electrode showed a substantial dependence on light exposure typical of photoresponsive semiconductor materials. It is important to underline the importance of light-insensitive transducers to applied research.\textsuperscript{51}

Medium-term stability was evaluated for f-MWCNT based carbonate-selective membranes over 24-h, resulting in a drift of just 40 µV.h\textsuperscript{-1}(see, Figure S2). To ensure the reversibility of the sensor, the concentration of carbonate was alternately varied from 1 mM to 0.1mM (Figure S3). As continuous carbon dioxide dissolution into the solution produces a carbonate concentration increase, the solution was degassed with nitrogen.

The accumulation of water at the inner interface (metal/transducer) and its consequence on the potentiometric signal has been explored in-depth in the literature.\textsuperscript{52,53} Water may originate from impurities of the solvent used to cast the membrane and, inevitably, by partitioning of water from the sample solution in contact with the membrane.\textsuperscript{54,55}

Lipophilic compounds such as carbon nanotubes should ideally repel the formation of an undesired water layer between the electrode and the ion-transducing layer. The water layer test according to Sutter et al.\textsuperscript{52} was performed and is shown in Figure S4. The f-MWCNT electrode did not exhibit a significant drift toward both the primary analyte and the interfering ion, indicating the absence of a water layer. In addition, this result suggests a suitable functioning of the transducer, which is in contrast to a bare coated wire electrode behavior.
Figure 4. Comparison between POT and f-MWCNTs transducers. a) Potentiometric medium term stability in a solution containing 0.1 mM Na$_2$CO$_3$ + 0.1M Tris-H$_2$SO$_4$ buffer (pH=8.6). b) Light test using a 20-W valve placed at 50 cm far from the potentiometric cell. The valve was turning on/off in order to mimic real day/night conditions (D=dark, L=light). Note that the commercial reference electrode was covered with an aluminum foil during this experiment.

The chemical nature of the transducer might have an undesired effect on the recognition event (ionophore-primary analyte) and consequently on the selectivity of the membrane. The presence of potentially interfering ions in the membrane, which are commonly used as counter ions or doped ions, (i.e., perchlorate, chloride, polystyrene sulfonate, etc.) may deteriorate the selectivity properties of the membrane. In order to confirm that a layer of f-MWCNTs does not produce any negative effect, selectivity coefficients were determined using the separate solution method (SSM) (Figure S5). The obtained selectivity pattern corresponds to the one for an aqueous inner solution electrode. This indicates that the presence of MWCNTs, in contrast to other transducers, does not exhibit a harmful effect on sensor quality. No clear potentiometric response is observed for chloride and nitrate at 1 mM levels, and the logarithmic selectivity coefficients should be understood as minimal values. To our surprise, the selectivity coefficient for carbonate over hydroxide is highly unfavorable, with log K$_{CO_3,OH}$ = 5.3 ± 0.1, which was not reported in the original paper. Fortunately, at pH 8.6, this interference is reasonably suppressed.

The selectivity coefficients for electrodes selective for nitrate, nitrite and dihydrogen phosphate were calculated by the same methodology (SSM) and summarized in Table S2. As above, with some interfering ions such as chloride that did not exhibit a Nernstian response slope even at high concentrations (0.1 M), these values should be considered minimum values. Beyond the poor selectivity coefficients over perchlorate and thiocyanate, the values were not significantly
different with respect to the ones reported for a similar membrane composition but with an inner liquid configuration.\textsuperscript{45,49} This indicates that the selectivity of the studied electrodes is a function of the membrane composition rather than the nature of the inner transducing element.

The transduction mechanism of carboxylated carbon nanotubes (CNT-COOH, 20% functionalization) was characterized by non-faradaic electrochemical impedance spectroscopy (in the absence of a redox couple in solution).\textsuperscript{37} The information extracted from the Nyquist spectrum indicates a purely capacitive mechanism that in principle is not modulated by oxygen levels in solution.\textsuperscript{37} Accordingly, the inner potential (glassy carbon/CNTs/membrane) is held to a defined value and added to the outer potential (membrane/solution).

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{figure5.png}
\caption{Electrochemical impedance spectroscopy (EIS) measurements for f-MWCNTs and n-MWCNTs in 0.1M KCl.}
\end{figure}

Figure 5 shows a Nyquist plot of f-MWCNTs electrode (~200 μm thickness) in contact with a 0.1M KCl solution. As expected, the impedance spectrum follows the behavior of a capacitor with a straight and vertical line centered on the real resistance (sum of all resistances in the electrochemical cell). Having confirmed this effect with this type of functionalized MWCNTs, the double layer capacitance is estimated with the data acquired at the lowest frequency (0.1-Hz) as ~1-mF. In another experiment, a membrane containing non-functionalized carbon nanotubes was also measured by electrochemical impedance. Here, the Nyquist plot exhibits a diffusion contribution (non-pronounced vertical line) that is essentially attributed to the inhomogeneous carbon nanotube film. This aspect related to the quality of the film formation is overcome by preparing a solution (f-MWCNTs) instead of a dispersion (n-MWCNTs) of carbon nanotubes in THF. In addition, the capacitance of f-MWCNTs is increased by factor of
three compared to n-MWCNTs, suggesting that an f-MWCNT layer is a more suitable transducer (bare glassy carbon ~1μF, Figure S6).

In view of performing in-situ measurements, a sample from the river Arve (pH, 8.2) was utilized as natural matrix for measuring carbonate. Both external calibration and external additions were carried out, obtaining 12.1 ± 0.2 µM and 12.3 ± 0.2 µM respectively. Evidently, the amount of chloride in the Arve sample (0.2 mM) bears no influence on the quantification of carbonate. A non-significant difference (12.5 ± 0.1 µM) was observed with the reference method (automatic titrator with pH potentiometric detection, Figure S7).

2.4 Conclusions

We demonstrated here that lipophilic multi-walled carbon nanotubes (f-MWCNTs) efficiently work as an ion-to-electron transducer for anion ionophore-based membrane electrode. A similar purely capacitive mechanism reported earlier for SWCNTs-COOH (20% functionalization) is reasoned from the electrochemical impedance measurements (EIS) providing a double layer capacitance of about 1-mF (one thousand times greater than bare glassy carbon). As a consequence of the high capacitance at the electrode interface, insignificant variation of the electromotive force over time is observed. This all-solid-state electrode exhibits similar analytical performances (LOD, sensitivity, selectivity coefficients, medium-term stability, etc.) as systems with classical inner liquid solution. Many important advantages, including their insensitivity to pressure and light, mechanical and chemical robustness, and the possibility of vertical or horizontal orientation, makes them a promising platform for the determination of nitrate, nitrite, dihydrogen phosphate, and carbonate in-situ.

2.5 Supporting information

2.5.1 Experimental

2.5.1.1 Materials, reagents and samples

Muti-walled carbon nanotubes (MWCNT) were purchased from HeJi, Inc (0.5-200 μm length and 30-50 nm diameter, M4905). Thionyl chloride (SOCl₂), octadecylamine (ODA), bis(2-ethylhexyl) sebacate (DOS), sulphuric acid (97%), nitric acid (65%), Poly(vinyl-chloride) (PVC, high molecular weight), bis(2-ethylhexyl) adipate (DOA), N,N-dioctyl-3α,12α-bis(4-trifluoroacetylbenzoyloxy)-5β-cholan-24-amide (carbonate ionophore VII), nitrite ionophore (IV), TDMAN (tridodecylmethylammonium nitrate) POT tridodecylmethylammonium
chloride (TDMACl), tetradecylammonium chloride (TDDA) 2-amino-2-hydroxymethyl-propane-1,3-diol (Tris), 1-morpholinoethanesulfonic acid (MES), Poly(3-octylthiophene-2,5-diyl) regioregular (electronic grade, 99.995% trace metals basis, average Mn ~25,000) tetrahydrofuran (THF), hydrochloric acid solution (1M), sodium hydroxide solution (2M), sodium chloride and sodium nitrate were purchased from Sigma-Aldrich (analytical grade). Synthesis of uranyl salophene III (with t-butyl substituents) as an ionophore for dihydrogen phosphate was performed by according to Wroblewski et al. An environmental sample was obtained from the Arve river (Geneva, Switzerland) and sealed immediately in a plastic container for analysis.

2.5.1.2 Synthesis of lipophilic multi-walled-carbon nanotubes

1 g of MWCNTs were refluxed (100 °C) in H₂SO₄/HNO₃ (3:1) for 1h. The MWCNTs were then filtered on a Millipore membrane (Polycarbonate PC, 0.10μm), washed with Milli-Q water and dried fully in an oven (60 °C). The resultant MWCNT-COOH was mixed with 20 ml of thionyl chloride and 1 ml of dimethylformamide, the mixture was stirred and refluxed at 70 °C overnight. After finishing the reaction, the solvent was evaporated by a rotary evaporation to remove the residual solvents. Finally, 1g of excess ODA was added and the mixture was heated at 100°C for 96 h. After cooling to room temperature, the excess ODA was removed by sonication and washing with ethanol for five times. The solid was filtered on a mentioned Millipore membrane and washed with ethanol to remove remnant octadecylamine. The resultant carbon nanotubes were then dried and stored for the final application.

2.5.1.3 ISE membranes and electrodes

A mixture of ionophore, ion exchanger, plasticizer and PVC were used to prepare the cocktail for each ion-selective electrode. (i) 8.3 mg carbonate ionophore VII, 2 mg TDMAC, 60 mg PVC and 100 μL DOA were dissolved in 2mL THF solvent for carbonate detection. (ii) 2 mg uranyl salophene III, 0.4 mg TDDA, 32.2 mg PVC and 64.3 mg o-NPOE were dissolved in 1 mL THF solvent for dihydrogen phosphate detection. (iii) 6.0 mg TDMAN, 31.3 mg PVC and 62.6 mg o-NPOE were dissolved in 1 mL THF solvent for nitrate detection. (iv) 1.1 mg nitrite ionophore (IV), 0.3 mg TDMAC, 32.5 mg PVC and 65.4 mg DOS were dissolved in 1 mL THF solvent for nitrite detection. 150 μL of each cocktail (3×50 μL) was pipetted and drop cast on either the bare glassy carbon electrode or the f-MWCNTs or POT electrodes. The carbonate, dihydrogen phosphate, nitrate and nitrite electrodes were conditioned in 1mM
Na$_2$CO$_3$, 10 mM sodium chloride, 1mM sodium nitrate and 1 mM sodium nitrite, respectively, in order to allow for quantitative ion replacement during a period of 24 h.

### 2.5.1.4 Electrochemical equipment

A Metrohm 827 pH meter (Metrohm Autolab, Utrecht, The Netherlands) was used to prepare the buffer and measure the pH during the experiment. A double-junction Ag/AgCl/3 M KCl/1 M LiOAc reference electrode was used in potentiometric measurements (Model 6.0726.100, Metrohm AG, Ionenstrasse, Switzerland). Glassy carbon electrode contained a GC-electrode-tip (6.1204.300) with a diameter of 3.00 ± 0.05 mm and was sourced from Metrohm (Switzerland). A platinum-working rod (3.2 cm$^2$ surface area) was used as a counter electrode for EIS measurements. Electrode bodies (Oesch Sensor Technology, Sargans, Switzerland) were used to mount the polymeric membranes. Potentiometric measurements were determined by zero current potentiometry employing a high impedance input 16-channel EMF monitor (Lawson Laboratories, Inc., Malvern, PA). The titration was performed with a 765-automatic Dosimat (Metrohm Autolab, Utrecht). The GC/f-MWCNTs electrodes, immersed in aqueous 0.1 M KCl were studied by EIS (Autolab PGSTAT101 Metrohm Autolab, Utrecht, The Netherlands) at open circuit potential. The impedance spectra were recorded in the frequency range of 100 kHz to 10 mHz, which is sufficiently wide to cover the processes of interest, by using a sinusoidal excitation signal (single sine) with an excitation amplitude ($\Delta E_{ac}$) of 10 mV.

### 2.5.1.5 Protocols

All calibrations were performed in 0.1M Tris-H$_2$SO$_4$ buffer at pH 8.6 unless otherwise specified. The titration was performed with an automatic titrator as a reference method to validate the methodology. For this purpose, 10 mL of Arve river sample was pipetted into the titration recipient followed by adding 10 mL of 0.1M NaOH. About 30 mL of Millipore water was added into the same beaker and the pH electrode was placed into the sample. The titration was controlled and monitored automatically by a titrator program. Each titration required 30 min to finish and a titration curve with two endpoints was obtained. The carbonate concentration was calculated by subtracting the volume for the two separate endpoints.
2.5.2 Supporting figures

![Graphs showing potentiometric time traces for nitrate, dihydrogen phosphate, and nitrite, respectively, with the three respective ion-selective electrodes. The logarithmic concentrations are indicated above each trace.](image)

**Figure S1.** Potentiometric time trace for nitrate, dihydrogen phosphate, and nitrite, respectively, with the three respective ion-selective electrodes. The logarithmic concentrations are indicated above each trace.
Figure S2. Medium-term stability. Top: coated wire electrode (CWE). Bottom: f-MWCNTs electrode. The experiments were performed in 0.1 mM Na$_2$CO$_3$ + 0.1M Tris-H$_2$SO$_4$ buffer (pH=8.6). The solutions were continuously degassed with nitrogen during the experiment.

Figure S3. Reversibility of the carbonate solid contact electrode at two concentration levels (1 mM and 0.1mM Na$_2$CO$_3$ in 0.1M Tris-H$_2$SO$_4$ buffer (pH=8.6)), for a) solutions that were not degassed and b) solutions degassed with nitrogen.
Figure S4. Water layer test. Top: GC/ISM. Bottom: GC/f-MWCNTs/ISM. Potentiometric responses were recorded in 10 mM Na₂CO₃ or 1 mM NaCl in a 0.1M Tris–H₂SO₄ buffer. During the experiment the solutions were continuously purged with nitrogen.

Figure S5. Selectivity determination for chloride, nitrate, hydroxide and carbonate for the carbonate-selective electrode.
Figure S6. Electrochemical impedance spectroscopy for a bare glassy carbon at the same operational conditions described in the experimental section.
Figure S7. Automatic titration and potentiometric response of the sample with carbonate-selective electrode: a) Arve river sample titration curve using 0.1 M HCl as titrant. Before titration, 10 mL of 0.1M NaOH and 30 mL purified water was added to a 10 mL sample. b) First-order derivative of the titration curve. c) Short time potentiometric response of the sample after calibration of the solid electrode.
### 2.5.3 Tables

**Table S1.** Lower detection limit (LDL), higher detection limit (HDL) and response time for anion selective electrodes.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>log LDL</th>
<th>log HDL</th>
<th>Response time(s)</th>
</tr>
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<tr>
<td>NO$_3^-$</td>
<td>-5.6</td>
<td>-1</td>
<td>5</td>
</tr>
<tr>
<td>NO$_2^-$</td>
<td>-6</td>
<td>-1</td>
<td>5</td>
</tr>
<tr>
<td>H$_2$PO$_4^-$</td>
<td>-5</td>
<td>-1</td>
<td>10</td>
</tr>
</tbody>
</table>

**Table S2.** Experimental selectivity coefficients for anion-selective electrodes by using SSM method

<table>
<thead>
<tr>
<th>Analyte</th>
<th>log $K_{ij}^{\text{pot}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO$_3^-$</td>
</tr>
<tr>
<td>NO$_3^-$</td>
<td>-</td>
</tr>
<tr>
<td>NO$_2^-$</td>
<td>0.7</td>
</tr>
<tr>
<td>H$_2$PO$_4^-$</td>
<td>-1.4*</td>
</tr>
</tbody>
</table>

*No clear potentiometric response is observed for interference ion at 1 mM levels, and the logarithmic selectivity coefficients should be understood as minimum values.
2.6 References


Chapter 3 Voltammetric Thin Layer Ionophore Based Films: Part 1. Experimental Evidence and Numerical Simulations

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Abstract

Voltammetric thin layer (~200 nm) ionophore-based polymeric films with defined ion-exchange capacity have recently emerged as a promising approach to acquire multi-ion information about the sample, in analogy to performing multiple potentiometric measurements with individual membranes. They behave under two different regimes that depend on the ion concentration. A thin layer control (no mass transport limitation of the polymer film or solution) is identified for ion concentrations of > 10 µM, in which case the peak potential serves as the readout signal in analogy to a potentiometric sensor. On the other hand, ion transfer at lower concentrations is chiefly controlled by diffusional mass transport from the solution to the sensing film, resulting in an increase of peak current with ion concentration. This concentration range is suitable for electrochemical ion transfer stripping analysis. The transition between the two mentioned scenarios is here explored experimentally, using a silver selective membrane as a highly selective proof-of-concept under different conditions (variation of ion concentration in the sample from 0.1 µM to 1 mM, scan rate from 25 to 200 mV s⁻¹, and angular frequency from 100 rpm to 6400 rpm). Apart from experimental evidence, a numerical simulation is developed that considers an idealized conducting polymer behavior and permits one to predict experimental behavior under diffusion or thin layer control.
3.1 Introduction

Today, ionophore-based membranes of a few hundred micrometer thickness (150-200 µm) are well established as the recognition element in potentiometric ion-selective sensors.1 Typically, the polymeric membrane is placed between two solutions (inner filling solution and sample) and the potential difference across the membrane is measured with a high input impedance potentiometer.2 By adjusting the experimental conditions in such a manner that the concentration of the inner solution remains constant during the experiment, the readout signal becomes proportional to the logarithmic sample activity. The necessity of using membranes of a few hundred micrometers has been a consequence of various fundamental and practical aspects,1,3-5 such as: (i) the reduction of the trans-membrane flux (from inner solution to sample phase) that negatively influences the lower limit of detection; (ii) decreasing the contamination of the inner interface by slowing the diffusion through the polymeric membrane (~12 h); (iii) minimization of the effect of the leaching out of membrane plasticizer and other components (giving a larger reservoir for thicker membranes); (iv) enhancement of the mechanical membrane robustness, in order to prevent its rupture during both the mounting process and experiments; (v) avoidance of mechanical bending in the membrane, as a result of variable pressure in both compartments.

Although the latter aspects would seem insignificant today, they have been a bottleneck in the miniaturization progress. With the arrival of solid contact transducers (mainly conducting polymers in the early nineties6,7 and nanostructured materials in the past decade8-10), the elimination of the inner liquid solution became feasible, and thereby most above-mentioned fundamental and technical issues were gradually addressed.11 Thinner membranes (a few tens of micrometers) were much easier to fabricate,12 enabling scientist to develop new analytical methodologies, such as voltammetry thin layer ionophore-based membranes.

In this direction, Amemiya and coworkers have established the use of “polarized membranes”, ~3 µm thick, backside contacted with conducting polymers such as Poly(3-octylthiophene) POT and PEDOT. The term “polarized membranes” has been introduced elsewhere13 to describe a membrane that can be polarized upon applying a potential. In order to prepare such membranes, a lipophilic electrolyte (ETH500 or TDDATFAB) is dissolved in a plasticizer solvent, together with the ionophore of interest. At a certain applied potential, the membrane is filled with the analyte, triggered by the oxidization or reduction of the conducting polymer. This principle is, in some way, analogous to that of the established thin mercury film electrode: an accumulation period of a few minutes for the preconcentration of analyte onto the electrode material under convective sample control is followed by anodic stripping voltammetry. With “polarized
membranes”, however, there is no oxidation-reduction reaction of the analyte itself involved, significantly broadening the range of potential species that can be detected. This elegant approach was found to significantly lower the limit of detection with respect to traditional potentiometry measurements.\textsuperscript{14,15} A selective extraction of a range of compounds (heparin,\textsuperscript{16} tetrapropylammonium,\textsuperscript{17} ammonium,\textsuperscript{18} potassium,\textsuperscript{18} perchlorate,\textsuperscript{19} fluoxetine, citalopram and sertraline\textsuperscript{20}) was carried out, as a result of coupling the redox properties of the conducting polymer to the ion-extraction membrane properties.

Later, preliminary experiments using even thinner membranes (~340 nm) doped with an excess of cation exchanger, with respect to anion exchanger (initially non-polarized membranes\textsuperscript{13}) were reported by Bakker and coworkers.\textsuperscript{21} Cyclic voltammetry was employed as readout, resulting in well-defined Gaussian-shaped ion-transfer peaks for both forward and backward scans. These experiments suggested that the oxidation/reduction of the conducting polymer might be understood as a confined surface process coupled to the ion-transfer at the membrane/sample interface under the thin layer assumption (no diffusion in the membrane phase). Other electroactive species such as 7,7,8,8-tetracyanoquinodimethane (TCNQ) or tetrathialfulvalene (TTF)\textsuperscript{22,23} were also used to modulate the ion-transfer process in a similar manner as the conducting polymers discussed above.

More recently and building on previous work by Bakker,\textsuperscript{21} a thin membrane (230±10 nm) containing active components similar to that of traditional potentiometric membrane electrodes (\(\sim 15\text{mmol/kg}\) cation exchanger and \(\sim 5\text{mmol/kg}\) ionophores) was examined via cyclic voltammetry at different concentrations of lithium and calcium.\textsuperscript{24} A gradual increase of calcium concentration (above 10 \(\mu\text{M}\)) in the solution provoked a shift of the ion transfer peak position to higher potentials, thereby obeying the Nernst equation for both monovalent and divalent cations. A model based on equilibrium assumptions was developed to explain the Nernstian displacement.\textsuperscript{24} A very similar model was further developed to predict the multianalyte response of a membrane containing two ionophores\textsuperscript{24,25} and later modified to correlate the shape of the voltammetric peak with different stoichiometries between analyte and ionophore.\textsuperscript{26,27} Nonetheless, changes in peak current below 10 \(\mu\text{M}\) could not be predicted using equilibrium assumptions.\textsuperscript{24}

Having introduced the two recent contributions to the field of ionophore-based membrane thin layer voltammetry, the main differences between the two directions by Amemiya\textsuperscript{19} and Bakker\textsuperscript{21} are: (i) the composition of the membrane, resulting in polarized and initially non-polarized membranes; (ii) the thickness of the membrane, ranging from 2-3 \(\mu\text{m}\)\textsuperscript{19} to 230-300 nm\textsuperscript{21}; (iii) the establishment of different electrochemical regimes, either limited by mass
transport (at low concentration of analyte) or under thin layer control (at moderate and high concentrations); (iv) the electrochemical protocol and readout signal: stripping voltammetry (peak current) or cyclic voltammetry (potential wave).

The use of different salts, either ion-exchangers or lipophilic electrolytes, dictated the doping of the conducting polymers and, consequently, the nature of the ion-transfer. In the case of POT, the addition of lipophilic cation exchanger renders the membrane initially permselective, containing the cation of interest.\textsuperscript{24,25} In contrast, the addition of a lipophilic electrolyte results in a membrane void of the ion of interest, requiring electrochemical perturbation for extraction. An alternative to the detection of cations was the replacement of POT by other conducting polymers (for example, oxidized PEDOT\textsuperscript{+} doped with lipophilic anions such as TFAB\textsuperscript{−} with a membrane containing lipophilic electrolyte)\textsuperscript{18,28} Here, the amount of cation extracted into the membrane should be equal to the amount of the anionic dopant in the PEDOT, which might be more difficult to control, compared to a simple addition of cation exchanger salt.\textsuperscript{24,25} Finally, the POT approach with cation-exchange membranes provides well-defined voltammetric peaks without applying background correction, even in blood and serum samples\textsuperscript{29} (absence of capacitive or residual current), which unfortunately does not appear to be the case for the PEDOT approach with lipophilic electrolytes.\textsuperscript{27} This may be problematic in challenging analytical applications.\textsuperscript{27}

Focused on the promising behavior of POT overlaid with cation-exchanger membranes, we report here on a model system based on the detection of silver by using a voltammetric thin layer film doped with cation exchanger and ionophore (with a formation constant of $\beta_{Ag}$, $L \sim 10^{12}$).\textsuperscript{30} This work aims to identify trends at low, medium and high solution concentrations, exploring the transition from diffusional mass transport control to thin layer behavior in ion transfer through thin film membranes backside contacted with a thin film of redox species (such as POT). An extended model considering the diffusional mass transport at the sample solution interface is shown here. This permits one to predict the voltammetric current and peak position in a wide concentration range of the analyte ion. Enhancement of mass transport by using rotating disk electrodes and normal stirring conditions were also used to test the model.

3.2 Experimental section

3.2.1 Reagents, materials and equipment.

Aqueous solutions were prepared by dissolving the appropriate salts in deionized water (>18 MΩ cm). Lithium perchlorate (>98%, LiClO\textsubscript{4}), 3-octylthiophene (97%, OT), silver nitrate (AgNO\textsubscript{3}), sodium nitrate (NaNO\textsubscript{3}), high molecular weight poly(vinyl chloride) (PVC), bis(2-
ethylhexyl)sebacate (DOS), sodium tetrakis[3,5-bis-(trifluoromethyl)phenyl]borate (NaTFPB), silver ionophore IV, acetonitrile (ACN) and tetrahydrofuran (>99.9 %, THF) were purchased from Sigma Aldrich.

GC-electrode tips (6.1204.300) with an electrode diameter of 3.00 ± 0.05 mm were sourced from Metrohm (Switzerland). Cyclic voltammograms were recorded with a PGSTAT 101 (Metrohm Autolab B.V., Utrecht, The Netherlands) controlled by Nova 1.11 software (supplied by Autolab) running on a PC. A double-junction Ag/ AgCl/3M KCl/1 M LiOAc reference electrode (6.0726.100 model, Metrohm, Switzerland) and a platinum electrode (6.0331.010 model, Metrohm, Switzerland) were used in the three-electrode cell. A rotating disk electrode (Autolab RDE, Metrohm Autolab B.V., Utrecht, The Netherlands) was used to spin coat the membranes on the electrodes at 1500 rpm as well as for the experiments with different rotating speeds.

Wolfram Mathematica® 9 software was used for the theoretical simulations.

3.2.2 Preparation of the electrodes.

Poly(3-octylthiophene) (POT) was electrochemically polymerized on GC surface by cyclic voltammetry (two scans, 0-1.5 V, 100 mV s⁻¹) and then discharged at 0 V for 120 s. A solution containing 0.1 M 3-octylthiophene and 0.1 M LiClO₄ in acetonitrile was used. This solution was purged with N₂ for 30 min before use. After the electropolymerization of POT, the electrode was immersed in pure acetonitrile for 30 min, to remove the electrolyte, and dried at room temperature for 15 min. Thereafter, a volume of 25 µL of diluted membrane cocktail (50 µL of the membrane cocktail + 150 µL of THF) was spin coated on the POT-based electrode. The composition of the silver-selective membrane cocktail was 30 wt.% of PVC, 60 wt.% of DOS, 40 mmol kg⁻¹ of NaTFPB and 80 mmol kg⁻¹ of silver ionophore IV. Conditioning of the membrane was not deemed necessary (estimated equilibration time of ~ 20 ms, using a film thickness of 200 nm and diffusion coefficient of 10⁻⁸ cm² s⁻¹).³¹
Figure 1. Scheme of the ion transfer processes that occur through a thin sensing film backside contacted with POT at different silver concentrations: (a) absence of silver, (b) low silver concentration and (c) high silver concentration. A fixed background of sodium concentration is considered. GCE is the glassy carbon electrode, POT/POT\(^+\) the conducting polymer, R\(^-\) the cation exchanger, \(Na^{\text{i}}\) the current for the sodium peak, \(Ag^{\text{i}}\) the current for the silver peak, I and II are the interfaces for the GCE/POT and membrane/aqueous solution (aq) respectively, \(\delta_{\text{POT}}\) and \(\delta_{\text{m}}\) are the thicknesses for the POT and membrane films and \(dx\) illustrates the finite elements in the solution domain (\(x\)). The ligand (L) was omitted to simplify the scheme.

3.3 Theory

The electrochemical system was described using two interfaces (see Figure 1a). The first one (I) corresponds to the interface between the conducting polymer (CP/CP\(^+\)) and the glassy carbon electrode (GCE). The second interface (II) is established between the same membrane (doped with cation exchanger and silver ionophore) and the sample solution with a variable amount (\(xM\)) of silver nitrate (AgNO\(_3\)). The electrochemical half-cell is written as follows:

\[
GCE|CP,CP^+|Na^{\text{i}}R^-,L(xM)Ag^{\text{i}}NO_3^-\] (1)

The first interface (I) is considered a fast process limited by electron transfer and not by the incorporation of the lipophilic anion (R\(^-\)) in the lattice of the conducting polymer. In other words, the lipophilic anion is assumed to be sufficiently available and in excess to fulfill the charge balance condition at this interface. The potential at this interface is therefore assumed to be at thermodynamic equilibrium, and the Nernst equation with half-electron transfer was used (eq 2).\(^{32}\)
\[ E_1 = \Delta \phi_1^0 + \frac{RT}{n_{CP}F} \ln \left( \frac{c_{CP^+}}{c_{CP}} \right) \]  \hspace{1cm} (2)

Mass balance for CP concentration also holds:

\[ c_{CP} = c_{CP^-} + c_{CP^+} \]  \hspace{1cm} (3)

Where, \( c_{CP^-} \) corresponds to the total concentration of the conducting polymer; \( c_{CP^+} \) is the concentration of the oxidized form and \( c_{CP^-} \) is the concentration of the reduced form; \( E_1 \) is the potential difference at the first interface with a standard redox potential (\( \Delta \phi_1^0 \)); \( n_{CP} \) is the average number of electrons transferred at the electrode surface for oxidation or reduction of a conducting polymer couple (CP/CP\(^+\)); \( R \) is the gas constant; \( T \) is the absolute temperature, and \( F \) the faraday constant.

Inserting eq 3 into eq 2, one obtains:

\[ E_1 = \Delta \phi_1^0 + \frac{RT}{n_{CP}F} \ln \left( \frac{c_{CP^-}}{c_{CP} - c_{CP^+}} \right) \]  \hspace{1cm} (4)

At the second interface (II), it is assumed that only Na\(^+\) or Ag\(^+\) may be transferred across the phase boundary. This interface was also treated with a Nernst type equation for silver and sodium (eq 5), because of the fact that ion transfer is generally considered a fast process that quickly reaches equilibrium (exceptions exist\(^{33}\)). \( \Delta \phi_{Na^+}^{0,aq\rightarrow m} \) and \( \Delta \phi_{Ag^+}^{0,aq\rightarrow m} \) are the respective standard ion transfer potentials for sodium and silver. Superscripts “\( m \)” and “\( aq \)” denote the sensing film (membrane) and aqueous phase, respectively. Silver and sodium concentration in the membrane (\( c_{Na^+}^m, c_{Ag^+}^m \)) and aqueous solution (\( c_{Na^+}^{aq}, c_{Ag^+}^{aq} \), strictly ion activities) were thus written in terms of the Nernstian relationship and equal to the potential at the second interface (\( E_2 \)) to give eq 5.

\[ E_2 = \Delta \phi_{Na^+}^{0,aq\rightarrow m} + \frac{RT}{n_{Na^+}F} \ln \left( \frac{c_{Na^+}^{aq}}{c_{Na^+}^m} \right) = \Delta \phi_{Ag^+}^{0,aq\rightarrow m} + \frac{RT}{n_{Ag^+}F} \ln \left( \frac{c_{Ag^+}^{aq}}{c_{Ag^+}^m} \right) \]  \hspace{1cm} (5)

As the applied potential (\( E_{app} \)) is distributed over both interfaces (I and II), the applied potential is expressed as a sum of both interfacial potentials neglecting the iR drop across the membrane\(^{17}\) (eq 6).

\[ E_{app} = \Delta \phi_1^0 + \frac{RT}{n_{CP}F} \ln \left( \frac{c_{CP^+}}{c_{CP} - c_{CP^+}} \right) + \Delta \phi_{Na^+}^{0,aq\rightarrow m} + \frac{RT}{n_{Ag^+}F} \ln \left( \frac{c_{Ag^+}^{aq}}{c_{Ag^+}^m} \right) \]  \hspace{1cm} (6)
In cyclic voltammetry, the applied potential is described with a triangular function, so eqs 5 and 6 are rewritten in the time domain as

\[ E_2(t) = \Delta \phi_{Na}^{aq-m} + \frac{RT}{n_{Na}} \ln \frac{c_{Na}^{aq}(t)}{c_{Na}^{m}} = \Delta \phi_{Ag}^{0,aq-m} + \frac{RT}{n_{Ag}^{+}} \ln \frac{c_{Ag}^{aq}(t)}{c_{Ag}^{m}} \] (7)

\[ E_{app}(t) = \Delta \phi_{1}^{0} + \frac{RT}{n_{CP}} \ln \frac{c_{CP}^{m}(t)}{c_{CP}^{m}} + \Delta \phi_{Ag}^{0,aq-m} + \frac{RT}{n_{Ag}^{+}} \ln \frac{c_{Ag}^{aq}(t)}{c_{Ag}^{m}} \] (8)

Where \( c_{Na}^{aq} \) is treated as a constant because of high background electrolyte concentration (NaNO\(_3\)).

The electroneutrality condition in the membrane phase and CP film (with area (A), membrane thickness (\( \delta_{m} \)), CP film thickness (\( \delta_{CP} \)), concentration of lipophilic anions (\( c_{R-} \)) must be fulfilled. The charge balance condition is then written as:

\[ c_{R-} \delta_{m} A = n_{CP} c_{CP}^{m}(t) \delta_{CP} A + n_{Na} c_{Na}^{aq}(t) \delta_{m} A = n_{Ag} c_{Ag}^{aq}(t) \delta_{m} A \] (9)

It is also considered that the aqueous solution is infinitively larger than the thin membrane layer. Therefore, the aqueous solution is approximated by a one-dimension space-time grid (\( x, t \)) whereas the electrolyte concentration is considered uniform inside the membrane (so-called “thin layer approximation”). A finite element method which takes equal space and time element distance(dx, dt) will be later introduced to discretize the aqueous and membrane silver concentration. The rate of the loss of silver from the membrane phase (\( m \)) (right term, eq 10) must be equal to the rate of the gain of silver (left term, eq 10) in the entire aqueous solution (right term, eq 10). This equation can be understood as a silver mass balance for the whole system, where \( c_{Ag}^{aq}(x,t) \) is the concentration of silver in the aqueous solution at position x and time t.

\[ A \int_{0}^{\infty} \frac{\partial c_{Ag}^{aq}(x,t)}{\partial t} dx = -A \delta_{m} \frac{\partial c_{Ag}^{m}(t)}{\partial t} \] (10)

A continuity equation (eq 11) is used to propagate the concentration changes to the subsequent time step and include the silver diffusion coefficient:

\[ \frac{\partial c_{Ag}^{aq}(x,t)}{\partial t} = D_{Ag}^{aq} \frac{\partial^{2} c_{Ag}^{aq}(x,t)}{\partial x^{2}} \] (11)

Inserting eq 11 in eq10, a useful relationship, valid for all t and x, is obtained:
With the boundary conditions:

\[ c_{Ag^+}^{aq}(x,0) = c_{Ag^+}^- \]  

(13)

\[ c_{Ag^+}^{aq}(\infty,t) = c_{Ag^+}^- \]  

(14)

Where \( c_{Ag^+}^- \) is the bulk silver concentration in the aqueous phase.

The \( c_{CP^-}(t) \) was calculated by solving eqs 7-9 and 10-12 with the finite difference method (see Supporting Information for more details about discretization). Finally, the current (\( i \)) is found by its proportionality to the rate of oxidized or reduced CP (see eq 15):

\[ i = n_{CP} F A \delta_{CP} \frac{\partial c_{CP^-}(t)}{\partial t} \]  

(15)

For experiments using rotating disk electrodes, the aqueous diffusion layer thickness \( \delta_{Ag^+}^{aq} \) was calculated according to the Levich equation,

\[ \delta_{Ag^+}^{aq} = 1.61 D_{Ag^+}^{eq} \frac{\omega^{1/3}}{v^{1/6}} \eta^{-1/2} \]  

(16)

where \( \omega \) is the angular velocity of the rotation electrode and \( \eta \) is the kinematic viscosity of the aqueous solution.\(^{34}\)

### 3.4 Results and discussion

Figure 1 schematically illustrates the model system employed here to allow one to predict the response for different experimental conditions for thin layer voltammetry ionophore-based membranes. A thin polymer film (\( \delta_m = 220 \pm 20 \text{ nm} \)) containing cation exchanger in sodium form (\( \text{Na}^+ \text{R}^- \)) and silver ionophore (\( \text{L} \)) (omitted in the scheme for simplification) was backside contacted with a thin poly(3-octylthiophene, POT) film (\( \delta_{POT} = 55 \pm 1 \text{ nm} \))\(^{35}\) electrosynthesized on a commercial glassy carbon electrode (GCE).

As described in the theory section, two interfaces (I and II) were considered. The first one (I) is related to the oxidation of the CP (\( i_{CP} \)) and the intrinsic charge compensation with the lipophilic anion (\( \text{R}^- \)) (Figure 1a, top). The second interface corresponds only to the ion transfer process between membrane and solution triggered by the oxidation of CP species at the first interface. As a result, an ion current is established across this interface (\( i_{Na^+} \)). In the case that only \( \text{Na}^+ \) is present in both the solution and the film (Figure 1a, bottom), one Gaussian-shaped
voltammetric peak attributed to sodium transfer is expected. Note that the current at the first interface is the same as the one at the second interface \((i_{CP} = i_{Na^+})\).

As the concentration of silver is gradually increased in the sample phase, sodium starts to be replaced by silver (ion exchanging at zero net current, as in potentiometry) before applying any potential, the membrane therefore initially contains both cations (with silver at a lesser amount) (Figure 1b, top). An anodic linear sweep potential (forward) results in two well-resolved peaks (red line). Because sodium is energetically less stabilized than silver in the membrane phase, owing to the presence of the silver receptor (L), then sodium is expelled first, followed by silver, thereby establishing a net current for both ions \((i_{Na^+}, i_{Ag^+})\). During the cathodic potential (backward) sweep, the membrane is initially devoid of \(Na^+\) and \(Ag^+\) ions, silver is the first ion taken up (as it is most preferred, since a molecular receptor is present) and then sodium.

In this particular case, when the concentration of silver is significantly lower than that of sodium in the sample phase, the overall process is limited by diffusional mass transport of silver in solution. This suggests that a gradual increase of silver concentration in solution may result in an enlargement of the silver peak current, accompanied by a diminishment of the sodium signal (see green line, Figure 1b, bottom). Presumably, this effect should be more pronounced as mass transport in the solution becomes more effective (see rotating disk electrode experiments and scan rate variations below). The aforementioned theory considers diffusional aspects in the sample phase that was not considered before and, for first time, these types of voltammograms can be rationalized and predicted.

Upon increasing the concentration of silver in solution further, only the silver peak remains (Figure 1c, top/bottom). Under such conditions, the current model converges to the previous one\(^\text{24}\), in which the concentration of the primary ion at the membrane/sample interface is considered invariable during the experiment.

Figure 2a shows experimental cyclic voltammograms for increasing silver concentration (up to 50 µM, top blue curve in the silver wave at 825 mV) in 10 mM \(NaNO_3\) background electrolyte. In the absence of silver in solution (red curve), only the sodium ion-transfer peak is observed at 333 mV, with an integrated charge of 3.15 µC. As the concentration of silver is increased from 0.1 µM to 50 µM (indicated in Figure 2a), a silver transfer peak appears at 825 mV that rises gradually, eventually yielding a constant current of 1.05 µA (dark blue and purple curves in Figure 2a).
Figure 2. (a) Experimental voltammograms for increasing silver concentrations (0, \(10^{-8}\), \(10^{-7}\), \(10^{-6}\), \(2.5\times10^{-6}\), \(5\times10^{-6}\), \(10^{-5}\), \(2.5\times10^{-5}\) and \(5\times10^{-5}\) M). 10 mM NaNO\(_3\) background electrolyte. Scan rate: 100 mV s\(^{-1}\). (b) Calculated voltammograms for the same concentrations used in experimental curves shown in (a).

The increase in the Ag peak height is linked to a proportional decrease in the Na peak, noting that the same initial charge (3.15 µC in the absence of silver) is now distributed between two peaks (e.g., for 2.5 µM silver in 10 mM NaNO\(_3\), the integrated charge was 0.764 µC and 2.359 µC for silver and sodium, respectively; see Table S1 in the supporting information). Furthermore, a linear relationship between Na and Ag current peaks, as a function of silver concentration in the solution, is obtained in the range of 1-10 µM silver concentration (Figure 3a). In this concentration region, the sensor can presumably be used for the stripping voltammetric detection of silver.

Figure 2b presents the calculated cyclic voltammograms under the same experimental conditions as Figure 2a. The qualitative correspondence between the simulated and experimental curves suggest that the proposed approach is generally appropriate to describe the voltammetry thin layer ionophore-based membranes. Specifically, the calculated cyclic voltammograms consistently reproduced the experiments in terms of current levels (described with eq 15), potential (described with eq 7 and eq 8, using the reported formation constant for
silver/ionophore (IV) complexes,\textsuperscript{30} resulting in standard ion-transfer potential of $\Delta \phi^{0,\text{Ag}^+}\rightarrow\text{m} \approx -0.8$ V) and the symmetric/asymmetric Gaussian shapes of the peaks (including the mixed potential response for sodium silver binary samples).

Despite the above-mentioned similarities between experimental and calculated voltammograms (that partly corroborate the usefulness of the model), the actual peak shapes are broader for the experimental data, which unfortunately cannot be modeled without a significant increase of complexity. While beyond the scope of this work, the CP oxidation treatment and the non-capacitive assumption may likely be improved. The use of the Nernst equation for describing POT electron transfer is the simplest approximation so far, although the assumption of one electron transfer for POT resulted in a calculated peak half height ($W_{1/2}$) of 100 mV, which is slightly larger, compared with the 90.6 mV expected for surface confinement reactions \textsuperscript{34} but significantly smaller than the 200 mV observed experimentally (Figure 2a).

Despite the fact that the literature of POT is particularly broad, there is not yet a theoretical and accepted interpretation of its cyclic voltammetry behavior.\textsuperscript{35} Nonetheless, it was claimed elsewhere that the behavior of POT, like other conducting polymers, could be described with a fraction of electron transfer reaction.\textsuperscript{32} By decreasing the value of $n_{cp}$, the peak becomes broader and fits better with the experimentally observed peak widths.

Figure S1a shows the silver transfer wave (100 µM) at different electron transfer numbers ($n_{cp} = 1, 0.5$ and $0.25$). As observed, a diminishment in the number of electrons translates into wider peaks (i.e., $W_{1/2} \approx 95, 150,$ and $260$ mV respectively) with an optimum value within $0.25 < n_{cp} < 0.5$. In addition, calculated peaks for a mixture containing 10 mM sodium and 10 µM silver, as a function of electron number is shown in Figure S1b in the supporting information. In this latter case, calculated widths for the Ag peak are slightly different ($W_{1/2} \approx 100, 140$ and 210 mV for $n_{cp} = 1, 0.5$ and 0.25), likely due to the fact that the peak shape is affected by silver mass transport contribution at low silver concentrations. In contrast to such improvements, this modification is not equally representative, in terms of peak height and shape (pronounced tailing at $n_{cp} = 0.25$). Therefore, a compromise situation between height, width and shape was set by using $n_{cp} = 0.5$. 

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Figure 3. (a) Silver and sodium peak currents vs. silver concentrations (from 1 to 10 µM). (b) Integrated charge vs. logarithmic of silver concentrations. Points for the higher silver concentrations (25-100 µM) are corrected by considering the capacitive charge of the voltammograms in the region of the silver peak.

The most sophisticated algorithm for treating POT oxidation/reduction as a quasi-reversible system may include experimental kinetic parameters, as proposed by Otero et al., although this treatment was widely criticized by other authors. On the other hand, it was recently demonstrated that POT oxidation could be appropriately fitted by a Gaussian function; however, a major issue arises from the broad fingerprint wave at cathodic currents. Having introduced a brief review of POT electrochemistry and its controversies, we prefer here to treat the POT interface as an idealized CP. Finally, the absence of capacitive and ohmic drop terms in the model do explain the zero current levels for the calculated voltammograms and the negligible changes in $E_{\text{peak}}$ and $\Delta E_{\text{peak}}$.

Having investigated the electrochemical system on the basis of diffusional mass transport in the aqueous phase for $c_{\text{Ag}}^a < 50$ µM, we further explore the behavior of thin layer films at higher concentrations of silver ($c_{\text{Ag}}^a > 50$ µM) to visualize the transition from diffusion control in the aqueous phase to POT oxidation control in the sensing film (Figure S2 in the supporting information). It has already been demonstrated that the POT oxidation process is limited by the
amount of cation-exchanger (R') in the membrane at higher concentrations (~ mM) of primary ion.\textsuperscript{24}

Under the critical conditions (\(c_{Ag}^{eq} \sim 25 \mu M\)), the Na peak disappears completely whereas the Ag peak reaches a limiting current value (~ 1.1 \(\mu A\)). Above this threshold, the silver peak shifts towards more positive potentials as predicted by the Nernst equation in the range of 25-250 \(\mu M\) of silver (see Figures S2a and S3 in the Supporting Information). In this concentration range, the sensor can be used for the potentiometric detection of silver. A slope of 59.8 ± 0.2 mV dec\(^{-1}\), with an intercept of 989 ± 7 mV, was obtained experimentally. The integration of the forward and backward silver peaks differed by less than 2% (e.g., 3.428 and 3.345 \(\mu C\) for 100 \(\mu M\) silver, see Figure S2a). In addition, the peak separation between forward and backward peaks was always close to ~70 mV (see Table S-1 in the Supporting Information).

The upper linear range of the calibration curve (>250 \(\mu M\), where super-Nernstian behavior is clearly visible, see Figure S3b) is likely caused by the deposition of silver (Ag\(^0\)) particles on the membrane surface, thereby turning the membrane partially black after this experiment. It is presumably responsible for the deterioration of the peak shape and the appearance of negative currents in the range of -0.5 V to 0.3 V (see Figure S2a). A similar effect was observed with a bare POT electrode in the absence of sensing film but in contact with a AgNO\(_3\) solution (1 mM; see Figure S4 in the Supporting Information).

Figure 3b shows the evolution of the integrated charge for each peak (Ag\(^+\) or Na\(^+\)), as a function of the logarithmic concentration of adding silver salt to solution. Note the excellent correspondence between total and individual charge amplitudes for sodium and silver, and the change of response regime with the silver concentration solution that coincides with the plateau in the integrated charge of both peaks.

Calculated voltammograms in the entire concentration range (Figure S3b) present an analogous trend to the experiments shown in Figure 3a. For example: (i) the Na peak current linearly decreases until it disappears (Figure S5a), (ii) the Ag peak current linearly increases up to a concentration of 50 \(\mu M\) of silver salt (Figure S5a), and (iii) at silver concentration of > 50 \(\mu M\), the peak shifts to more positive potentials, according to the Nernst equation (Figure S5b). Metallic silver formation is not considered in the theory, and thus, a Nernstian behavior is predicted for the entire concentration range (Figure S5b).
Silver and oxidized POT concentration profiles at two different bulk silver ion concentrations (1 µM and 1 mM in the presence of 10 mM NaNO₃) are shown in Figures S6 and S7 in the Supporting Information, along with the applied anodic potential, in view of emphasizing the versatility of the thin ionophore-based thin film sensing approach and its dependence on the experimental conditions. Comparing these two experimental scenarios, one may rationalize the importance of diffusional mass transport. For instance, the released concentration of silver with respect to the bulk silver concentration increases 8 and 0.05 times for 1 µM and 1 mM respectively (Figures S6b and S7b). This indicates the necessity to include a diffusion term for lower concentrations of silver in contrast to the higher ones. The converted POT under these simulated conditions is around 17% (Figures S6d and S7d).

With the objective of perturbing the concentration gradient at the sample/membrane interface, two experiments were carried out. The first one consisted of varying the scan rate dependence of the applied potential whereas the second experiment used the rotating disk electrode at a constant concentration of silver and sodium.

Figure 4a shows experimental cyclic voltammograms for 10 µM silver nitrate in 10 mM NaNO₃ at different scan rates, from 200 mV s⁻¹ to 25 mV s⁻¹. At the highest scan rate (200 mV s⁻¹), the
intensity of Na peak is found to be 1.2 times higher than that of Ag peak. By decreasing the scan rate, this effect is gradually reversed (i.e., at 75 mV s\(^{-1}\) the peak current for Ag was 1.4 times higher than that for Na peak) reaching the limiting case at 25 mV s\(^{-1}\) where only a silver wave is observed. This suggests that silver mass transport is more effective at lower scan rates rather than higher ones.

Note that the Na peak current varies linearly with scan rate, while the Ag peak current dependence is with the square root of scan rate (Figures 4b and 4c respectively). This also turns out to be the case with the backward scan (Figures S8a and S8b). This important evidence confirms that: (i) Na\(^+\) ion-transfer obeys the so-called thin layer approximation, and (ii) Ag\(^+\) ion transfer is controlled by diffusion in the aqueous phase at these concentration levels. Calculated voltammograms at different scan rates (Figure 4d) exhibit similar features as the ones experimentally observed (Figures 4e and 4f).

In conclusion, the present theory successfully predicts an effective mass transport of silver at low scan rates. By contrast, at higher silver concentrations (10-fold higher, 100 µM) diffusional mass transport in the sample solution is no longer the rate-limiting step as is visualized in Figure S9 (transition from square root to linear scan rate dependence, Figures S9c and S9d). Here again, the current model converges into the previous one for higher concentration of silver salt.\(^{24}\)

Figure 5a illustrates a series of experiments that allow one to visualize the influence of rotation speed (\(\omega\)) on thin films interrogated with linear sweep voltammetry at 2.5 µM silver. While the peak position for sodium and silver changes only slightly with rotation speed (379 ± 25 and 860 ± 30 mV, respectively), the Na peak decreases until its disappearance, and simultaneously, the intensity of the Ag peak gradually increases, yielding the limiting current value (from 0.2886 µA at 0 rpm to 1.060 µA at 6400 rpm).
A typical plot ($i_{\text{peak}}$ vs. $\omega^{1/2}$) shown in Figure 5b exhibits a linear relationship until 900 rpm (the second curve from top) with a subsequent leveling off. It is here demonstrated that below 900 rpm, the overall process is limited by silver diffusion in the sample (Figure S10j). However, above 900 rpm, mass transport becomes more effective, because of the reduction of the diffusion layer (rotating disk electrode theory\textsuperscript{34}), resulting in an enhancement of the inward silver flux, which ultimately avoids the depletion of silver at the membrane interface.

A diffusion-controlled phenomenon (i.e., below 900 rpm) must be dependent on sample concentration. Therefore, a range of silver concentrations (see Figure S10) were used at the same angular frequencies. At lower concentrations, the linearity is extended up to 3000 rpm whereas at higher concentrations the proportionality breaks down at only 400 rpm. In other words, for larger concentration gradients (driving force), less convection coming from the angular rotation (translating into a diminishment of the diffusion layer thickness) is required to sustain the silver uptake from the membrane. Evidently, for lower concentration gradients, very fast rotations are necessary to compensate the weak driving force at the interface. Note that the loss of linearity again represents the transition between regimes of mass transport diffusion to...
thin layer behavior (see Figure S11). Figure 5c presents the calculated curves for a cation concentration of 2.5 µM by introducing the Levich equation in the current theory. Apart from the proper agreement with the experimental voltammograms (Figure 5a), the observed plateau is also predicted (see Figure 5d) by the simulation.

3.5 Conclusions

We have demonstrated here that thin layer ionophore-based films interrogated with a controlled potential technique exhibited responses that are dependent on the chosen experimental conditions. The membrane was initially doped with cation exchanger, which limited the ion capacity of the membrane. Through a wide range of experimental designs, we identified two different cases modulated by: (i) silver mass transport diffusion or (ii) oxidation of the conducting polymer under a thin layer assumption. The appropriate selection of the experimental conditions (i.e., concentration of the target interest, speed of the scan rate, or angular frequency) would depend on the final application of these materials. The model and simulation presented here are able to predict all key experimental results under different conditions (scan rate and angular frequency) for this model system, and therefore, is a fundamental step forward in the field of thin layer materials, whether doped with molecular receptors or not. The developed model should be equally useful for membranes containing only lipophilic electrolytes (anion transport), in which case the Nernst equation (eq.5) and the charge balance equation (eq.9) should be reformulated for anions. Chapter 4 describes a simplified semi-empirical treatment that allows one to easily predict the limit of detection, as well as the transition between one regime and the other for thin layer membranes with defined ion exchange capacity. Our current efforts are focused on understanding fundamental aspects of multi-receptor thin layer membranes to determine very low amounts of targets. Efforts to treat the electrochemical properties of conducting polymer (CPs) beyond the typical Nernst equation are currently in progress.
3.6 Supporting information

3.6.1 Discretization

Equations from the main manuscript:

\[
A \int_0^\infty \left( \frac{\partial c_{eq}^{aq}}{\partial t} \right) dx = -A \delta_m \frac{\partial c_{eq}^m}{\partial t} \tag{10}
\]

\[
\frac{\partial c_{eq}^{aq}}{\partial t} (x,t) = D_{eq}^{aq} \frac{\partial^2 c_{eq}^{aq}}{\partial x^2} \tag{11}
\]

Finite difference method to discretize eq 10 (main manuscript):

\[
\sum_{x=0}^{n-1} A(c_{eq}^{aq}, (x,t+\Delta t) - c_{eq}^{aq} (x,t))dx = -\delta_m A(c_{eq}^m, (t+\Delta t) - c_{eq}^m (t)) \tag{S.1}
\]

where \( n \) is the number of element in which the diffusion layer is divided. Arranging eq S.1:

\[
\sum_{x=1}^{n-1} (c_{eq}^{aq} (x,t+\Delta t) - c_{eq}^{aq} (x,t))dx = -\delta_m (c_{eq}^m, (t+\Delta t) - c_{eq}^m (t)) - (c_{eq}^{aq} (0,t+\Delta t) - c_{eq}^{aq} (0,t))dx \tag{S.2}
\]

This equation is used below for the development eq S.7.

Eq 11 (main manuscript) is discretized to eq S.3:

\[
c_{eq}^{aq} (x,t+\Delta t) - c_{eq}^{aq} (x,t) = D_{eq}^{aq} \frac{\Delta t}{(dx)^2} \left( c_{eq}^{aq} (x-1,t) - 2c_{eq}^{aq} (x,t) + c_{eq}^{aq} (x+1,t) \right) \tag{S.3}
\]

with \( 1 \leq x \leq n - 1 \). Rewriting this equation from \( x = 1 \) to \( x = n - 1 \):

\[
\sum_{x=1}^{n-1} (c_{eq}^{aq} (x,t+\Delta t) - c_{eq}^{aq} (x,t))dx = D_{eq}^{aq} \frac{\Delta t}{dx} \left( c_{eq}^{aq} (0,t) - c_{eq}^{aq} (1,t) - c_{eq}^{aq} (n-1,t) + c_{eq}^{aq} (n,t) \right) \tag{S.4}
\]

Assuming that there is no diffusion in the aqueous phase (\( n \gg\gg \), from \( n \) to \( n - 1 \)), eq S.4 is simplified to:

\[
\sum_{x=1}^{n-1} (c_{eq}^{aq} (x,t+\Delta t) - c_{eq}^{aq} (x,t))dx = D_{eq}^{aq} \frac{\Delta t}{dx} \left( c_{eq}^{aq} (0,t) - c_{eq}^{aq} (1,t) \right) \tag{S.5}
\]

Incorporating e. S.2 to equation S.5, eq S.6 is obtained:

\[
\delta_m (c_{eq}^m (t+\Delta t) - c_{eq}^m (t)) + (c_{eq}^{aq} (0,t+\Delta t) - c_{eq}^{aq} (0,t))dx = D_{eq}^{aq} \frac{\Delta t}{dx} \left( c_{eq}^{aq} (1,t) - c_{eq}^{aq} (0,t) \right) \tag{S.6}
\]
To solve $c_{Ag}^{aq}(0, t + \Delta t)$, eqs 7, 8 and 9 (main manuscript) are rewritten in terms of $t + \Delta t$:

$$E_{app}(t + \Delta t) = \Delta \phi^0 + \frac{RT}{n_{POT}F}\ln \frac{c_{CP}^{aq}(t + \Delta t)}{c_{CP}^{aq}(t + \Delta t)} + \Delta \phi_{Na^+}^{0, \text{aq-\text{mem}}} + \frac{RT}{n_{Na}F}\ln \frac{c_{Na^+}^{aq}}{c_{Na^+}^{aq}(t + \Delta t)} \quad (S.7)$$

$$E_{2}(t + \Delta t) = \Delta \phi_{Na^+}^{0, \text{aq-\text{mem}}} + \frac{RT}{n_{Na}F}\ln \frac{c_{Na^+}^{aq}}{c_{Na^+}^{aq}(t + \Delta t)} = \Delta \phi_{Ag^+}^{0, \text{aq-\text{mem}}} + \frac{RT}{n_{Ag}F}\ln \frac{c_{Ag^+}^{aq}(0, t + \Delta t)}{c_{Ag^+}^{aq}(t + \Delta t)} \quad (S.8)$$

$$c_{r} \delta_{r} A = n_{cp}c_{CP}^{c}(t + \Delta t)\delta_{r} A + n_{Na}c_{Na}^{m}(t + \Delta t)\delta_{r} A + n_{Ag}c_{Ag}^{m}(t + \Delta t)\delta_{r} A \quad (S.9)$$

The applied potential is expressed as:

$$E_{app}(t) = \begin{cases} E_{\text{init}} + vt, & 0 \leq t \leq t_{\lambda} \\ E_{\text{turn}} - v(t - t_{\lambda}), & t_{\lambda} \leq t \leq 2t_{\lambda} \end{cases} \quad (S.10)$$

Eqs S.3 and S.6 to S.10 are combined to obtain $c_{CP}^{c}(t + \Delta t)$.

Finally, the current is expressed as:

$$i(t) = n_{cp}FA\delta_{CP}\frac{c_{CP}^{c}(t + \Delta t) - c_{CP}^{c}(t)}{\Delta t} \quad (S.11)$$
3.6.2 Parameters used for calculated peaks:

Figure 2b:

\[ A = 6 \times 10^{-4} \text{dm}^2; \quad F = 96486 \text{ C mol}^{-1}; \quad \delta_{\text{film}}^{\text{PVC}} = 2.3 \times 10^{-6} \text{dm}; \quad \delta_{\text{film}}^{\text{POT}} = 0.55 \times 10^{-6} \text{dm}; \quad c_{\text{POT}} = 0.75 \text{M}; \quad c_r = 0.015 \text{M}; \]

\[ E_{\text{POT}}^0 = 0.8 \text{ V}; \quad E_{\text{Na}}^0 = -0.3 \text{ V}; \quad E_{\text{Ag}}^0 = 0.23 \text{ V}; \quad s = 0.059 \text{ V}; \quad n_{\text{POT}} = 0.5; \quad n_{\text{Na}} = 1; \quad n_{\text{Ag}} = 1; \quad v = 100 \text{ mV s}^{-1}; \]

\[ dx = 10^4 \text{ dm}; \quad \Delta t = 10^2 \text{ s}; \quad D_{\text{Ag}}^{\text{eq}} = 0.6 \times 10^{-7} \text{ dm}^2 \text{ s}^{-1}; \quad E_{\text{init}} = -0.5 \text{ V}; \quad E_{\text{turn}} = 1.5 \text{ V}; \quad c_{\text{Ag}}^{\text{eq}} = 10 \text{ mM}; \]

\[ c_{\text{Ag}} = 10^{-6}, 10^{-7}, 10^{-8}, 2.5 \times 10^{-8}, 5 \times 10^{-8}, 10^{-5}, 2.5 \times 10^{-5}, 5 \times 10^{-5} \text{ M} \]

Figures 4d, 4e and 4f:

\[ A = 6 \times 10^{-4} \text{dm}^2; \quad F = 96486 \text{ C mol}^{-1}; \quad \delta_{\text{film}}^{\text{PVC}} = 2.3 \times 10^{-6} \text{dm}; \quad \delta_{\text{film}}^{\text{POT}} = 0.55 \times 10^{-6} \text{dm}; \quad c_{\text{POT}} = 0.75 \text{M}; \quad c_r = 0.015 \text{M}; \]

\[ E_{\text{POT}}^0 = 0.8 \text{ V}; \quad E_{\text{Na}}^0 = -0.3 \text{ V}; \quad E_{\text{Ag}}^0 = 0.23 \text{ V}; \quad s = 0.059 \text{ V}; \quad n_{\text{POT}} = 0.5; \quad n_{\text{Na}} = 1; \quad n_{\text{Ag}} = 1; \quad v = 200, 100, 75, 50, 25 \text{ mV s}^{-1}; \]

\[ dx = 10^4 \text{ dm}; \quad \Delta t = 10^2 \text{ s}; \quad D_{\text{Ag}}^{\text{eq}} = 0.6 \times 10^{-7} \text{ dm}^2 \text{ s}^{-1}; \quad E_{\text{init}} = -0.5 \text{ V}; \quad E_{\text{turn}} = 1.5 \text{ V}; \quad c_{\text{Na}}^{\text{eq}} = 10 \text{ mM}; \quad c_{\text{Ag}}^{\text{eq}} = 10^{-4} \text{M}. \]

Figures 5c and 5d:

\[ A = 6 \times 10^{-4} \text{dm}^2; \quad F = 96486 \text{ C mol}^{-1}; \quad \delta_{\text{film}}^{\text{PVC}} = 2.3 \times 10^{-6} \text{dm}; \quad \delta_{\text{film}}^{\text{POT}} = 0.55 \times 10^{-6} \text{dm}; \quad c_{\text{POT}} = 0.75 \text{M}; \quad c_r = 0.015 \text{M}; \]

\[ E_{\text{POT}}^0 = 0.8 \text{ V}; \quad E_{\text{Na}}^0 = -0.3 \text{ V}; \quad E_{\text{Ag}}^0 = 0.23 \text{ V}; \quad s = 0.059 \text{ V}; \quad n_{\text{POT}} = 0.5; \quad n_{\text{Na}} = 1; \quad n_{\text{Ag}} = 1; \quad v = 100 \text{ mV s}^{-1}; \]

\[ dx = 10^4 \text{ dm}; \quad \Delta t = 10^2 \text{ s}; \quad D_{\text{Ag}}^{\text{eq}} = 0.6 \times 10^{-7} \text{ dm}^2 \text{ s}^{-1}; \quad E_{\text{init}} = -0.5 \text{ V}; \quad E_{\text{turn}} = 1.5 \text{ V}; \quad c_{\text{Na}}^{\text{eq}} = 10 \text{ mM}; \quad c_{\text{Ag}}^{\text{eq}} = 2.5 \times 10^{-4} \text{M}. \]

0 rpm: \( dx = 10^4 \text{ dm}, \Delta t = 10^2 \text{ s}; \) 100 rpm: \( dx = 1.05 \times 10^4 \text{ dm}, \Delta t = 10^3 \text{ s}; \) 200 rpm: \( dx = 9.89 \times 10^5 \text{ dm}, \Delta t = 10^3 \text{ s}; \) 400 rpm: \( dx = 1.05 \times 10^4 \text{ dm}, \Delta t = 10^2 \text{ s}; \) 800 rpm: \( dx = 7.42 \times 10^5 \text{ dm}, \Delta t = 10^3 \text{ s}; \) 1600 rpm: \( dx = 5.25 \times 10^5 \text{ dm}, \Delta t = 10^2 \text{ s}; \) 2200 rpm: \( dx = 4.48 \times 10^5 \text{ dm}, \Delta t = 10^2 \text{ s}; \) 3200 rpm: \( dx = 3.71 \times 10^5 \text{ dm}, \Delta t = 5 \times 10^3 \text{ s}; \)
3.6.3 Tables

Table S-1. Peak parameters for sodium and silver peaks in Figure 2 (n=5 consecutive scans).

| $c_{Ag}$ (M) | $q_{Na\text{ peak}}$ (µC) | $q_{Ag\text{ peak}}$ (µC) | $q_{\text{total}}$ (µC) | $\Delta E$ (f-b) (mV) |
|-----|-----------------|-----------------|-----------------|-----------------|------|
| $0^a$ | 3.152 | 0 | 3.152 | 80.3 | |
| $1\times10^{-5}$ | 3.084 | 0.009 | 3.093 | 70.5 | |
| $1\times10^{-7}$ | 2.950 | 0.113 | 3.063 | 70.5 | |
| $1\times10^{-6}$ | 2.717 | 0.363 | 3.082 | 70.5 | |
| $2.5\times10^{-6}$ | 2.359 | 0.764 | 3.122 | 70.5 | |
| $5\times10^{-6}$ | 1.851 | 1.246 | 3.097 | 55.5 | |
| $1\times10^{-5}$ | 1.237 | 1.779 | 3.012 | 31.7 | |
| $2.5\times10^{-5}$ | 0 | 3.466 | 3.466 | 70.4 | |
| $5\times10^{-5}$ | 0 | 3.596 | 3.597 | 90.1 | |
| $1\times10^{-4}$ | 0 | 3.428 | 3.428 | 83.2 | |
| $2.5\times10^{-4}$ | 0 | 3.463 | 3.463 | 71.4 | |
| $5\times10^{-4}$ | 0 | 3.454 | 3.454 | 87.3 | |
| $1\times10^{-3}$ | 0 | 3.440 | 3.440 | 103.1 | |

$^a$ 10 mM NaNO₃ background solution. f=forward; b=backward scan.
Figure S1. Calculated cyclic voltammogram for different electron transfer number of POT ($n_{\text{POT}}$=1, 0.5 or 0.25) at (a) 100 µM of silver and (b) 10 µM of silver. Parameters used for calculated peaks: $A=6\times10^{-4}$dm$^2$; $F=96486$ Cmol$^{-1}$; $\delta_{\text{PVC}}=2.3\times10^{-6}$dm; $\delta_{\text{film}}=0.55\times10^{-6}$dm; $c_{\text{POT}}=0.75$M; $c_{\text{Ag}}=0.015$M; $E_{\text{POT}}^0=0.8$ V; $E_{\text{Ag}}^0=-0.3$ V; $E_{\text{Na}}^0=0.23$ V; $s=0.059$ V; $n_{\text{POT}}=0.25, 0.5, 1$; $n_{\text{Na}}=1$; $n_{\text{Ag}}=1$; $v=100$ mV s$^{-1}$; $dx=10^{-4}$dm; $x_{\text{max}}=40$; $\Delta t=10^{-2}$s; $D_{\text{Ag}}^{\infty}=0.6\times10^{-7}$dm$^2$s$^{-1}$; $E_{\text{init}}=-0.5$ V; $E_{\text{turn}}=1.5$ V; $c_{\text{Na}}^{\infty}=10$ mM; $c_{\text{Ag}}^{\infty}=10^{-5}$, 10$^{-3}$M.
Figure S2. (a) Experimental voltammograms for increasing silver concentrations (0, 10⁻⁸, 10⁻⁷, 10⁻⁶, 2.5×10⁻⁶, 5×10⁻⁶, 10⁻⁵, 2.5×10⁻⁵, 5×10⁻⁵, 10⁻⁴, 2.5×10⁻⁴, 5×10⁻⁴, 10⁻³ M). 10 mM NaNO₃ background electrolyte. Scan rate: 100 mV s⁻¹. (b) Calculated voltammograms for the same concentrations used in experimental curves showed in (a). Parameters used for the calculated peaks: A=6×10⁻⁴ dm² F=96486 C mol⁻¹ δ_pvc=2.3×10⁻⁶ dm²; δ_pot=0.55×10⁻⁶ dm²; c_pot=0.75M; c_R=0.015M; E_pot=0.8 V; E_{Na⁺}^² = -0.3 V; E_{Ag⁺}^² = 0.23 V; s=0.059 V; n_pot=0.5; n_{Na⁺}=1; n_{Ag⁺}=1; v=100 mVs⁻¹; dx=10⁻⁴ dm; xₘₕₐₓ =40; Δt=10⁻² s; D_{Ag⁺}^{aq} =0.6×10⁻⁷ dm² s⁻¹; E_{ini}= -0.5 V; E_{turn}=1.5 V; c_{Na⁺}^{aq}=10 mM;

c_{Ag⁺}^{aq} = 0, 10⁻⁸, 10⁻⁷, 10⁻⁶, 2.5×10⁻⁶, 5×10⁻⁶, 10⁻⁵, 2.5×10⁻⁵, 5×10⁻⁵, 10⁻⁴, 2.5×10⁻⁴, 5×10⁻⁴, 10⁻³ M
Figure S3. Experimental calibration curves for silver (peak potential vs. logarithmic silver concentration) obtained in two different concentration ranges.
Figure S4. Cyclic voltammogram obtained using a GC/POT electrode in 1mM AgNO$_3$ solution. Background electrolyte: 10 mM NaNO$_3$. Scan rate: 100mV s$^{-1}$. 

Figure S5. (a) Calculated peak current for sodium and silver vs. silver concentration (from $10^{-8}$ to $10^{-5}$ M). (b) Calculated calibration curve for silver (peak potential vs. logarithmic concentration).
Figure S6. Calculated concentration profiles ($c_{Ag^+}/c_{Ag^{\ast}}$) vs. distance from the membrane interface ($x=0$) to the bulk solution ($x=400$ µm) for 1 µM silver at different $c_{POT^-}/c_{POT^+}$ ratios coinciding with the beginning (a), maximum (b) and ending (c) of the calculated silver peak. Time scale for each curve is 1 s (a), 0.2 s (b) and 0.4 s (c). Dashed lines in (c) are calculated for longer times (last curve for $c_{Ag^+}/c_{Ag^{\ast}}=1$ is obtained for $t=800$ s). (d) Concentration profile calculated for oxidized POT ($c_{POT^-}/c_{POT^+}$ vs. time).
Figure S7. Calculated concentration profiles ($c_{Ag^+/Ag} / c_{Ag^{+}}$ vs. distance from the membrane interface ($x=0$) to the bulk solution ($x=400 \, \mu m$)) for 1 mM silver at different $c_{POT^-}/c_{POT}$ ratios coinciding with the beginning (a), maximum (b) and ending (c) of the calculated silver peak. Time scale for each curve is 1 s (a), 0.2 s (b) and 0.4 s (c). Dashed lines in (c) are calculated for longer times (last curve for $c_{Ag^+/Ag^{+}}=1$ is obtained for $t=800$ s). (d) Concentration profile calculated for oxidized POT ($c_{POT^-}/c_{POT}$ vs. time).
Figure S8. (a) Experimental peak current for sodium backward peak vs. scan rate at $10^{-5}$ M silver. (b) Experimental peak current for silver backward peak vs. square root of scan rate at $10^{-5}$ M silver.
Figure S9. (a) Experimental voltammograms for 10^{-4} M silver at different scan rates. (b) Calculated voltammograms for 10^{-4} M silver at different scan rates. (c) Experimental peak current vs. scan rate. (d) Calculated peak current vs. scan rate. Background electrolyte: 10mM NaNO₃. Scan rates: 200 mV s⁻¹, 100 mV s⁻¹, 75 mV s⁻¹, 50 mV s⁻¹ and 25 mV s⁻¹.
Figure S10. (a-i) Experimental cyclic voltammograms for increasing rotation speeds at different concentrations of silver. Rotation speeds start from 0 to 6400 rpm. Sample concentration is indicated in each graph. (j) Peak current for sodium vs. square root of the rotation speed at different silver concentrations. Background electrolyte: 10mM NaNO$_3$. Scan rate: 100 mV s$^{-1}$. 
Figure S11. Calculated cyclic voltammograms for increasing rotation speeds at different concentrations of silver. Rotation speeds start from 0 to 6400 rpm. Sample concentration is indicated in each graph. An efficient mass transport occurs together with a reduction of the thickness of the diffusion layer in the aqueous phase down to a constant value of $\delta_{Ag^{+}}^{aq} = 10 \mu$m, generating a plateau for the peak current as increasing concentration of silver. In the developed model, this plateau occurs when $\delta_{Ag^{+}}^{aq} = dx = 10\mu$m that is reached with the breakdown of the Levich equation (eq 16 in the main manuscript) at each concentration.
3.7 References

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Chapter 4 Voltammetric Thin Layer Ionophore Based Films: Part 2. Semi-Empirical Treatment

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Abstract

This work reports on a semi-empirical treatment that allows one to rationalize and predict experimental conditions for thin layer ionophore-based films with cation-exchange capacity read out with cyclic voltammetry. The transition between diffusional mass transport and thin layer regime is described with a parameter ($\alpha$), which depends on membrane composition, diffusion coefficient, scan rate, and electrode rotating speed. Once the thin layer regime is fulfilled ($\alpha = 1$), the membrane behaves in some analogy to a potentiometric sensor with a second discrimination variable (the applied potential) that allows one to operate such electrodes in a multianalyte detection mode owing to the variable applied ion transfer potentials. The limit of detection of this regime is defined with a second parameter ($\beta = 2$) and is chosen in analogy to the definition of the detection limit for potentiometric sensors provided by the IUPAC. The analytical equations were validated through the simulation of the respective cyclic voltammograms under the same experimental conditions. While simulations of high complexity and better accuracy satisfactorily reproduced the experimental voltammograms during the forward and backward potential sweeps (Chapter 3), the semi-empirical treatment here, while less accurate, is of low complexity and allows one to quite easily predict relevant experimental conditions for this emergent methodology.
4.1 Introduction

While in the last two decades ionophore-based membranes have been primarily utilized for developing potentiometric and optical sensors \(^{1,2}\), recent research has established the versatility of these materials for use in electrochemical ion transfer, triggered by the oxidation/reduction of compounds (i.e., conducting polymers) situated between the membrane and a metallic electrode.\(^{3,5}\) The use of membranes of micrometer thickness or lower has been a critical requirement to establish these types of sensors.\(^{3,6,7}\) Under thin layer conditions, the mass transport diffusion inside of the membrane can be neglected, and the membrane can then be considered a one-dimensional element. As a consequence of this experimental condition, the voltammetric ion transfer peak may become Gaussian\(^{5}\), narrow, symmetric (in the forward and backward scans), without capacitive current and ohmic drop resistance, in analogy to surface-confined electrochemical reactions.\(^{8}\) These electrochemical characteristics also indicate that the amount of ions initially present in the membrane phase (or after the uptake) are exhaustively released at the ion-transfer peak.

Thin layer ionophore-based membranes interrogated with dynamic electrochemical techniques have been developed along two different paths. The first direction utilizes ion-exchange membranes and focused on peak potential in similar fashion to potentiometry, ideally giving Nernstian responses to ion activity. The addition of multiple ionophores in the same membrane has been shown to allow one to measure multiple ions within the same potential sweep in less than 10 s (1 V full scale at 100 mV s\(^{-1}\) scan rate) for up to three analyte ions.\(^{5,9}\) The importance of the thin layer film was evident in the resolution factor. The thinner the membrane (around 200 nm), the narrower the obtained ion transfer peak (~200 mV). For thin membranes, a much better resolution was observed without requiring the separation of overlapping peaks by a deconvolution algorithm required for thicker membranes. Moreover, the recent use of polyurethane films gave a much improved chemical and mechanical robustness\(^{10-12}\) in addition to the already established biocompatibility of this material for ion detection in biological fluids.\(^{4,13,14}\)

A simplified model that considers the concentration at the membrane/sample interface to be equal to the concentration of the bulk sample predicted a Nernstian shift of peak potential at relatively high concentrations of the ion of interest.\(^{5,7}\) Because diffusion was not taken into account in this model, only high concentrations in the sample phase could be simulated.

Amemiya and coworkers further developed this model\(^{5}\) by considering different stoichiometries of complexation between ionophore and analyte in the sensing phase\(^{15}\) as well as more recently including the contribution of a secondary ion in the complexation process.\(^{16}\)
These experiments were carried out with initially oxidized PEDOT$^+$ and membranes doped with lipophilic electrolytes (TDDATFAB or other varieties).

The second direction uses similar membranes containing lipophilic electrolyte (and selective ionophore), although typically thicker than the ones employed for multianalyte detection, that act as a reservoir into which the ion of interest can be selectively accumulated upon applying an appropriate potential, followed by subsequent ion stripping.$^{3,17-21}$ This elegant strategy resulted in lowering the limit of detection of several ions by reading out the peak current of the stripping signal. A theory was formulated in terms of diffusional mass transport in the sample phase, assuming a constant diffusion layer thickness produced by a rotating disk electrode.$^{19}$ Despite the authors defining a useful pre-concentration factor (ion concentration ratio in membrane and sample) and most likely because of the intention to decrease the limit of detection, no experimental evidence was presented about the behavior of this system at higher concentrations.

It was not until Chapter 3 that the transition from one mode to the other was experimentally and theoretically elucidated by using the same membrane composition at different sample concentrations, scan rates and electrode rotation speeds. Both regimes were found to be interconnected and dependent on experimental conditions. As a general rule, at nanomolar levels, the systems must be described in terms of diffusion, whereas at millimolar levels a thin layer approach is more appropriate. The time dependent solution described in Chapter 3 for chemically reversible systems $^{22}$ may be used to simulate most desired conditions owing to the fact that differential equations are the closest description to anticipated reality.

In this work, a series of simple equations based on pseudo-steady state conditions are developed that may be very useful to plan experiments $a$ $priori$, as successfully performed earlier with potentiometric sensors to predict and describe limits of detection, selectivity, and response time $^{1,23}$. We explore here a semi-empirical treatment that allows one to predict the transition between both modes as well as the limit of detection in the potentiometric (peak potential) readout mode by the use of two factors ($\alpha$, $\beta$).
4.2 Experimental section

4.2.1 Reagents, materials and equipment

Aqueous solutions were prepared by dissolving the appropriate salts in deionized water (>18 MΩ cm). Lithium perchlorate (>98%, LiClO₄), 3-octylthiophene (97%, OT), silver nitrate (AgNO₃), sodium nitrate (NaNO₃), high molecular weight poly(vinyl chloride) (PVC), bis(2-ethylhexyl)sebacate (DOS), sodium tetrakis[3,5-bis-(trifluoromethyl)phenyl]borate (NaTFPB), silver ionophore IV, acetonitrile (ACN) and tetrahydrofuran (>99.9 %, THF) were purchased from Sigma Aldrich and used as received.

GC-electrode tips (6.1204.300) with an electrode diameter of 3.00 ± 0.05 mm were sourced from Metrohm (Switzerland). Cyclic voltammograms were recorded with a PGSTAT101 (Metrohm Autolab B.V., Utrecht, The Netherlands) controlled by Nova 1.11 software (supplied by Autolab) running on a PC. A double-junction Ag/AgCl/3M KCl/1 M LiOAc reference electrode (6.0726.100 model, Metrohm, Switzerland) and a platinum counter electrode (6.0331.010 model, Metrohm, Switzerland) were used in a three-electrode cell. A rotating disk electrode (Autolab RDE, Metrohm Autolab B.V., Utrecht, The Netherlands) was used to spin coat the membranes on the electrodes at 1500 rpm as well as for the experiments with different rotating speeds. Wolfram Mathematica® 9 software was used for the theoretical validation of the proposed equations.

4.2.2 Preparation of the electrodes

Poly(3-octylthiophene) (POT) was electrochemically polymerized on GC electrode surface by cyclic voltammetry (two scans, 0-1.5 V, 100 mV s⁻¹) and then discharged at 0 V for 120 s. A solution containing 0.1 M OT and 0.1 M LiClO₄ in acetonitrile was used. This solution was purged with N₂ for 30 min before use. After the POT film electropolymerization, the electrode was immersed in pure acetonitrile for 30 min, to remove the electrolyte, and dried at room temperature for 15 min. Thereafter, a volume of 25 µL of diluted membrane cocktail (50 µL of the membrane cocktail + 150 µL of THF) was spin coated on the POT-based electrode. The composition of the silver-selective membrane cocktail was 30 wt.% of PVC, 60 wt.% of DOS, 40 mmol kg⁻¹ of NaTFPB and 80 mmol kg⁻¹ of silver ionophore IV. Conditioning of the membrane was not deemed necessary (estimated equilibration time of ~ 20 ms, using a film thickness of 200 nm estimated by ellipsometry¹⁰ and diffusion coefficient of 10⁻⁸ cm² s⁻¹).
4.3 Theory

4.3.1 Semi-empirical model

Figure 1 illustrates the model system consisting of two interfaces (I and II) and the establishment of reversible silver ion transfer across interface II, triggered by reduction or oxidation of a conducting polymer (CP/CP⁺) placed between the selective membrane and the electron conductor. The membrane initially contains cation exchanger (Na⁺R⁻) and a selective ionophore (L) though to simplify only the silver process is indicated. The existence of two regimes in voltammetric thin layer ionophore-based membranes was experimentally confirmed in part I. Moreover, the transition from one regime to the other was clearly described. Herein, a simplified theory based on steady state assumptions allows one to predict experimental conditions for either diffusion control (at very low concentrations) or thin layer control (at higher concentrations).

**Figure 1.** Schematic illustration of the investigated electrochemical system. I and II refer to the interfaces, \( m \): membrane; \( aq \): sample; \( \delta_{POT} \): thickness of POT layer; \( \delta_m \): thickness of membrane layer; \( dx \): sample dimension; GCE: glassy carbon; \( i_{POT} \): current owing to the oxidation (orange line POT to POT⁺) or reduction (green line, POT⁺ to POT) of POT; \( i_{Ag} \): silver ion-transfer current (uptake green line and release orange line). Grey, purple and light blue boxes represent POT, membrane and sample layers respectively.
Figure 2. Scheme of the mass transport regime at low silver concentrations. Case 1 corresponds to the accumulation of silver at small diffusion layer thickness whereas Case 2 is for larger diffusion layer thickness. The accumulation time is illustrated in the lower cyclic voltammogram. This process is accompanied with an increase of the amount of silver in the membrane phase ($c_{Ag}^+$). $t_1$, $t_2$ refer to the intermediate times to reach the maximum diffusion layer ($t_{dl}$). $t_a$: accumulation time described as the double difference between initial ($t_i$) and peak time ($t_{peak}$). $\delta_m$: thickness of membrane layer; $dx$: sample dimension; $c_{Ag}^+*$: bulk silver concentration. For simplicity, the GCE, POT layer, cation exchanger (R-) sites and silver ionophore (L) were omitted here.

4.3.2 Mass transport regime (low concentrations)

In this case, owing to the low amount of silver in the sample phase, silver is always depleted at the membrane/sample interface (Figure 2). Thereby, the inward flux of silver ($J_I$) can be described by a steady state approximation (eq 1) as follows:

$$J_I = D_{Ag}^{aq} \frac{c_{Ag}^+}{\delta_{Ag}^{aq}}$$  \hspace{1cm} (1)

where $D_{Ag}^{aq}$ is the diffusion coefficient of silver in the aqueous phase, $c_{Ag}^+$ the concentration of silver in the bulk solution, and $\delta_{Ag}^{aq}$ the diffusion layer thickness under steady state conditions.

When a cyclic sweep potential is applied, the accumulation starts from the right base of the backward silver peak until the left base of the forward silver peak. During this period, accumulation occurs by spontaneous exchange of sodium by silver in the absence of current.
The accumulation time ($t_a$) of silver in the sensing film ($c_{Ag^+}^m$) can be described as a function of the ion transfer potential ($E_{peak}$), the initial applied potential ($E_{initial}$) and the scan rate ($v$) assuming a symmetric forward and backward silver peak:

$$ t_a = \frac{2(E_{peak} - E_{initial})}{v} \quad (2) $$

The diffusion layer thickness was approximated with eq 3, with $t_{dl}$ the required time to establish a given diffusion layer thickness.

$$ \delta_{Ag^+}^{eq} = 2\sqrt{D_{Ag^+}^{eq}t_{dl}} \quad (3) $$

After rearranging eq 3, $t_{dl}$ is obtained as

$$ t_{dl} = \frac{\delta_{Ag^+}^{eq}^2}{4D_{Ag^+}^{eq}} \quad (4) $$

Having defined $t_a$ and $t_{dl}$, two limiting cases can be distinguished. The first case occurs for $t_a \geq t_{dl}$ where a steady state is accomplished by convective means (stirring the solution or rotating the electrode, Figure 2, Case 1). Here, the number of moles of silver taken up per unit area by the membrane ($n_{Ag^+}^m$) can be described by eq 5:

$$ n_{Ag^+}^m = J_1(t_a - t_{dl}) + \frac{1}{2}c_{Ag^+}^s\delta_{Ag^+}^{eq} \quad (5) $$

with $n_{Ag^+}^m = c_{Ag^+}^m\delta_m$. The first term on the right side, $J_1(t_a - t_{dl})$, defines the amount of silver taken up during steady state whereas the second term, $\frac{1}{2}c_{Ag^+}^s\delta_{Ag^+}^{eq}$, represents the corresponding amount of silver up to the time the linear concentration gradient is obtained. eq 5, therefore, predicts the total amount of silver transferred during one voltammetry scan.

In the second case ($t_a < t_{dl}$, Figure 2, Case 2), the diffusion layer thickness is not constant (quiescent solution or rapid scan) and can be described as a function of diffusion coefficient and the accumulation time ($t_a$) as $2\sqrt{D_{Ag^+}^{eq}t_a}$. The number of moles of silver ions taken up is now written quite simply from geometrical consideration as:

$$ n_{Ag^+}^m = c_{Ag^+}^s\sqrt{D_{Ag^+}^{eq}t_a} \quad (6) $$
The capacity of the membrane to be saturated with silver may be appropriately described with a parameter ($\alpha$, eq 7) that is defined as the ratio between the concentration of silver in the membrane ($c^m_{Ag^+}$) and the total concentration of cation exchanger ($c_{R^-}$) in the same phase. As a result, this parameter takes values in the interval $0 \leq \alpha \leq 1$ as the maximum value of $c^m_{Ag^+}$ is limited by $c_{R^-}$ present in the membrane.

$$\alpha = \frac{c^m_{Ag^+}}{c_{R^-}}$$

This parameter $\alpha$ can now be derived for the two aforementioned cases.

For $\delta^{eq}_{Ag^+} \leq 2 \sqrt{D^{eq}_{Ag^+} \frac{2(E_{peak} - E_{initial})}{v}}$ (steady state),

$$\alpha = \frac{2D^{eq}_{Ag^+} c^*_{Ag^+}(E_{peak} - E_{initial})}{\delta^{eq}_{Ag^+} c_{R^-}} + \frac{\delta^{eq}_{Ag^+} c^*_{Ag^+}}{4}$$

(8)

While for $\delta^{eq}_{Ag^+} > 2 \sqrt{D^{eq}_{Ag^+} \frac{2(E_{peak} - E_{initial})}{v}}$ (without steady state),

$$\alpha = \frac{c^*_{Ag^+} \delta^{eq}_{Ag^+} \frac{2(E_{peak} - E_{initial})}{v}}{\delta^{eq}_{R^-} c_{R^-}}$$

(9)

Eqs 8 and 9 provide useful relationships to calculate the degree of saturation of the membrane semi-empirically as a function of scan rate, concentration of silver in the sample, and concentration of cation exchanger. When $\alpha=1$, the membrane is saturated with silver, resulting in a transition of the regime to thin layer control.
Figure 3. Representation of the thin layer regime at high silver concentrations. Left column corresponds to the uptake of silver whereas the right column is the release of silver. This process is accompanied with an increase/decrease of silver amount in the membrane phase ($c_{Ag^+}^m$) to the saturation level ($\alpha=1$, red line). The aqueous concentration at the interface to the stripping time ($t_s$) was denoted as $c_{Ag^+}^{aq}(0, t_s)$. The stripping time was approximated to the width at half maximum ($W_{1/2}$). $\delta_m$: thickness of membrane layer; $dx$: sample dimension. The GCE, POT layer, cation exchanger (R-) sites and silver ionophore (L) were again omitted here to simplify.

Figure 4. Differentiation between two limiting cases in the thin layer regime. Left: in the stirring case, the diffusion layer thickness ($\delta_{aq,imposed}$) was determined by the rotation speed. For, $t_s \geq t_{dl}$ an extra term was necessary to include owing to the amount of silver that diffuse to the bulk solution (eq 10). Right: in the no-stirring case, the diffusion layer grows indefinitely ($\delta_{aq,max}$), thereby the $t_s < t_{dl}$ and the total amount of silver released was described by eq 18. $\delta_m$: thickness of membrane layer; $dx$: sample dimension.
4.3.3 Thin layer regime (high concentrations)

Exposing the thin layer membrane to higher silver concentrations must result in a spontaneous exchange process accompanied with the saturation of the membrane ($\alpha = 1$) during a backward scan (Figure 3, left column uptake). Under such conditions, the silver concentration at the membrane/solution interface is assumed to be equal to the concentration in the bulk sample at the initial time (thin layer assumption, Figure 3, right column release).

Upon application of an anodic potential, silver starts to be released from the membrane, reaching a maximum level at $E_{peak}$ (Figure 3). The outward silver flux ($J_2$) for a constant diffusion layer thickness is given by Fick’s first law as

$$J_2 = D_{Ag} \frac{c_{Ag}^{aq} (0,t) - c_{Ag}^*}{\delta_{Ag}^{aq}}$$

(10)

The stripping time ($t_s$) is related to the peak width at half maximum ($W_{1/2}$, see Figure 3), approximated here as

$$t_s = \frac{W_{1/2}}{v}$$

(11)

In analogy to the two mass control regimes, we consider two cases illustrated in Figure 4: stirred ($t_s \geq t_{dl}$) and unstirred ($t_s < t_{dl}$) solutions.

When $t_s \geq t_{dl}$, the number of moles released ($n_{Ag}^m$) up to the peak current can be written with eq 12. The first term on the right side of eq 12 corresponds to the number of moles released into the diffusion layer while the second term corresponds to the loss of silver by diffusional mass transport from the diffusion layer to the bulk of the solution (Figure 4, case 1). This term is included because the diffusion layer is allowed to be constant under these conditions (convective sample control).

$$n_{Ag}^m = \frac{1}{2} (c_{Ag}^{aq} (0,t_s) - c_{Ag}^*) \delta_{Ag}^{aq} + \int_{t_s}^t J_2 dt$$

(12)

Here, $n_{Ag}^m = r c_r \delta_m$, where $r$ is the peak asymmetry factor (i.e., the silver peak area up to the peak maximum divided by the total peak area).

A parameter $\beta$ is here defined to express the ratio between silver concentration at the interface for the time equal to the stripping time ($t_s$) with respect to the silver concentration in the bulk solution:
\[
\beta = \frac{c_{Ag^{\text{aq}},}(0, t_s)}{c_{Ag^{\text{aq}}}}
\]  

(13)

\(\beta\) is always larger than 1 since at the beginning of the stripping \(c_{Ag^{\text{aq}},}(0, t) = c_{Ag^{\text{aq}}}^*\).

Assuming that \(J_2\) is constant at \(E_{\text{peak}}\) when \(t_{dl}\) is close to \(t_s\), eq 12 can be rewritten as:

\[
r c_K \delta_m = \frac{1}{2} (\beta - 1) \delta_{Ag^{\text{aq}},} c_{Ag^{\text{aq}}}^* + \frac{D_{Ag^{\text{aq}},} (\beta - 1) c_{Ag^{\text{aq}}}^*}{\delta_{Ag^{\text{aq}},}^2} (t_s - t_{dl})
\]  

(14)

After insertion into eq 14 the time to build up the diffusion layer (\(t_{dl}\), eq 4) and the stripping time (\(t_s\), eq 11), \(\beta\) may be calculated as:

\[
\beta = \frac{r c_K \delta_m \delta_{Ag^{\text{aq}},}^2 v}{D_{Ag^{\text{aq}},} c_{Ag^{\text{aq}},} W_{l/2} + \frac{1}{4} \delta_{Ag^{\text{aq}},}^2 c_{Ag^{\text{aq}},} v} + 1
\]  

(15)

With \(\beta = 2\) (see results and discussion for the reasoning of choice of \(\beta = 2\)) and \(r = 0.5\) (assuming a symmetrical peak), we predict the limit of detection for this regime as:

\[
c_{Ag^{\text{aq}},}^* (DL) = \frac{2 c_K \delta_m \delta_{Ag^{\text{aq}},}^2 v}{\delta_{Ag^{\text{aq}},}^2 v + 4 D_{Ag^{\text{aq}},} W_{l/2}}
\]  

(16)

As we assumed \(t_s > t_{dl}\), \(\delta_{Ag^{\text{aq}},}^2 v < 4 D_{Ag^{\text{aq}},} W_{l/2}\). This results in a simplified form of eq 16 for stirred solutions:

\[
c_{Ag^{\text{aq}},}^* (DL) \approx \frac{c_K \delta_m \delta_{Ag^{\text{aq}},}^2 v}{2 D_{Ag^{\text{aq}},} W_{l/2}}
\]  

(17)

If, on the other hand, \(t_s < t_{dl}\), the number of moles released (\(n_{Ag^{\text{aq}}}^m\)) at the peak current can be written according to eq 18. Note that only the first term is kept from eq 14, as the diffusion layer is in continuous growth. It is therefore not necessary to include the diffusion to the sample bulk (Figure 4, case 2).

\[
n_{Ag^{\text{aq}}}^m = \frac{1}{2} (\beta - 1) \delta_{Ag^{\text{aq}},} c_{Ag^{\text{aq}}}^*
\]  

(18)
**Table 1 – Summary of key equations for both regimes.**

<table>
<thead>
<tr>
<th>Mass Transport Regime((\alpha&lt;1))</th>
<th>Condition</th>
<th>Expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ \delta^{eq}<em>{Ag^+} \leq 2 \sqrt{D^{eq}</em>{Ag^+} \frac{2(E_{peak} - E_{initial})}{v}} ]</td>
<td>[ \alpha = \frac{2D^{eq}<em>{Ag^+}c^*</em>{Ag^+} (E_{peak} - E_{initial})}{\delta^{eq}<em>{Ag^+} v} + \frac{\delta^{eq}</em>{Ag^+} c^*_{Ag^+}}{4} ]</td>
<td></td>
</tr>
<tr>
<td>[ \delta^{eq}<em>{Ag^+} &gt; 2 \sqrt{D^{eq}</em>{Ag^+} \frac{2(E_{peak} - E_{initial})}{v}} ]</td>
<td>[ \alpha = \frac{c^<em><em>{Ag^+} \sqrt{D^{eq}</em>{Ag^+} \frac{2(E_{peak} - E_{initial})}{v}}}{\delta^{eq}_{Ag^+} c^</em>_{R^+}} ]</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thin Layer Regime ((\alpha=1))</th>
<th>Condition</th>
<th>Expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ \delta^{eq}<em>{Ag^+} \leq 2 \sqrt{D^{eq}</em>{Ag^+} \frac{W_{1/2}}{v}} ]</td>
<td>[ \beta = \frac{r_{C^+} \delta^{eq}<em>{Ag^+} v}{D^{eq}</em>{Ag^+} c^<em><em>{Ag^+} W</em>{1/2} + \frac{1}{4} \delta^{eq}_{Ag^+} 2 c^</em>_{Ag^+} v} + 1 ]</td>
<td></td>
</tr>
<tr>
<td>[ \delta^{eq}<em>{Ag^+} &gt; 2 \sqrt{D^{eq}</em>{Ag^+} \frac{W_{1/2}}{v}} ]</td>
<td>[ \beta = \frac{r_{C^+} \delta^{eq}<em>{Ag^+} v}{c^*</em>{Ag^+} \sqrt{D^{eq}<em>{Ag^+} W</em>{1/2}} / v} + 1 ]</td>
<td></td>
</tr>
<tr>
<td>[ \delta^{eq}<em>{Ag^+} \leq 2 \sqrt{D^{eq}</em>{Ag^+} \frac{W_{1/2}}{v}} ]</td>
<td>[ c^*<em>{Ag^+} (DL) = \frac{2c</em>{R^+} \delta^{eq}<em>{Ag^+} v}{\delta^{eq}</em>{Ag^+} 2 v + 4D^{eq}<em>{Ag^+} W</em>{1/2}} ]</td>
<td></td>
</tr>
<tr>
<td>[ \delta^{eq}<em>{Ag^+} \geq 2 \sqrt{D^{eq}</em>{Ag^+} \frac{W_{1/2}}{v}} ]</td>
<td>[ c^*<em>{Ag^+} (DL) \approx \frac{c</em>{R^+} \delta^{eq}<em>{Ag^+} v}{2D^{eq}</em>{Ag^+} W_{1/2}} ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>[ c^*<em>{Ag^+} (DL) = \sqrt{\frac{v}{4D^{eq}</em>{Ag^+} W_{1/2}}} c_{R^+} \delta^{eq}_{m} ]</td>
<td></td>
</tr>
</tbody>
</table>
\( \beta \) can be expressed with eq 18 by replacing \( n_{Ag}^{\beta} = r c_k \delta_m, \delta_{Ag}^{eq} = 2 \sqrt{D_{Ag}}n_{Ag}^{\beta}t_s \) and the stripping time \( (t_s, eq \ 11), \)

\[
\beta = \frac{r c_k \delta_m}{c_{Ag}^{*} \sqrt{D_{Ag}^{\beta} W_{1/2} / v}} + 1 \tag{19}
\]

With \( \beta=2 \) (see results and discussion for the reasoning of choice of \( \beta=2 \)) and \( r=0.5 \) (symmetrical peak), we again describe the limit of detection for the limiting case of unstirred solutions as

\[
c_{Ag}^{*} (DL) = \sqrt{\frac{v}{4D_{Ag}^{\beta} W_{1/2}}} c_{Ag}^{*} \delta_m \tag{20}
\]

Both parameters and detection limits are listed in Table 1 and have been experimentally and theoretically validated for different scenarios.

**Figure 5.** Simulated voltammograms (a) and extracted \( E_{peak} \) vs. \( \log c_{Ag}^{eq} \) (b). Experimental voltammograms (c) and extracted \( E_{peak} \) vs. \( \log c_{Ag}^{eq} \) (d). The semi-empirical conditions are indicated for \( \alpha = 1 \) (red vertical line) and \( \beta = 2 \) (green vertical line) in both b) and d). Note that the red, green and blue dots in b) and d) correspond to the respective voltammograms with the same color in a) and c). The intersection of the dash lines refers to the traditional limit of detection for potentiometric sensors.
4.4 Results and discussion

The significance of this work lies on the description of voltammetric thin layer ionophore-based membrane by using two parameters. One describes the amount of silver in the membrane phase during accumulation ($\alpha$) while the other relates to the concentration of silver at the interface during the stripping process with respect to the bulk concentration ($\beta$).

As described by eq 7, the saturation of the membrane dictates the change of the regime. To demonstrate this, a simulation using finite difference method (see Chapter 3) was performed for higher concentration of silver (between $10^{-5}$ to $10^{-3}$ M) assuming a diffusion layer thickness of 400 µm, thereby describing an experimental situation of neither stirring nor rotation. Figure 5a shows the calculated voltammograms for various concentration of silver, whereas Figure 5b corresponds to the calibration curve of the extracted potentials at the maximum peak current as a function of the logarithmic silver concentration. When the membrane was saturated (red line in Figure 5a or red dot in Figure 5b), the peak potentials were indeed displaced to more positive positions with increasing silver concentrations. This condition was equally obtained for $\alpha=1$.

The calculated limit of detection according to the IUPAC recommendations for potentiometric sensors is the intersection of Nernstian segment of the calibration curve and the extrapolated background signal. Mathematically, this point deviates from ideal Nernstian behavior by $RT/zF \times \ln 2$, or $59.2/z \times \log 2$ at 298 K, where $z$ is the valency of the ion of interest. If the detection limit is given by concentration polarization, as in the present case, then it is reached with surface concentration that exhibits a factor 2 deviation from the bulk value. This case coincides with the concentration calculated with $\beta=2$ (See Figure SI-1 for $\beta$ at detection limit). This relationship permits one to predict the detection limit of the sensor in the potentiometric mode using eq. 16, 17 or eq 20. To confirm the appropriate prediction of the saturation and detection limit parameters, experimental curves have been plotted in Figure 5c,d. A negligible deviation between the experimental detection limit and the calculated one with $\beta=2$ (eq 20, less than 2%, see SI for details of calculation) corroborates the usefulness of the proposed approach. It should be noted that the discrepancy in the limit of detection between Figures 5b,d is due to the peak width (which is attributed to the electrochemical behavior of the conducting polymer) and does not affect the prediction of $\alpha$ and $\beta$.

Figure 6 shows three experimental voltammetric responses in the thin-layer regime at different rotation speeds. As expected, the limit of detection as well as the linear range is improved by ~1 order of magnitude from non-stirring conditions to stirring conditions (1600 rpm). The limit
of detection for each calibration curve was also predicted by eq 16 (See SI of calculation details) and was in agreement with the experimental set of data.

**Figure 6.** Effect of rotation speed in the limit of the detection at the thin layer regime. The dashed lines refer to the calculated detection limit with $\beta = 2$.

Figure 7a displays the degree of saturation ($\alpha$) as a function of the concentration of silver in the sample phase for four different diffusion layer thicknesses (400, 50, 10 and 2 µm). The solid lines represent the semi-empirical treatment whereas the markers correspond to the numerical simulation. For concentration higher than 20 µM (blue dots, $\delta_{aq}=400\mu$m), $\alpha$ becomes equal to 1, which in addition indicates the saturation of the membrane and the transition from one mode to the other. With this diffusion layer thickness ($\delta_{aq}=400\mu$m, corresponding to non-stirring or non-rotation experimental conditions), $t_s < t_{dt}$, and therefore, eq 9 was used for the blue line, which accounts for exactly half the amount of silver ($\frac{1}{2}c_{Ag}^{aq} \delta_{aq}$) depleted in the whole diffusion layer with an assumption of bulk concentration level in the diffusion layer prior to the accumulation process. The deviation between the dots and the solid line indicates that the simplified treatment was less accurate because the concentration profile must be dynamic and not a constant bulk value before the backward scan starts (see Figure S6, Chapter 3).

By decreasing the diffusion layer thickness (e.g., experiments with rotating disk electrodes) down to 2 µm, the whole curve shift to lower concentrations. This suggests that the condition of saturation is fulfilled at lower sample concentrations of silver because mass transport is enhanced. In these cases, the flux $J_1$ dominates the amount of silver accumulated in the membrane (eq 5), making the result less dependent on the concentration profile in the diffusion
layer prior to accumulation. This makes the semi-empirical treatment more accurate (see Tables in *Supporting Information* for more numerical comparisons).

![Figure 7](image)

**Figure 7.** Simulated (markers) and calculated (solid lines) parameters ($\alpha$ and $\beta$ as a function of $\log c_{Ag^{+}}$) at four diffusion layer thicknesses. a) Dashed lines refers to the concentration of silver that fulfil the condition of $\alpha=1$. b) Dashed vertical lines and dotted horizontal lines refer to the concentration of silver that fulfill the condition of $\alpha=1$ and the limit of detection ($\beta = 2$) respectively.

Figure 7b shows the dependence of $\beta$ on the concentration of silver in the sample phase at the same four diffusion layer thicknesses as shown in Figure 7a. The solid line represents the semi-empirical function for $\beta$ whereas the markers are from the simulation (Chapter 3). The lines at 400 µm and 50 µm overlap with each other due to very closely calculated results. As stated in the theory section, $\beta$ has a chemical meaning once $\alpha$ is equal to 1, and for this reason, the simulation and the simplified treatment correspond well in such a concentration interval. Note that for the right most curve (corresponding to an experiment without any rotation or stirring), the first value that satisfies $\alpha$ equal to 1, $\beta$ is around 4. This roughly indicates that the concentration at the membrane/sample interface was 4 times greater than in the bulk solution. By contrast, at higher concentrations (~10 mM), $\beta$ reaches a value of 1, which confirms the assumption in our two recent papers that no depletion or enrichment occurs at the membrane.
surface relative to the sample bulk. As the diffusion layer thickness decreases (in the case of rotating the electrode), \( \beta \) curves also shift to the left, just like \( \alpha \).

Note that the simulated values agree well with the semi-empirical treatment at relatively large diffusion layer thicknesses (blue marker, in this case eq 19 with \( \delta_{aq}=400\mu m \) and green marker, eq 15 with \( \delta_{aq}=50\mu m \) were used). On the other hand, the simulated values are slightly larger than those from the semi-empirical treatment at relatively small diffusion layer thicknesses (black and red markers, in this case only eq 15 was used). This can be explained from the assumption of constant flux \( J_2 \) for the derivation of \( \beta \), which is not strictly correct for \( t_{dl} \) much smaller than \( t_s \). The simulated plateau (blue and green markers) at low silver concentrations was not predicted by the semi-empirical treatment. Here, \( \alpha \) was always equal to 1, which is not a realistic assumption when the silver concentration is very low.

Having introduced the importance of both parameters and their reasonable agreement to the simulated results, a limit of detection for the thin layer regime is predicted as a function of aqueous diffusion layer thickness and scan rate for different concentrations of cation exchanger in the membrane phase. The results from the two cases described by eq 16 and eq 20 are shown for a range of variables in Figure 8.

Figure 8a shows the calculated logarithmic values of the limit of detection as a function of logarithmic diffusion layer thickness at four different cation exchanger concentrations. The detection limit remains constant when the diffusion layer thickness was larger than a critical value (red line, \( \delta_{aq}=58\mu m \)) and starts to decrease with smaller diffusion layer thickness. At a thickness of \( \delta_{aq}=2\mu m \) (blue line, very high rotation speed, more than 7200rpm), the limit of detection would be reduced by around 1.5 orders of magnitude.

The logarithmic value of the limit of detection as a function of scan rate was also calculated, see Figure 8b. The blue and red lines indicate scan rates of 10 mV s\(^{-1}\) and 200 mV s\(^{-1}\) respectively. By reducing the scan rate down to 10 mV s\(^{-1}\), the limit of detection may be reduced by 1 order of magnitude. In both figures (Figure 8a,b), the detection limits were reduced by 1 logarithmic unit as the concentration of cation exchanger decreases by 1 order of magnitude.

As pointed out in our previous work, a lower amount of 0.5 mM of cation exchanger resulted in a remarkable deterioration of the signal. Therefore, the cation exchanger concentration cannot be indiscriminately decreased as the idealized representation shown in Figure 8a,b. Accordingly, these three experimental conditions may be optimized for yielding a minimum detection limit if desired, which is expected to be reasonably achievable in the sub-micromolar concentration range.
Figure 8. Calculated limit of detections at several experimental conditions: a) as a function of the logarithmic value of diffusion layer thickness ($\delta_{aq}$) at four different concentrations of cation exchanger ($c_R$); b) as a function of logarithmic value of the scan rate at four different concentrations of cation exchanger ($c_R$). The cation exchanger concentrations are indicated on each curve.

4.5 Conclusions

We demonstrate here the theoretical prediction of the operational regime for ion transfer processes within voltammetric thin-layer ionophore-based films. While diffusional mass transport controls the process at low ion analyte concentrations, the thin layer regime was found to occur at high concentrations. The transition between these two regimes was described by defining two parameters ($\alpha$ and $\beta$) that evaluate both the silver content in the membrane prior to stripping and the ratio of the silver amount at the membrane/aqueous interface with respect to the bulk concentration, respectively. The derived equations for these parameters allow one to predict the silver concentration at which the transition occurs (for $\alpha=1$). On the other hand, the calculated concentration for $\beta=2$ coincided with the limit of detection of the electrode for its use as a potentiometric sensor. The limit of detection could be predicted with $\beta=2$ as a function of scan rate, diffusion layer thickness, and amount of cation exchanger in the thin layer membrane. Further work will be focused on the optimization of these parameters for
obtaining the lowest detection limit with multi-analyte detection based on multi-ionophore membranes.

4.6 Supporting information

4.6.1 Tables

Table SI-1. Calculated α and β values at a diffusion layer thickness of 400μm

<table>
<thead>
<tr>
<th>Silver concentration(M)</th>
<th>( \alpha ) Calculated from simulation</th>
<th>( \alpha ) Calculated from eq 9</th>
<th>( \beta ) Calculated from simulation</th>
<th>( \beta ) Calculated from eq 19</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.74 x 10^{-6}</td>
<td>0.1533</td>
<td>0.1002</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6.83 x 10^{-6}</td>
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<td>0.2494</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1.37 x 10^{-5}</td>
<td>0.7300</td>
<td>0.5002</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2.00 x 10^{-5}</td>
<td>0.8700</td>
<td>0.7301</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2.74 x 10^{-5}</td>
<td>1.0000</td>
<td>1.0000</td>
<td>3.8030</td>
<td>3.5203</td>
</tr>
<tr>
<td>6.90 x 10^{-5}</td>
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<td>1</td>
<td>1.9460</td>
<td>2.0024</td>
</tr>
<tr>
<td>1.00 x 10^{-4}</td>
<td>1</td>
<td>1</td>
<td>1.6540</td>
<td>1.6916</td>
</tr>
<tr>
<td>1.00 x 10^{-3}</td>
<td>1</td>
<td>1</td>
<td>1.0670</td>
<td>1.0684</td>
</tr>
<tr>
<td>1.00 x 10^{-2}</td>
<td>1</td>
<td>1</td>
<td>1.0070</td>
<td>1.0070</td>
</tr>
</tbody>
</table>
Table S1-2. Calculated $\alpha$ and $\beta$ values at a diffusion layer thickness of 50$\mu$m

<table>
<thead>
<tr>
<th>Silver concentration (M)</th>
<th>$\alpha$ Calculated from simulation</th>
<th>$\alpha$ Calculated from eq 8</th>
<th>$\beta$ Calculated from simulation</th>
<th>$\beta$ Calculated from eq 15</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.01 x $10^{-6}$</td>
<td>0.0966</td>
<td>0.0974</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2.60 x $10^{-6}$</td>
<td>0.2447</td>
<td>0.2488</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5.25 x $10^{-6}$</td>
<td>0.4876</td>
<td>0.4996</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7.92 x $10^{-5}$</td>
<td>0.7255</td>
<td>0.7504</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1.06 x $10^{-5}$</td>
<td>0.9396</td>
<td>1.0000</td>
<td>7.2330</td>
<td>7.1119</td>
</tr>
<tr>
<td>6.63 x $10^{-5}$</td>
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<td>1</td>
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</tr>
<tr>
<td>1.00 x $10^{-4}$</td>
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<td>1.7200</td>
<td>1.6684</td>
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<tr>
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</tr>
<tr>
<td>1.00 x $10^{-2}$</td>
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<td>1.0070</td>
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</tr>
</tbody>
</table>
### Table S1-3. Calculated $\alpha$ and $\beta$ values at a diffusion layer thickness of 10$\mu$m

<table>
<thead>
<tr>
<th>Silver concentration (M)</th>
<th>$\delta_{d_{eq}} = 10\mu$m</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\alpha$</td>
</tr>
<tr>
<td></td>
<td>Calculated from simulation</td>
</tr>
<tr>
<td>1.00 x 10$^{-8}$</td>
<td>0.0000</td>
</tr>
<tr>
<td>1.00 x 10$^{-7}$</td>
<td>0.0432</td>
</tr>
<tr>
<td>1.00 x 10$^{-6}$</td>
<td>0.432</td>
</tr>
<tr>
<td>1.44 x 10$^{-6}$</td>
<td>0.6172</td>
</tr>
<tr>
<td>2.50 x 10$^{-6}$</td>
<td>0.9907</td>
</tr>
<tr>
<td>5.00 x 10$^{-6}$</td>
<td>1</td>
</tr>
<tr>
<td>1.00 x 10$^{-5}$</td>
<td>1</td>
</tr>
<tr>
<td>1.00 x 10$^{-4}$</td>
<td>1</td>
</tr>
<tr>
<td>1.00 x 10$^{-3}$</td>
<td>1</td>
</tr>
</tbody>
</table>
Table SI-4. Calculated $\alpha$ and $\beta$ values at a diffusion layer thickness of 2μm

<table>
<thead>
<tr>
<th>Silver concentration (M)</th>
<th>$\delta_{Ag}^{eq} = 2\mu m$</th>
<th>$\alpha$</th>
<th>$\beta$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Calculated from simulation</td>
<td>Calculated from eq 8</td>
<td>Calculated from simulation</td>
</tr>
<tr>
<td>1.00 x 10^{-8}</td>
<td>0.0246</td>
<td>0.0246</td>
<td>-</td>
</tr>
<tr>
<td>4.95 x 10^{-8}</td>
<td>0.1164</td>
<td>0.1218</td>
<td>-</td>
</tr>
<tr>
<td>1.00 x 10^{-7}</td>
<td>0.2404</td>
<td>0.2459</td>
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</tr>
<tr>
<td>2.45 x 10^{-7}</td>
<td>0.6149</td>
<td>0.6022</td>
<td>-</td>
</tr>
<tr>
<td>4.03 x 10^{-7}</td>
<td>0.9919</td>
<td>0.9926</td>
<td>18.3681</td>
</tr>
<tr>
<td>4.96 x 10^{-7}</td>
<td>1</td>
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</tr>
<tr>
<td>1.00 x 10^{-6}</td>
<td>1</td>
<td>1</td>
<td>7.6090</td>
</tr>
<tr>
<td>1.00 x 10^{-5}</td>
<td>1</td>
<td>1</td>
<td>1.6880</td>
</tr>
<tr>
<td>1.00 x 10^{-4}</td>
<td>1</td>
<td>1</td>
<td>1.0750</td>
</tr>
</tbody>
</table>
Table SI-5. Peak parameters for sodium and silver peaks shown in Figure 5c (n=5, consecutive scans).

<table>
<thead>
<tr>
<th>$c_{\text{Ag}}$ (M)</th>
<th>$q_{\text{Na peak}}$ (µC)</th>
<th>$q_{\text{Ag peak}}$ (µC)</th>
<th>$q_{\text{total}}$ (µC)</th>
<th>$\Delta E$ (f-b) (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1×10^{-5}</td>
<td>1.237</td>
<td>1.779</td>
<td>3.012</td>
<td>31.7</td>
</tr>
<tr>
<td>2.5×10^{-5}</td>
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<td>3.466</td>
<td>3.466</td>
<td>70.4</td>
</tr>
<tr>
<td>5×10^{-5}</td>
<td>0</td>
<td>3.596</td>
<td>3.597</td>
<td>90.1</td>
</tr>
<tr>
<td>1×10^{-4}</td>
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<td>3.428</td>
<td>3.428</td>
<td>83.2</td>
</tr>
<tr>
<td>2.5×10^{-4}</td>
<td>0</td>
<td>3.463</td>
<td>3.463</td>
<td>71.4</td>
</tr>
</tbody>
</table>

$^a$ 10 mM NaNO$_3$ background solution. f=forward; b=backward scan.

4.6.2 Calculations

4.6.2.1 Critical concentration of silver for $\alpha = 1$:

For a silver concentration of 10$^{-5}$ M, $\alpha$ was calculated as 0.59 (from experimental data shown in Table SI-5, ($\alpha = q_{Ag}/q_{total}$). Therefore, the critical silver concentration corresponds to the saturation of the membrane ($\alpha = 1$) and was calculated as $c_{\text{critical}}^* = 1.69 \times 10^{-5}$ M, considering the relationship between $\alpha$ and $c_{\text{Ag}}^*$.

4.6.2.2 Semi-empirical calculation of the limit of detection at different rotation speeds

$$c_{\text{Ag}}^*(DL) = \frac{2c_K \delta_m \delta_{\text{aq}}^2}{4D_{\text{m}}^* W_{1/2}} \delta_{\text{aq}}^2 v + 4D_{\text{m}}^* W_{1/2} \delta_{\text{aq}}^2 \delta_m$$  \hspace{1cm} (eq 16) \hspace{1cm} ($\delta_{\text{aq}}^2 \leq 2 D_{\text{m}}^* W_{1/2} / v$)

$$c_{\text{Ag}}^*(DL) = \sqrt{\frac{v}{4D_{\text{m}}^* W_{1/2}}} c_K \delta_m$$  \hspace{1cm} (eq 20) \hspace{1cm} ($\delta_{\text{aq}}^2 > 2 D_{\text{m}}^* W_{1/2} / v$)

The diffusion layer thickness is calculated according to Levich equation$^1$

$$\delta_{\text{aq}}^2 = 1.61 D_{\text{Ag}}^* \frac{1/3}{\omega^{1/2} \eta^{1/6}}$$  \hspace{1cm} (S1)

with $D_{\text{Ag}}^* = 1.70 \times 10^{-5}$ cm$^2$s$^{-1}$, $\omega = 0$, 100 and 1600 rpm and $\eta = 1.004 \times 10^{-4}$ m$^2$s$^{-1}$ at 20 ℃. The concentration of cation exchanger and thickness of the thin layer membrane (estimated by
ellipsometry\(^2\) are: \(c_{x^v} = 1.5 \times 10^{-2} \text{M} \) and \(\delta_m = 2.3 \times 10^{-6} \text{dm} \). The extracted half peak width is approximate to \(W_{1/2} = 0.3094 \text{ V} \) (see Figure 5c) and the scan rate is \(v = 0.1 \text{ V s}^{-1} \).

The criteria for either choosing eq.16 or choosing eq.20 is as follows:

\[
2\sqrt{D^{w_c}_v \cdot W_{1/2}} / v = 145 \text{ \(\mu\)m} \\
\text{(S2)}
\]

(i) \(0 \text{ rpm (no rotation)}\)

The diffusion layer thickness was around 400 \(\mu\)m, therefore eq 20 was used.

\[
c_{x^v}^{\ast} (LD) = 2.37 \times 10^{-5} \text{M} \\
\text{(S3)}
\]

(ii) \(100 \text{ rpm}\)

The calculated diffusion layer thickness was 59.4 \(\mu\)m, therefore eq 16 was used.

\[
c_{x^v}^{\ast} (LD) = 1.66 \times 10^{-5} \text{M} \\
\text{(S4)}
\]

(iii) \(1600 \text{ rpm}\)

The calculated diffusion layer thickness was 14.8 \(\mu\)m, therefore eq 16 was used.

\[
c_{x^v}^{\ast} (LD) = 4.82 \times 10^{-6} \text{M} \\
\text{(S5)}
\]
4.6.3 Figures

**Figure SI-1.** Calculated concentration profiles for silver in the aqueous phase for a bulk concentration equal to the limit of detection (see Figure 5b in main manuscript). Inset: corresponding cyclic voltammogram. The blue line is the concentration profile before the peak starts while the red line is the concentration profile at the peak position (β coincides with value of 2 at peak position).

4.7 References

(22) Yuan, D.; Cuartero, M.; Crespo, G. A.; Bakker, E. 2016, Submitted as Part I.
Chapter 5 Probing Ion-Ionophore Interactions in Thin Layer Polymeric Membranes

This work is in preparation for publication in Anal. Chem.

Abstract

Ion-selective membranes of submicrometer thickness, backside contacted with an ion to electron transducing layer such as poly(3-octylthiophene) are attractive tools to electrochemically probe ion–ionophore interactions. It is shown here that a simple voltammetric scan gives direct information on complex stoichiometry, complex formation constants, and selectivity coefficient as a function of ion-exchanger. These are key data in the field of ion sensors based on molecular receptors that in the past required tedious and often error prone experiments. As diffusion kinetics are sufficiently rapid in the time scale of a voltammetric scan, thin membrane systems can in ideal cases be described with thermodynamic theory. Indeed, oxidation of the underlying transducing layer is accompanied by the removal of cation-exchanger sites in the overlaying sensing membrane so that the resulting charge can be understood in analogy to the controlled dosing of ion-exchanger. The main challenge with this approach is the poorly understood electrochemical behavior of the underlying transducing layer. It is here overcome by recording the behavior of the membrane towards a bulky reference ion, tetrabutylammonium. This cation exhibits voltammetric phase transfer that is well described theoretically and confirmed experimentally to be independent of ionophore. This information is used to arrive at a relationship between charge and potential for the transducing layer alone, which is then subtracted in subsequent experiments from the experimental cell potential. This allows one to describe, in a single linear scan, the change in phase boundary potential as a function of ion-exchanger concentration. The principle is put forward with valinomycin as model ionophore but thought to be readily applicable to a wide range of other molecular receptors that exhibit reversible binding kinetics.
5.1 Introduction

Ion-selective membranes (ISMs) are based on a matrix normally composed of polymer and plasticizer, lipophilic ion exchanger and selective ion receptor (ionophore).\textsuperscript{1} Ionophore-free membranes always show the same selectivity pattern in the order of hydration energy. Distinctly different selectivity may be observed in the presence of a lipophilic molecular receptor (ionophore), driven by the complex formation constants between the extracted ion and the ionophore.\textsuperscript{2} Ion-ionophore complexation constants often dramatically differ from those observed in bulk solution as obtained spectroscopically (NMR titrations), owing to the specific solvent environment of ion-selective membranes.\textsuperscript{3,4}

Scheme 1. Working mechanism of thin layer membrane containing ionophore valinomycin forward linearly scanned in tetrabutylammonium ion solution a) or b) in M\textsuperscript{+} solution (M\textsuperscript{+}=K\textsuperscript{+} or Na\textsuperscript{+}). L does not interact with TBA\textsuperscript{+} but with M\textsuperscript{+}. GC=Glassy Carbon; ISM=Ion Sensing Membrane; POT=poly(3-octylthiophene); R = lipophilic cation exchanger; L=Ionophore; TBA\textsuperscript{+}= tetrabutylammonium ion; A=Anion. $\Delta \phi_{POT}$ is the potential associated to POT oxidation; $\Delta_{\text{aq}}^{\text{m}} \Phi_{TBA^+}$ and $\Delta_{\text{aq}}^{\text{m}} \Phi_{M^+}$ are the Galvani potential differences for the transfer of TBA\textsuperscript{+} and M\textsuperscript{+}, respectively.

The optimum molar ratio of ionophore to ion exchanger in the membrane depends on the complex stoichiometries, with a selectivity modifying influence that can be quite dramatic.\textsuperscript{5} Some ionophores also may form mixed complexes and the optimal ratio will depend on the relative strength of the resulting complexes.\textsuperscript{6-8}
Only a limited number of experimental techniques are available to assess ion-ionophore complex formation constants directly in the membrane,\textsuperscript{9-12} of which the sandwich membrane approach is perhaps the most widely used.\textsuperscript{10} This method is based on the potential measurement of a two-layer sandwich membrane, where only one side contains the ionophore, mounted in an ion-selective electrode (ISE) of the inner solution type. The initial potential of the asymmetric membrane reflects the ion activity ratio at both membrane-aqueous interfaces (inner filling solution|membrane|sample solution), and this is used to calculate ion-ionophore complex formation constants.\textsuperscript{13} The principle of the approach rests on the effective uncoupling of both phase boundary potentials by inducing a well-defined initial ion concentration profile in the membrane.\textsuperscript{13} While the method is quite precise and accurate, it is experimentally tedious as it gives just a single data point per experimental run, each reflecting just one membrane composition. Alternatively, membranes have also started to be characterized by dynamic electrochemistry, for example by controlling current (pulstrodes) to achieve instrumentally tunable selectivity,\textsuperscript{14} but this approach is less robust as the current signal is limited by membrane mass transport kinetics.

Recently, relatively thin ISMs on the order of one micrometer or less and backside contacted with a conducting polymer have been introduced.\textsuperscript{12,15} Their voltammetric response has been theoretically modelled,\textsuperscript{12,16} showing that under optimal experimental conditions the influence of mass transport on the current response can be eliminated. Such systems are in principle promising tools to characterize ion–ionophore interactions in ion-selective membranes,\textsuperscript{15} because a local electrochemical equilibrium may be imposed at each applied potential within a linear scan. This corresponds to an electrochemical dosing of ionic reagents, affording an exquisite level of information with a single scan. Unfortunately, this is only possible if one has quantitative information on the potential contribution of the inner transducing as a function of extent of charge conversion. Earlier work assumed simply a linear relationship between charge and potential change for the conducting polymer layer.\textsuperscript{12} Unfortunately, this assumption is likely not adequate for quantitative work as it lacks a rigorous experimental confirmation. It is also not extendable to other transducing materials such as lipophilic redox probes.\textsuperscript{17,18}

We put forward here a new approach that allows for a more accurate isolation of the sample–membrane boundary potential from the overall cell potential. This should allow one to assess ion–ionophore interactions as a function of ion loading in a single
voltammetric scan and hence may become a powerful and convenient method for such studies.

5.2 Experimental section

5.2.1 Reagents, materials and equipment.

Aqueous solutions were prepared by dissolving the appropriate salts in deionized water (>18 MΩ cm). Lithium perchlorate (>98%, LiClO4), 3-octylthiophene (97%, OT), potassium chloride (KCl, ≥99.5%), sodium chloride (NaCl, ≥99.5%), tetrabutylammonium sulfate solution (50 wt.% in H2O), high molecular weight poly(vinyl-chloride) (PVC), polyurethane pellet (PU, SelectophoreTM), bis(2-ethylhexyl)sebacate (DOS), sodium tetrakis[3,5-bis-(trifluoromethyl)phenyl]borate (NaTFPB), potassium ionophore I (Valinomycin), acetonitrile (ACN) and tetrahydrofuran (>99.9 %, THF) were purchased from Sigma Aldrich.

GC-electrode tips (6.1204.300) with an electrode diameter of 3.00 ± 0.05 mm were sourced from Metrohm (Switzerland). Cyclic voltammograms were recorded with a PGSTAT 101 (Metrohm Autolab B.V., Utrecht, The Netherlands) controlled by Nova 1.11 software (supplied by Autolab) running on a PC. A double-junction Ag/AgCl/3M KCl/1 M LiOAc reference electrode (6.0726.100 model, Metrohm, Switzerland) and a platinum electrode (6.0331.010 model, Metrohm, Switzerland) were used in the three-electrode cell. A rotating disk electrode (Autolab RDE, Metrohm Autolab B.V., Utrecht, The Netherlands) was used to spin coat the thin membranes on the POT modified electrodes at 1500 rpm. A 16-channel EMF interface (Lawson Laboratories, Inc., Malvern, PA) was used for potentiometric measurements. Wolfram Mathematica® 9 software was used to develop the theory and the final data fit.

5.2.2 Preparation of electrodes based on thin membranes.

Poly(3-octylthiophene) (POT) was electrochemically polymerized on GC surface by cyclic voltammetry (two scans, 0-1.5 V, 100 mV s-1) and then discharged at 0 V for 120 s. A solution containing 0.1 M 3-octylthiophene and 0.1 M LiClO4 in acetonitrile was used. This solution was purged with N2 for 30 min before use. After the electropolymerization of POT, the electrode was immersed in pure acetonitrile for 30 min, to remove the electrolyte, and dried at room temperature for 15 min. The POT underlayer was then coated with 25 uL of the diluted membrane cocktail (dilution of 1:4 in THF). Table S1 shows the compositions of the membrane cocktails (referred to a total weight of 100 mg) prepared in 1mL THF.
5.3 Results and discussion

Figure 1. a) Linear cyclic voltammograms observed in 10mM tetrabutylammonium ion (TBA\(^+\)) with membranes MI (no ionophore) and MII (valinomycin). b) Linear cyclic voltammogram observed in 10mM KCl solution using membrane MII.

Figure 1a shows the linear scans for two different membrane formulations, one with and one without the ionophore valinomycin (MI and MII, see Table S1 for details of membrane compositions), towards aqueous tetrabutylammonium ion (TBA\(^+\), 10 mM). The forward peak is explained with the removal of the anionic tetraphenylborate derivative from the membrane by the conducting polymer being oxidized with increasing potential, thereby becoming positively charged. This is accompanied by an expulsion, by ion transfer, of the tetrabutylammonium ion from the membrane. To clarify, these reactions are schematically shown in Scheme 1a. The exhaustive nature of this process explains the bell-shaped curve of the voltammogram. If an ionophore is present in the membrane that exhibits an affinity to the cation of interest, it moves the observed peak to more positive potentials. It is this shift that forms the basis of the method discussed here.

As shown in Figure 1a, the presence of ionophore has no significant influence on the shape and position of the TBA\(^+\) peak, at 0.8386 ± 0.0169 V (SD, n=3) without and 0.8406 ± 0.0301 V (SD, n=3) with ionophore, respectively. This suggests that the interaction between tetrabutylammonium and valinomycin can be neglected. This ion was used earlier as sterically hindered reference ion in potentiometric studies and the lack of interaction was confirmed with sandwich membrane experiments.\(^{10}\) As the phase boundary potential for this simple case can be most easily predicted, it forms the basis for the uncoupling of the individual potential contributions of the electrochemical cell.
The approach is experimentally illustrated for tetrabutylammonium in Figure S1a and Figure 2. Figure S1a represents the baseline corrected forward linear scan for tetrabutylammonium that describes electrochemical turnover as a function of applied oxidative potential. The data needs to be represented as a function of ionic concentration, which requires the integration of the current with time to give relative charge, q, as given in Figure 2a (see eq S3 for integration). With the ion to electron transducer used here, zero charge corresponds to the initial cation-exchanger concentration, \( c_{R^-}^{m,0} \), while the maximum charge (q = 1) scales to a zero concentration. As shown in the Supporting Information, this relationship is written as

\[
c_{R^-}^{m} = c_{R^-}^{m,0} (1-q)
\]  

(1)

where \( c_{R^-}^{m} \) is the available concentration of the cation-exchanger \( R^- \) in the membrane at any applied potential. The transformed data are expressed as cell potential vs. concentration and shown as the top curve in Figure 2b. The theoretical dependence of the boundary potential for the transfer of \( TBA^+ \) as a function of ion-exchanger concentration is now calculated quite readily based on the following Galvani potential relationship:

\[
\Delta_{aq}^m \phi_{TBA^+} (c_{R^-}^{m}) = \Delta_{aq}^m \phi_{TBA^+}^0 + \frac{RT}{F} \ln \frac{c_{aq}^{eq} \text{TBA}^+}{c_{R^-}^{m}}
\]  

(2)

where \( \Delta_{aq}^m \phi_{TBA^+}^0 \) and \( \Delta_{aq}^m \phi_{TBA^+} (c_{R^-}^{m}) \) are the respective standard ion transfer potential and ion transfer potential between membrane and aqueous phase for tetrabutylammonium; R is gas constant; T is absolute temperature and F is faradaic constant; and \( c_{aq}^{eq} \text{TBA}^+ \) is the aqueous concentration of the tetrabutylammonium ion.

This function is plotted as the middle trace in Figure 2b. It may now be subtracted, for each potential, from the experimental data (top trace) to describe the electrochemical behavior of the underlying conducting polymer. It is evident that the potential of this ion to electron transducer exhibits a non-linear relationship with ion-exchanger concentration, and therefore oxidation state. This challenges the simplifying assumptions used earlier\(^\text{19}\) to describe the electrochemistry of the inner transducing layer.
Earlier work found a linear dependence of peak current on the scan rate within a certain range, suggesting that POT oxidation kinetics may be neglected in this surface confined experiment. To further confirm this assumption, a membrane containing only cation exchanger was scanned in 10 mM KCl solution at different scan rates (Figure S2a) and all the forward peaks were likewise transformed into a form of relative charge as a function of potential (Figure S2b) as discussed above. The five curves closely overlap each other with negligible deviation. This suggests that under the selected experimental conditions, POT transducer oxidation is sufficiently rapid to allow for a thermodynamic treatment, allowing one to extract the ion to electron transducer potential function.

The potential–charge relationship related to the ion to electron transducing layer extracted above (bottom trace, Figure 2b) is now used to isolate the process for the transfer for other ions. Figure 1b shows the linear scan for a thin membrane containing molar excess of cation-exchanger over the ionophore valinomycin in contact with aqueous 10 mM KCl solution. As illustrated in Scheme 1b, this composition results in two distinct ion transfer waves, as the removal of cation-exchanger upon oxidation of the ion to electron transducer first expels uncomplexed potassium ion from the membrane and only subsequently the ions bound to ionophore.
Figure 3. a) Plot of integrated relative charge as a function of applied potential for K⁺ in Figure S1b. b) Plot of isolated potential for POT oxidation (top solid trace), experimental applied potential (middle solid trace, ion transfer + POT) and isolated Galvani potential difference (bottom dotted trace) as a function of cation exchanger in the membrane.

Figure S1b shows the baseline corrected forward peak for the linear scan and the observed charge for the entire peak (5.92 μC, integration of the two peaks) is very similar to that for TBA⁺ (6.04 μC, see Figure S1a), as the same cation-exchanger is the limiting reagent in both cases. The normalized charge as a function of the applied potential is shown in Figure 3a. The two distinct ion transfer processes are again clearly visible as consecutive s-shaped responses. The normalized charge is now represented as cation-exchanger concentration (eq 1) and the inversion of the plot results in the middle trace shown in Figure 3b. This allows one to subtract the same relationship for the ion to electron transducing layer extracted in Figure 2 (shown again as top trace in Figure 3b). One arrives now at the desired potential change at just the sample–membrane phase boundary, shown as bottom trace in Figure 3b. The discrete nature of this trace originates from sub-sampling, as the subtracted potentials in the two data sets are not exactly the same. The initial decrease of the phase boundary potential at very low ion-exchanger concentration changes in Figure 3b is thought to originate from small variations of the cation-exchanger concentration between the different samples and is considered an artifact that should not be taken into account for the extraction of binding data. The data are now in analogy to a titration curve, where a potassium salt is consecutively added to the valinomycin contained in the membrane. Once potassium is in excess of valinomycin, the potential decreases drastically, corresponding to an increase of the free potassium concentration.
Quantitative data are extracted by fitting with equilibrium theory, see eqs. S11-S15 in Supporting Information. The model assumes a 1:1 complex stoichiometry for the potassium–valinomycin complex and appropriate mass and charge balances for the membrane phase, together with the phase boundary potential equation, to give:

\[
\begin{align*}
    c_{K}^m &= \frac{\psi(1 + \psi \beta_{ML} + \beta_{ML} L_{tot})}{1 + \psi \beta_{ML}} \\
    \psi &= e^{-\frac{F(\Delta \phi^L_{pot} - \Delta \phi^H_{pot})}{RT}}.
\end{align*}
\]  

with \(\psi\) is the total concentration of ionophore valinomycin in the membrane while \(\beta_{ML}\) is the overall complex formation constant for this 1:1 complex stoichiometry.

The best fit from 3 replicates (separate membranes) gives \(\log \beta_{KL} = 9.58 \pm 0.08\) (SD, \(n=3\)), shown in Figure 4 as solid trace together with the isolated phase boundary potential data. The same procedure was also applied to 10 mM NaCl for the same membrane (see Figure S3 in Supporting Information), with the appropriate traces and data points shown in Figure 4 as well. The associated stability constant is found as \(\log \beta_{NaL} = 5.25 \pm 0.20\) (SD, \(n=3\)). Mixed 1:1 and 1:2 complexes might describe the binding behavior for sodium even better, although this was not pursued in more detail. The values found for the complex formation constants for potassium and sodium in thin membranes compare favorably to those previously reported using sandwich membranes, \(\log \beta_{KL} = 9.86 \pm 0.08\) and \(\log \beta_{NaL} = 5.36 \pm 0.08\) respectively.\(^{13,20}\)
In addition to the obtained complex formation constant, the potential differences between the complete potassium and sodium potential traces provide a direct insight into membrane selectivity, see Figure S4. At concentrations of ion exchanger larger than that of valinomycin, the modest selectivity for potassium reflects its smaller hydration energy (Hofmeister sequence), with a logarithmic selectivity coefficient of -0.58 ± 0.02 (SD, n=3). The best selectivity is found for R_T < L_T, with a corresponding value of -4.74 ± 0.15 (SD, n=3), which agrees with the conventional composition for potassium ion selective membranes.

The approach was also explored for a different membrane material, plasticized polyurethane (PU), which has demonstrated improved robustness compared to the PVC studied above. The phase boundary potential change was extracted by otherwise the exact same procedure (see Supporting Information, Figure S5). It gave smaller values for the formation constants of valinomycin with potassium and sodium, \( \log \beta_{KL} = 8.07 ± 0.05 \) (SD, n=3) and \( \log \beta_{NaL} = 3.53 ± 0.17 \) (SD, n=3). These values were cross-validated with the potentiometric sandwich membrane method (see Supporting Information, Sandwich membrane experiment), giving \( \log \beta_{KL} = 7.94 ± 0.22 \) (SD, n=3) and \( \log \beta_{NaL} = 3.45 ± 0.35 \) (SD, n=3). The decrease in formation constants is understood by the presence of coordinating functional groups in polyurethane that may solvate uncomplexed ions.

5.4 Conclusions

In summary, the approach put forward here may serve as an attractive method for characterizing ion-ionophore interactions. It is able to provide information not only of the complex stoichiometry and the complex formation constant but also the selectivity coefficient of primary ion towards interfering ion for a continuously varying membrane composition. The thin layer membrane configuration here minimizes mass transport limitations and thereby largely simplifies mathematical treatment. Some potential limitations of the approach are noted. It requires materials of sufficient lipophilicity and stability for the experiment. The ion of interest should not exhibit a chemical affinity to the underlying transducing material. For example, anions may interact electrostatically with cationic oxidized POT and have experimentally shown to negatively impact polymer stability. One should experimentally confirm the absence of chemical interaction between ionophore and the selected reference ion. If ion pairing is important, the theoretical model should incorporate this effect. The voltammetric signal may be
kinetically limited by the ion–ionophore recognition as well, in which case the model should be developed accordingly.\textsuperscript{22,23}

5.5 Supporting information

5.5.1 Sandwich membrane experiment

Formation constants of the complex between valinomycin and potassium/or sodium in PU/DOS (1:1) membranes were estimated according to the procedure described for sandwich membranes.\textsuperscript{10,20} Potassium selective membranes were prepared by dissolving 90 mg of PU, 90 mg of DOS, 0.84 mg of NaTFPB and 4.23 mg of valinomycin in 2mL THF. This solution was then poured into a glass ring (22 mm inner diameter) placed on a glass slide and dried overnight at room temperature. Small disks of the obtained membrane were punched and mounted on Ostec electrode bodies (Ostec, Sargans, Switzerland). Blank membranes containing same amounts for PU, DOS and NaTFPB but no valinomycin were also prepared following the same procedure. The membranes were conditioned overnight in either 10 mM KCl or 10 mM NaCl solutions. Inner filling solution of each electrode was exactly the same as for the conditioning.

The potential of the membrane containing the ionophore was first registered in 10 mM KCl (200 rpm of stirring). Then the potential of the sandwich membrane composed of the same ionophore membrane and the blank membrane is registered in the same solution. The observed potential jump is used for the calculation of the valinomycin-K complex formation constant in the PU membrane. The same procedure was followed in 10 mM NaCl for the calculation of valinomycin-Na complex formation constant in the PU membrane.

5.5.2 Supporting theory

The following theoretical approach is applied for the anodic scan of voltammetric waves for a cation transfer process in ionophore-based thin layer membranes. The applied potential $E_{\text{app}}(t)$ is assumed to be based on two contributions, namely, the phase boundary potential corresponding to the ion transfer across the membrane/aqueous interface, $\Delta_a \phi_{M^+}(t)$, and the potential associated to the oxidation of the POT underlayer, $\Delta \phi_{POT}(t)$.

$$E_{\text{app}}(t) = \Delta_a \phi_{M^+}(t) + \Delta \phi_{POT}(t)$$

(S1)

Since the available concentration of the lipophilic part of the cation exchanger ($R^-$) in the membrane depends on the applied potential because $R^-$ stabilizes the gradual oxidation of POT to POT$^+$, equation S1 is rewritten as a function of $c_{R^-}^m$. 

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\[ E_{\text{app}}(c_R^m) = \Delta_m^{\text{aq}} \phi^0_{M^+} (c_R^m) + \Delta \phi_{\text{POT}} (c_R^m) \]  
\hspace{1cm} (S2)

where \( c_R^m \) is the available concentration of cation exchanger in the membrane.

5.5.2.1 Conversion of the experimental \( i - E_{\text{app}} \) curve into \( q - E_{\text{app}} \) curve.

After the baseline correction of the experimental voltammogram (\( i - E_{\text{app}} \) curve), this is converted into the \( q - E_{\text{app}} \) curve (coulouvammogram) using equation S3.

\[ q = \int_{t_1}^{t_2} i \, dt / \int_{t_1}^{t_2} i \, dt \]  
\hspace{1cm} (S3)

where \( t_1 \) is the time when the peak starts, \( t_2 \) is the time when the peak ends and \( t \) is a time variable between \( t_1 \) and \( t_2 \). Note that a relative charge is defined by considering the total charge of the peak.

5.5.2.2 Conversion of \( q - E_{\text{app}} \) curve into \( E_{\text{app}} - c_{R^-} \) curve.

Thereafter, \( q - E_{\text{app}} \) is converted into \( E_{\text{app}} - c_{R^-} \) curve using equation S4, which considers that the available concentration of \( R^- \) in the membrane (\( c_{R^-}^m \)) depends on the charge transferred across the membrane/aqueous interface that is in turn externally controlled by the applied potential:

\[ c_{R^-}^m = c_{R^-}^{m,0} (1 - q) \]  
\hspace{1cm} (S4)

where \( c_{R^-}^{m,0} \) is the total concentration of cation exchanger initially added in the membrane (i.e. 40 mmol kg\(^{-1}\) in our case).

5.5.2.3 Calculation of \( \Delta_{\text{aq}}^{\text{m}} \phi_{\text{TBA}^+} - c_{R^-}^m \) curve and \( \Delta \phi_{\text{POT}} - c_{R^-}^m \) curve for voltammetric TBA\(^+\) peak.

At high TBA\(^+\) concentration (10 mM), the interfacial concentration of TBA\(^+\) is assumed to be constant and equal to the bulk concentration in the aqueous phase. As TBA\(^+\) does not interact with valinomycin (as demonstrated in the main manuscript comparing voltammograms with and without valinomycin), the phase boundary potential is thermodynamically described with the Nernstian equation:

\[ \Delta_{\text{aq}}^{\text{m}} \phi_{\text{TBA}^+} (c_R^m) = \Delta_{\text{aq}}^{\text{m}} \phi_{\text{TBA}^+}^0 + \frac{RT}{F} \ln \frac{c_{\text{TBA}^+}^{\text{aq}}}{c_{\text{TBA}^+}^m} \]  
\hspace{1cm} (S5)

where \( \Delta_{\text{aq}}^{\text{m}} \phi_{\text{TBA}^+}^0 \) and \( \Delta_{\text{aq}}^{\text{m}} \phi_{\text{TBA}^+} (c_R^m) \) are the respective standard ion transfer potential and ion transfer potential between membrane and aqueous phase for tetrabutylammonium; \( R \) is gas
constant, \( T \) is absolute temperature and \( F \) is faradaic constant; \( c_{\text{TBA}^+}^{\text{aq}} \) and \( c_{\text{TBA}^+}^{\text{m}} \) are the concentrations of tetrabutylammonium ion in aqueous phase and membrane phase, respectively. In order to fulfill the electroneutrality condition in the membrane, the membranous \( \text{TBA}^+ \) concentration is always equal to the concentration of \( R^- \):

\[
c_{R^-}^{m} = c_{\text{TBA}^+}^{m}
\]

(S6)

Thus, eq S5 is rewritten as:

\[
\Delta_{\text{aq}}^m \phi_{\text{TBA}^+} (c_{R^-}^m) = \Delta_{\text{aq}}^m \phi_{\text{TBA}^+}^0 + \frac{RT}{F} \ln \frac{c_{\text{TBA}^+}^{\text{aq}}}{c_{K^+}^{m}}
\]

(S7)

This equation is used for the theoretical prediction of the experimental \( \Delta_{\text{aq}}^m \phi_{\text{TBA}^+} - c_{R^-}^m \) curve. The \( \Delta \phi_{\text{POT}} - c_{R^-}^m \) curve is then calculated by subtracting the \( \Delta_{\text{aq}}^m \phi_{\text{TBA}^+} - c_{R^-}^m \) curve to the \( E_{\text{app}} - c_{R^-}^m \) curve:

\[
\Delta \phi_{\text{POT}} (c_{K^+}^m) = E_{\text{app}} (c_{K^+}^m, \text{TBA}^+) - \Delta_{\text{aq}}^m \phi_{\text{TBA}^+} (c_{K^+}^m)
\]

(S8)

5.5.2.4 Calculation of \( \Delta_{\text{aq}}^m \phi_{M^+} - c_{R^-}^m \) curve for voltammetric Na\(^+\) and K\(^+\) peaks.

The \( \Delta_{\text{aq}}^m \phi_{M^+} - c_{R^-}^m \) curves corresponding to the pure transfer of Na\(^+\) and K\(^+\) across the membrane are obtained by subtracting the \( \Delta \phi_{\text{POT}} - c_{R^-}^m \) curve to the corresponding \( E_{\text{app}} - c_{R^-}^m \) curve:

\[
\Delta_{\text{aq}}^m \phi_{\text{Na}^+} (c_{K^+}^m) = E_{\text{app}} (c_{K^+}^m, \text{Na}^+) - \Delta \phi_{\text{POT}} (c_{K^+}^m)
\]

(S9)

\[
\Delta_{\text{aq}}^m \phi_{\text{K}^+} (c_{K^+}^m) = E_{\text{app}} (c_{K^+}^m, \text{K}^+) - \Delta \phi_{\text{POT}} (c_{K^+}^m)
\]

(S10)

5.5.2.5 Theoretical fitting of the experimental \( \Delta_{\text{aq}}^m \phi_{M^+} - c_{R^-}^m \) curve for Na\(^+\) and K\(^+\).

The phase boundary potential at the membrane-aqueous interface is theoretically described by the Nernst equation, since kinetic effects can be totally neglected:

\[
\Delta_{\text{aq}}^m \phi_{M^+} = \Delta_{\text{aq}}^m \phi_{M^+}^0 + \frac{RT}{F} \ln \frac{1}{c_{M^+}^m}
\]

(S11)

where \( c_{M^+}^m \) denotes the “free” ion concentration in the membrane phase (M\(^+\)=Na\(^+\) or K\(^+\)). Note that the aqueous concentration is treated as unity and the resulting systematic errors are all incorporated into the standard ion transfer potential. The mass balance for the ionophore is
given by equation S12, assuming 1:1 stoichiometry for Na\(^+\) and K\(^+\) complexes with valinomycin.

\[ L_{\text{tot}} = c_{ML} + L \]  
(S12)

where \( L_{\text{tot}} \) refers to the total concentration of ionophore initially added in the membrane, \( c_{ML} \) is the concentration of the ML complex and \( L \) is the free concentration of the ionophore in the membrane. In addition, charge balance is also considered:

\[ c_{M}^{m} = c_{ML} + c_{M}^{m}. \]  
(S13)

The complexation constant is traditionally described as following:

\[ \beta_{ML} = \frac{c_{ML}}{c_{M}^{m} \cdot L} \]  
(S14)

Combining equations S11-S14, the following equation is obtained:

\[ c_{R}^{m} = \frac{\psi \left( 1 + \psi \beta_{ML} + \beta_{ML} L_{\text{tot}} \right)}{1 + \psi \beta_{ML}} \]  
(S15)

with \( \psi = e^{\frac{F \left( \Delta_{\text{aq}} \phi_{M} - \Delta_{\text{aq}} \phi_{M'} \right)}{RT}} \). The theoretical fitting of the experimental \( \Delta_{\text{aq}} \phi_{M} - c_{R}^{m} \) curves for Na\(^+\) and K\(^+\) is based on this final equation by modulating the involved parameters.

### 5.5.2.6 Parameters used for the fitting of the experimental \( \Delta_{\text{aq}} \phi_{M} - c_{R}^{m} \) curves.

**a) Thin membrane based on PVC (MII).**

For potassium:

\( L_{\text{tot}}: 0.0142 \text{ mmol kg}^{-1} \); \( \Delta_{\text{aq}} \phi_{M}: -0.813 \text{ V} \); \( \beta_{KL}: 10^{9.50} \); \( R: 8.314 \text{ J K}^{-1} \text{ mol}^{-1} \); \( T: 293.15 \text{ K} \); \( F: 96485 \text{ C mol}^{-1} \);

For sodium:

\( L_{\text{tot}}: 0.0112 \text{ mmol kg}^{-1} \); \( \Delta_{\text{aq}} \phi_{M}: -0.845 \text{ V} \); \( \beta_{NaL}: 10^{5.50} \); \( R: 8.314 \text{ J K}^{-1} \text{ mol}^{-1} \); \( T: 293.15 \text{ K} \); \( F: 96485 \text{ C mol}^{-1} \);

**b) Thin membrane based on PU (MIII).**

For potassium:

\( L_{\text{tot}}: 0.0145 \text{ mmol kg}^{-1} \); \( \Delta_{\text{aq}} \phi_{M}: -0.720 \text{ V} \); \( \beta_{KL}: 10^{8.10} \); \( R: 8.314 \text{ J K}^{-1} \text{ mol}^{-1} \); \( T: 293.15 \text{ K} \); \( F: 96485 \text{ C mol}^{-1} \);

For sodium:
$L_{\text{tot}}$: 0.0124 mmol kg$^{-1}$; $\Delta_{\text{aq}}^{m} \varphi_{M}^{\text{c}}$: -0.720 V; $\beta_{\text{NaL}}$: 10$^{3.70}$; R: 8.314 J K$^{-1}$ mol$^{-1}$; T: 293.15 K; F: 96485 C mol$^{-1}$;

Note that slightly different values of $L_{\text{tot}}$ were used for potassium and sodium due to the following experimental reason. Cyclic voltammograms for these two ions were obtained always in the same order, first sodium and then potassium, changing the solution for each experiment. As is already known, thin membranes based on PVC suffer from response deterioration when facing rinsing process (the change of solution somehow provokes the same effect) due to the leaching of the cation exchanger from the membrane. Thus, the amount of the cation exchanger may be slightly lower in the experiment of potassium and therefore the total integrated charge (sum of the two peaks corresponding to the cation transfer mediated or not by valinomycin) is also lower. This is reflected also in the $\Delta_{\text{aq}}^{m} \varphi_{M}^{\text{c}} + c_{\text{c}}^{\text{m}}$ curves (Figure 4 in the main manuscript), where the inflexion point of the potassium curve is placed at a little bit higher $c_{\text{c}}^{\text{m}}$ than for sodium.

### 5.5.3 Tables

**Table S1.** Composition of the membrane cocktails referred to a membrane total weight of 100 mg.

<table>
<thead>
<tr>
<th>components</th>
<th>membrane</th>
<th>PVC$^{[a]}$</th>
<th>PU$^{[a]}$</th>
<th>DOS$^{[a]}$</th>
<th>NaTFPB$^{[b]}$</th>
<th>Valinomycin$^{[b]}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>31</td>
<td>63</td>
<td>40</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>31</td>
<td>63</td>
<td>40</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>47</td>
<td>47</td>
<td>40</td>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[a] Mass percentage. [b] mmol kg$^{-1}$
5.5.4 Figures

Figure S1. Baseline corrected forward scan a) of voltammogram for TBA$^+$ ion that was shown as solid line in Figure 1a and b) of voltammogram for K$^+$ ion that was shown in Figure 1b.

Figure S2. a) Cyclic voltammograms of membrane MI observed in 10 mM KCl with different scan rates (ν): 10 mV s$^{-1}$, 25 mV s$^{-1}$, 50 mV s$^{-1}$, 100 mV s$^{-1}$, 200 mV s$^{-1}$. b) Plot of integrated relative charge of forward scan peak as a function of applied potential from five different scan rates voltammograms of a). The five curves are closely overlapped with each other.
Figure S3. a) Linear cyclic voltammogram of membrane MII scanned in 10mM NaCl Solution. b) Baseline corrected forward peak of voltammogram shown in a). c) Plot of the integrated relative charge as a function of applied potential. d) Plot of isolated potential for POT oxidation (top solid trace), experimental applied potential (middle solid trace, ion transfer+POT) and isolated galvani potential difference (bottom dotted trace) as a function of cation exchanger in the membrane.
Figure S4. Logarithmic selectivity coefficient value of potassium towards sodium as a function of ratio of amount of cation exchanger against ionophore. This curve was derived by subtraction of fitted potassium curve with fitted sodium curve in Figure 4.

Figure S5. a) Voltammograms observed in 10 mM solution of Na⁺, K⁺ and TBA⁺ salts using a thin membrane containing 40 mmol kg⁻¹ of cation exchanger and 10 mmol kg⁻¹ of the potassium ionophore valinomycin (MIII in Table S1). (b) Theoretical fitting of the ion transfer curve for potassium and sodium, isolated from experiments shown in a).
5.6 References

(9) Nazarov, V. A.; Andronchik, K. A.; Egorov, V. V.; Matulis, V. E.; Ivashkevich, O. A. Electroanalysis 2011, 23, 1058-1066.
Chapter 6 Overcoming Pitfalls in Boundary Elements Calculations with Computer Simulations of Ion Selective Membrane Electrodes

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**Abstract**

Finite difference analysis of ion-selective membranes is a valuable tool for understanding a range of time dependent phenomena such as response times, long and medium term potential drifts, determination of selectivity and (re)conditioning kinetics. It is here shown that an established approach based on the diffusion layer model applied to an ion-exchange membrane fails to use mass transport to account for concentration changes at the membrane side of the phase boundary. Instead, such concentrations are imposed by the ion-exchange equilibrium condition, without taking into account the source of these ions. The limitation is illustrated with a super-Nernstian potential jump, where a membrane initially void of analyte ion is exposed to incremental concentrations of analyte in the sample. To overcome this limitation, the two boundary elements, one at either side of the sample–membrane interface, are treated here as a combined entity and its total concentration change is dictated by diffusional fluxes into and out of the interface. For each time step, the concentration distribution between the two boundary elements is then computed by ion-exchange theory. The resulting finite difference simulation is much more robust than the earlier model and gives a good correlation to experiments.
6.1 Theory

Computer simulation is an excellent tool to analyze the electrochemical time dependent response behavior of ion selective membranes, especially near the detection limit, in the super-Nernstian jump region, for determining ion selectivity, and when interrogated by dynamic electrochemistry. Two different dynamic models are normally applied for this purpose, the Nernst-Planck-Poisson model (NPP) and the diffusion layer model (DLM). While NPP is more comprehensive, we will focus here on DLM as it is mathematically simpler, is more transparent with simulation parameters and gives good predictive power, and therefore has been successfully applied in numerous contributions. A mathematical discretization is introduced to give an approximate solution of the diffusion equations in the aqueous and membrane phase. For this purpose, the finite difference method is often used for its mathematical simplicity. Radu et al. utilized this approach to trace the real-time potential response of polymeric membrane ion selective electrodes. They identified that solving all relevant diffusion equations is a mathematical weak problem, subject to the nonlinear constraint at the interface. Unfortunately, no explicit formula was put forward to calculate the boundary elements, and the equations used were rather too complex and difficult to be applied by non-specialists. Later, Morf et al. also used this general approach to analyze the dependence of potential response on the experimental parameters such as diffusion layer thickness, ion diffusion coefficients and total ion exchanger concentration. Here, all the formulas for calculating every finite element were clearly presented, making the approach much more accessible. The key formulas to calculate the boundary elements for each time step, $\tau + \Delta \tau$, based on the concentrations at the previous time, $\tau$, (not indicated on the right side for simplicity) are rewritten here as eqs 1-2:

$$C'_{i,0}(\tau + \Delta \tau) = C'_{i,0} + pq(C'_{i,1} - C'_{i,0})$$ (1)

$$C_{i,0}(\tau + \Delta \tau) = \frac{X_{tot} a'_{i,0} X'_{i,0}}{a'_{i,0} + K_j a'_{i,0}} \approx \frac{X_{tot} C'_{i,0}}{C'_{i,0} + K_j C''_{j,0}}$$ (2)

with

$$\tau = \frac{D_{i,m}}{\delta^2} t$$

$$p = \frac{D_{i,ag}}{D_{i,m} \delta'^2}$$

$$q = \frac{\delta}{\delta'}$$
where $C_{i,0}'_{t}$, $C_{i,-1}'_{t}$ are the concentrations of the analyte ion, i, of element 0 and element -1 at the aqueous side of the interface; $C_{i,0}$ and $C_{i,1}$ are the corresponding analyte ion concentrations of element 0 and element 1 at the membrane side; $\tau$ and $\Delta \tau$ are the dimensionless form of time and each time increment step; $p$ is the permeability ratio and $q$ is the inverse thickness ratio between aqueous and membrane elements; $D_{i,m}$ and $D_{i,aq}$ are ion diffusion coefficients in membrane and aqueous phase, respectively; $\delta$ is the discretized element thickness at membrane side and $\delta'$ is the element thickness at membrane side; $X_{tot}$ is the total concentration of ion exchanger in the membrane; and $K_{ij}$ is the selectivity coefficient for analyte ion i over interfering ion j. Briefly, eq 1 is used for calculating the aqueous boundary element while eq 2 is for calculating the resulting membrane boundary element by assuming an ion-exchange phase boundary equilibrium where all ions have the same valency.\(^{15}\)

Equation 1 was derived from differentiation of the continuity law at the interface.\(^{4}\) It was later employed by others to describe the time behavior of controlled-potential thin layer coulometry\(^{7}\) and to predict the evolution of time dependent selectivity coefficients.\(^{13}\) Lewenstam\(^{16}\) et al. criticized the formula “...may be mathematically incorrect”, as they suggested that the interfacial flux is actually not necessarily differentiable. Although they realized this potential limitation, an alternative formula was not given. Instead, an attempt was made to deduce a diffusion exchange model from eq 1, which may be problematic.

Since the diffusion layer model has been widely used so far\(^{11}\) and will likely be applied in the future for many more ion selective electrode simulations, it is important to evaluate the applicability of this boundary equation and, in case of failure, to propose improvements. To critically assess eq 1, a dedicated virtual experiment was chosen. The calculation of other elements and the potential trace are otherwise the same as in Morf’s paper.\(^{4}\)

Figure 1 shows the two simulated interfacial analyte ion concentrations, one for each side of the phase boundary, and the resulting potential trace of an ion selective electrode exposed to varying sample concentrations. The parameters used for this virtual experiment are as follows: diffusion coefficient in aqueous phase, $D_{i,aq} = 10^{-5} \text{cm}^2/\text{s}$; diffusion coefficient in membrane phase, $D_{i,m} = 10^{-8} \text{cm}^2/\text{s}$; total ion exchanger concentration in membrane, $X_{tot} = 0.01 \text{M}$; selectivity coefficient of analyte to interfering ions. $\log K_{ij} = -5$ ; background ion concentration, $c_{j}' = 10 \text{ mM}$, considered constant during the experiment; the bulk sample concentration is chosen to increase from 10 $\mu$M to 10 mM, to subsequently return back from 10 mM to 10 $\mu$M and again increase successively to 10 mM; the time interval for each sample concentration is 30s; the membrane thickness and the aqueous diffusion layer thickness are set to $\delta_m = 200 \mu$m and $\delta_{aq} = 120 \mu$m, respectively. Simulations were carried out with $\Delta t$ of
0.005 s and element distance step of $\delta = \delta' = 20 \mu m$ (see Supporting Information for details of the programming).

Figure 1. a) Potential trace of an ion selective membrane initially void of primary ions exposed to virtually designed varying bulk sample concentrations (indicated as $pI^+$ values) and b) corresponding interfacial primary ion concentration (i.e., position 0) in membrane (red line) and aqueous phase (blue line). The dotted vertical lines indicate a time interval of 30 s for changing the concentration in the sample bulk. See text for virtual experimental parameters. The interfacial elements were calculated by eq 1 and eq 2.

As shown in Figure 1a, the potential trace exhibits a super-Nernstian potential response in the entire concentration range, which is due to the diffusion controlled ion-exchange reaction at the membrane/aqueous interface. This phenomenon has been previously described in detail.\textsuperscript{3,12,16} The blue trace (below one) in Figure 1b is the time trace of aqueous boundary concentration while the red line is the time trace for the corresponding membrane boundary concentration. While the aqueous boundary concentrations increase or decrease gradually when the sample bulk is altered (as indicated with $pI^+$ values), the membrane boundary concentrations (red line, above one) change very drastically at 30 s, 185 s and 210 s, much more so than the changes observed at the aqueous side of the boundary. The reason for this is that in eq 1 the time dependent concentration change from the flux gradient is attributed entirely to the interfacial aqueous element ($C_{i,0}'$). The calculation of the corresponding membrane element ($C_{i,0}$) is entirely performed by the equilibrium conditions, eq 2. Mathematically, the membrane concentration at the interface does therefore not originate from mass transport phenomena but is created, seemingly out of thin air. This is a fundamental flaw of eq 1, and this violation of the conservation of mass likely results in unacceptable errors.
Instead, it is chemically obvious that mass transport must contribute directly to the concentration change at the membrane side of the interface as well, and flux should also be used for calculating this membrane element, \( C_{i,0} \). Large deviations are indeed found for a simulation based on eqs 1-2 compared to that put forward in Radu’s work.\(^{12}\) Figure S1a shows the previously reported potential time response traces for a membrane containing 10% of analyte ions (relative to ion-exchanger), calculated for two different diffusion coefficients in the membrane, while Figure S1b gives the potential traces for simulations based on eqs 1 and 2. The simulation in Figure S1b gives chemically unreasonable values (negative concentrations) at low analyte concentrations and wrongly predicts the position of the super-Nernstian potential jump. Negative concentrations are easier to observe at low concentrations because the “creation” of \( C_{i,0} \) will be amplified if lower \( C'_{i,0} \) and smaller \( K_{ij}, C'_{j,0} \) are used as they constitute the denominator of eq 2. A smaller denominator results in a higher value of \( C_{i,0} \) and the results will deviate even more from mass balance. To compare, Figure 1 shows a full trace for the entire experiment as here \( K_{ij}C'_{j,0} \) is \( 10^{-7} \), while for Figure S1 \( K_{ij}C'_{j,0} \) is much lower, at \( 10^{-13} \).\(^{12}\)

To overcome this limitation, a more robust formula is introduced here that simultaneously considers the flux for both aqueous and membrane boundary elements. As shown in scheme 1, the aqueous diffusion layer is discretized into \( m+1 \) elements, each with an element thickness of \( \delta' \) while the membrane layer is discretized into \( n+1 \) elements, each of thickness \( \delta \). As above, position 0 denotes the interface. The numbers \( m \) and \( n \), as well as \( \delta' \) and \( \delta \) are not necessarily of the same value. Element thicknesses should be sufficiently small so that the flux from one element to its neighbor follows the linearization of Fick’s first law, shown here for \( J_{-1/0} \) and \( J_{0/1} \):

\[
J_{-1/0} = -D_{i,\text{aq}} \frac{C'_{i,0} - C'_{i,-1}}{\delta'} \\
J_{0/1} = -D_{i,\text{m}} \frac{C_{i,1} - C_{i,0}}{\delta}
\]

(6)

(7)

where \( J_{-1/0} \) is the flux from aqueous element -1 to the adjacent aqueous interfacial element 0, and \( J_{0/1} \) is the flux from the aqueous boundary element 0 to the neighboring aqueous element 1. The flux from the aqueous phase to the membrane phase is defined as positive, indicated as the direction of the arrows in scheme 1.
Scheme 1. Discretization of the membrane phase and aqueous diffusion layer with m+1 and n+1 elements of thicknesses $δ'$ and $δ$, respectively. Flux $J$ is considered across the border of two elements, indicated as right arrows. Rapid equilibration is assumed between the two interfacial elements $C_{i,0}'$ and $C_{i,0}$, and these two elements are taken as a single entity to describe the time dependent concentration change as a result of ion flux to and from the interface.

It is assumed that ion-exchange equilibrium (eq 2) holds at all times at the interface. For this reason, the two interfacial boundary elements are treated here as a linked entity, and concentration changes arising from fluxes into and from the neighboring elements are given by combining the two boundary elements as follows:

$$\frac{(C_{i,0}'(t+\Delta t) - C_{i,0}(t))\delta + (C_{i,0}(t+\Delta t) - C_{i,0}(t))\delta}{(J_{i,0} - J_{i,1})\Delta t}$$

(8)

Combining eq 8 with eqs 3-7 gives a direct replacement for equation 1:

$$\frac{(C_{i,0}'(\tau + \Delta \tau) - C_{i,0}(\tau)) + (C_{i,0}(\tau + \Delta \tau) - C_{i,0}(\tau))q = pq(C_{i-1}' - C_{i,0})\Delta \tau - q(C_{i,0} - C_{i,1})\Delta \tau}{J_{i,0} - J_{i,1} \Delta t}$$

(9)

Eq 9 is now used instead of eq 1 to calculate the boundary elements together with eq 2 (see Supporting Information for an explicit formula for $C_{i,0}'(\tau + \Delta \tau)$ derived from eqs 2 and 9).

Figure 2 shows the same virtual experiment of Figure 1, computed with eq 9 instead of eq 1. Compared to Figure 1a, the potential trace in Figure 2a exhibits a larger delay at low analyte concentrations (0s-90s, 180s-240s) and a larger potential jump at 1mM ($pI_{+} = 3$, 60s-90s). The membrane boundary concentration (above red line in Figure 2b) changes much more slowly compared to the results based on eq 1 (Figure 1b), which is chemically more reasonable because the membrane concentration should also be dependent on mass transport as explained above.
Figure 2. a) Potential trace of an ion selective membrane initially void of primary ions exposed to virtually designed varying bulk sample concentrations (indicated as pI+ values) and b) Interfacial primary ion concentration in membrane (red line) and aqueous phase (blue line). The interfacial elements were calculated by eq 2 and eq 9. The simulation parameters are the same as Figure 1.

The robustness of eq 9 is also demonstrated by resimulation of Figure S1a, where eq 1 had failed. Figure 3 shows an overlay of the newly simulated potential trace and the literature data. The trace for a membrane diffusion coefficient of $10^{-8}$ cm$^2$ s$^{-1}$ is equal to the literature data while small deviations are found for a diffusion coefficient of $10^{-9}$ cm$^2$ s$^{-1}$, which is likely due to using different simulation parameters (see Supporting Information for calculation details).

Another virtual experiment (Figure 5 in the Morf's paper) to assess calibration curves for hysteresis with electrodes exhibiting a super Nernstian jump was also recalculated by eq 9. Figure S2 shows the results of the calculation using the same parameters as that in Morf’s paper. The resulting hysteresis is stronger for shorter time periods between sample changes (2.5s for each sample concentration, Figure S2a) compared to that calculated by eq 1 (see Figure 5a in the paper). The hysteresis decreases gradually when increasing measuring times for each sample composition (10 s, 40 s, 160 s for Figure S2b-d), whereas by Morf’s method this loop vanishes at measuring times of 10s (Figure 5b in ref 4) but unreasonably appears again at measuring times of 40s and 160s (Figure 5c,d in ref 4). Eq 9 gave the same results even when increasing simulation time intervals ($\Delta t$) by 10 orders of magnitude (data not shown), while eq 1 introduced instabilities with increasing $\Delta t$ as shown in Figure S3a,b.
To further verify the general applicability of eq 9, a laboratory experiment was also simulated. Figure S4a is the extracted experimental potential trace and its corresponding simulated trace. Figure S4b,c are the simulation of this potential trace, respectively, using either eq 1 or eq 9. While the result computed from eq 1 is far from the experimental one, the predicted trace from eq 9 is very close to the experiment, more so than the one predicted in the reference paper.

After evaluating the two formulas for several virtual and real experimental cases, eq 9 is suggested to replace eq 1 for the calculation of boundary elements in diffusion layer model simulations. Although eq 9 is successfully validated, its derivation is based on an assumption that each finite element is treated as a thin layer. It is also noted that the ion-exchange equilibrium based on eq 2 assumes monovalent ions. For analyte and interfering ions of different charge, eq 2 is no longer relevant and expanded ion-exchange equilibrium equations are to be used, as reported earlier. The treatment assumes that interfacial equilibration is instantaneous in the time frame of the experiment, which may not be realistic in all cases of practical relevance, and in which case the more advanced NPP model may be more useful. The thin layer concept of finite element for deriving eq 9 in this paper may also be useful to treat boundary elements for the NPP model.
6.2 Supporting information

6.2.1 Explicit formula

The increment of boundary elements concentrations for each time step is using eq 9 in the main manuscript.

\[
(C'_{i,0}(\tau + \Delta \tau) - C'_{i,0}(\tau)) + (C_{i,0}(\tau + \Delta \tau) - C_{i,0}(\tau))q = pq(C'_{i-1} - C'_{i,0})\Delta \tau - q(C_{i,0} - C_{i,1})\Delta \tau \tag{1}
\]

The ion exchange reactions in boundary membrane and aqueous element are always at equilibrium for each time step, following eq 2 for ions with the same valency.

\[
C_{i,0}(\tau + \Delta \tau) = \frac{X_{na}a'_{i,0}}{a'_{i,0} + K_y a'_{j,0}} \approx \frac{X_{tot}C'_{i,0}(\tau + \Delta \tau)}{C_{i,0}(\tau + \Delta \tau) + K_y C'_{j,0}} \tag{2}
\]

The explicit formula for \(C'_{i,0}(\tau + \Delta \tau)\) is got by eliminating \(C_{i,0}(\tau + \Delta \tau)\) from the above two equations.

\[
\begin{align*}
C'_{i,0}(\tau + \Delta \tau) &= \frac{1}{2} (\lambda qX_{na} + qC_{i,0}(\tau) - K_y C'_{j,0} + C'_{i,0}(\tau)) \\
&+ \frac{1}{2} \sqrt{4(K_y \lambda C'_{j,0} + K_y qC_{i,0}(\tau)C'_{i,0} + K_y C'_{j,0}C'_{i,0}(\tau))}
\end{align*}
\]

where \(\lambda\) is \(\lambda = pq(C'_{i-1} - C'_{i,0})\Delta \tau - q(C_{i,0} - C_{i,1})\Delta \tau\).

This explicit formula is then used for calculating \(C'_{i,0}(\tau + \Delta \tau)\) at each time step.
6.2.2 Supporting figures

**Figure S1.** (a) Calculated time response for membranes showing a super-Nernstian response by exchanging 10% of primary ions with an interfering ions; this figure is reproduced directly from Figure 6(A) of reference.12 (b) Recalculated time response for membrane by using eqs 1-2 in the main manuscript with otherwise the same parameters as (a).
**Figure S2.** Recalculated EMF response of an ISE membrane with initial ions $J^+$ to sample solutions containing the preferred ions $I^+$ using eq 9 in the main manuscript. Computer-simulated values of the electrode potential $E$ relative to the standard reference potential $E^0_i$ are shown as a function of log $a_i$. The bulk sample activity was first decreased in steps from $10^{-1}$ to $10^{-7}$ M (full circles), and then again increased (open circles). The measuring time for each sample was 2.5s (a), 10s (b), 40s (c) and 160s (d), respectively. The Arrows in each figure indicate the direction of sample concentration change. All simulation parameters were obtained from the literature.⁴
Figure S3. Recalculation of Figure S2a using eq 1. The time intervals used, a) $\Delta t = 1\text{ms}$ b) $\Delta t = 5\text{ms}$. All other parameters are the same as for Figure S2a.
Figure S4. a) Experimental (top) and predicted (bottom) potential changes of a silver-selective membrane initially void of silver ions in response to alternating concentrations of silver nitrate (indicated as pAg values) in a background of $10^{-5}$ M LiNO$_3$. This figure is directly reproduced from Figure 3 of literature.\textsuperscript{12} b) Calculation of part a) experiment by using eqs 1-2 with the same parameters as the literature. c) Calculation of part a) experiment by using eq 2 and eq 9.
6.2.3 Programs

The programs are all computed in Mathematica 8.0®.

6.2.3.1 Symbols

\( k_{ij} \): selectivity coefficient

\( x_{tot} \): total ion exchanger concentration in membrane

\( t \): experimental time for each sample in s

\( \tau \): dimensionless form of \( t \)

\( \Delta t \): time increment value for each step in s

\( \Delta \tau \): dimensionless form of \( \Delta t \)

\( \delta \): discretized element thickness in membrane side

\( \delta' \): discretized element thickness in aqueous side

\( \delta_m \): total membrane thickness

\( \delta_{aq} \): aqueous diffusion layer thickness

\( D_{iaq} \): diffusion coefficient of ions \( i \) in aqueous phase

\( D_{im} \): diffusion coefficient of ions \( i \) in membrane phase

\( c_j \): concentration of background interfering ions \( j \)

\( c_{ia}[x,\tau] \): concentration of ions \( i \) at position of \( x \) for time step \( \tau \) at aqueous side

\( c_{im}[x,\tau] \): concentration of ions \( i \) at position of \( x \) for time step \( \tau \) at membrane side

\( m \): number of the last element in aqueous phase

\( n \): number of the last element in membrane phase

\( \Delta \tau = D_{im} \Delta t / \delta^2 \)

\( p = D_{iaq} \delta / (D_{im} \delta') \)

\( q = \delta / \delta' \)

6.2.3.2 Calculation for Figure 1

Parameters:

\( k_{ij} = 10^{-5} \)

\( c_j = 10^{-2} \text{ M} \)
xtot= 0.01M

δ_m=200 x 10^{-5} dm

δ_{aq} = 120 x 10^{-5} dm

δ = 20 x 10^{-5} dm

δ' = 20 x 10^{-5} dm

m=6

n=10

Diaq=10^{-7} dm^2 s^{-1}

Dim=10^{-10} dm^2 s^{-1}

t=30s

Δt = 0.005 s

Δτ=1.25 x 10^{-5}

tperiod= IntegerPart[30/Δt]=6000

p=10^3

q=1

Initial concentrations

Do[cia[x,1]]=0, {x,0,m}]

Do[cim[x,1]]=0, {x,0,n}]

Boundary sample concentrations

Do[cia[m,τ]]=10^{-5}, {τ,1,tperiod}];

Do[cia[m,τ]]=10^{-4}, {τ,tperiod+1,2 tperiod}];

Do[cia[m,τ]]=10^{-3}, {τ,tperiod+1,3 tperiod}];

Do[cia[m,τ]]=10^{-2}, {τ,3 tperiod+1,4 tperiod}];

Do[cia[m,τ]]=10^{-3}, {τ,4 tperiod+1,5 tperiod}];

Do[cia[m,τ]]=10^{-4}, {τ,5 tperiod+1,6 tperiod}];

Do[cia[m,τ]]=10^{-5}, {τ,6 tperiod+1,7 tperiod}];

Do[cia[m,τ]]=10^{-4}, {τ,7 tperiod+1,8 tperiod}];
Do[cia[m,τ]]=10^3, {τ,8 tperiod+1,9 tperiod}];
Do[cia[m,τ]]=10^2, {τ,9 tperiod+1,10 tperiod}];
tmax=10 tperiod

Inner side boundary membrane concentrations
Do[cim[n,τ]]=0, {τ,0,tmax}];

Evolutions
For [τ = 1, τ < tmax,
{ Do[cia[x, τ]=cia[x,τ-1]+ p q (cia[x-1,τ-1]-2cia[x,τ-1]+ cia[x+1,τ-1]) Δτ, {x,1,m-1}],
Do[cim[x, τ]=cim[x,τ-1]+(cim[x-1,τ-1]-2cim[x,τ-1]+ cim[x+1,τ-1]) Δτ, {x,1,n-1}],
cia[0,τ]= cia[0,τ-1]+ p q(cia[1,τ-1]-cia[0,τ-1]) Δτ - q(cim[0,τ-1]-cim[1,τ-1]) Δτ,
cim[0,τ]=xtot cia[0,τ] / (cia[0,τ]+kij cj)
},
τ++]

Outputs
Potential trace
ListLinePlot[ Table[{τ Δt, -59.2 Log[10, kij cj/xtot] + 59.2 Log[10, cia[0,τ]/cim[0,τ]]}, {τ, 800, tmax - 1, 100}], Frame -> True, PlotRange -> {{-30, 330}, {-30, 350}}, BaseStyle -> {16, FontFamily -> Helvetica"}, FrameLabel -> {"TIME / s", "EMF CHANGE / mV"}, LabelStyle -> (FontFamily -> "Helvetica"), AxesOrigin -> {-1000, -1000}, AspectRatio -> 1, PlotStyle -> {Thick, Red}, FrameStyle -> {Thick, Thick}, FrameTicks -> {{Table[u, {u, 0, 0.010, 0.002}], None}, {Table[u, {u, 0, 300, 60}], None}, {Table[u, {u, 0, 300, 60}], None}]]

Interfacial membrane and aqueous concentration
ListLinePlot[{Table[{τ Δt, cia[0, τ]}, {τ, 1,tmax-1, 100}], Table[{τ Δt, cim[0, τ]}, {τ, 800, tmax - 1, 100}]}, Frame -> True, PlotRange -> {{-30, 330}, {-0.001, 0.012}}, BaseStyle -> {16, FontFamily -> "Helvetica"}, FrameLabel -> {"TIME / s", "INTERFACIAL CONCENTRATION / M"}, LabelStyle -> (FontFamily -> "Helvetica"), AxesOrigin -> {-1000, -1000}, AspectRatio -> 1, PlotStyle -> {Thick}, FrameStyle -> {Thick}, FrameTicks -> {{Table[u, {u, 0, 0.010, 0.002}], None}, {Table[u, {u, 0, 300, 60}], None}]]
6.2.3.3 Calculation for Figure 2

Parameters, initial concentrations and boundary concentrations and outputs are the same as Figure 1

Evolutions

For $\tau=1, \tau<\text{tmax}$,

\[
\{ \text{Do}[\text{cia}[x, \tau] = \text{cia}[x, \tau-1] + p \ q \ (\text{cia}[x-1, \tau-1] - 2 \text{cia}[x, \tau-1] + \text{cia}[x+1, \tau-1]) \Delta \tau, \ {x, 1, m-1} \},
\]

\[
\text{Do}[\text{cim}[x, \tau] = \text{cim}[x, \tau-1] + (\text{cim}[x-1, \tau-1] - 2 \text{cim}[x, \tau-1] + \text{cim}[x+1, \tau-1]) \Delta \tau, \ {x, 1, n-1} \},
\]

\[
\lambda = p \ q \ (\text{cia}[1, \tau-1] - \text{cia}[0, \tau-1]) \Delta \tau - q (\text{cim}[0, \tau-1] - \text{cim}[1, \tau-1]) \Delta \tau,
\]

\[
\text{cia}[0, \tau] = \frac{1}{2} \left( \lambda - q \ x_{\text{tot}} + q \ cim[0, \tau-1] \right) - k_{ij} \ c_j + \text{cia}[0, \tau-1] +
\]

\[
\frac{1}{2} \sqrt{\left( \lambda - q \ x_{\text{tot}} + q \ cim[0, \tau-1] - k_{ij} \ c_j + \text{cia}[0, \tau-1] \right)^2 +}
\]

\[
4 \left( k_{ij} \ c_j + k_{ij} \ c_j \ q \ cim[0, \tau-1] + k_{ij} \ c_j \ cim[0, \tau-1] \right) \}
\]

\[
\text{cim}[0, \tau] = x_{\text{tot}} \ cia[0, \tau] / \ (cia[0, \tau] + k_{ij} \ c_j)
\]

\[
\tau++
\]

6.2.3.4 Calculation for Figure 3

Parameters:

\[
k_{ij} \ c_j = 10^{-13}
\]

\[
 x_{\text{tot}} = 0.001 \text{M}
\]

\[
 \delta_m = 200 \times 10^{-5} \text{dm}
\]

\[
 \delta_{\text{aq}} = 100 \times 10^{-5} \text{dm}
\]

\[
 \delta = 10^{-5} \text{dm}
\]

\[
 \delta' = 10 \times 10^{-5} \text{dm}
\]

\[
 n = 200
\]

\[
 m = 10
\]

\[
 \text{Diaq} = 10^{-7} \text{dm}^2 \text{s}^{-1}
\]

\[
 \text{Dim} = 10^{-10} \text{dm}^2 \text{s}^{-1} \text{ or } 10^{-11} \text{dm}^2 \text{s}^{-1}
\]

\[
 t = 300 \text{s}
\]
\Delta t = 0.04 \, s

\Delta \tau = 0.04 \, (\text{for } \text{Dim}=10^{-10} \, \text{dm}^2 \, \text{s}^{-1}) \, \text{or} \, 0.004 \, (\text{for } \text{Dim}=10^{-11} \, \text{dm}^2 \, \text{s}^{-1})

tperiod = \text{IntegerPart}[300/\Delta t] = 7500

p = 10^2 \, (\text{for } \text{Dim}=10^{-10} \, \text{dm}^2 \, \text{s}^{-1}) \, \text{or} \, 10^3 \, (\text{for } \text{Dim}=10^{-11} \, \text{dm}^2 \, \text{s}^{-1})

q = 0.1

Initial concentrations

\text{Do[cia[x,1]]} = 10^{-9}, \{x,0,m\}\]
\text{Do[cim[x,1]]} = 0, \{x,0,n\}\]

Boundary sample concentrations

\text{Do[cia[m,\tau]]} = 10^{-9}, \{\tau,1,\text{tperiod}\}\]
\text{Do[cia[m,\tau]]} = 10^{-8.5}, \{\tau,\text{tperiod}+1,2 \, \text{tperiod}\}\]
\text{Do[cia[m,\tau]]} = 10^{-8}, \{\tau,2 \, \text{tperiod}+1,3 \, \text{tperiod}\}\]
\text{Do[cia[m,\tau]]} = 10^{-7.5}, \{\tau,3 \, \text{tperiod}+1,4 \, \text{tperiod}\}\]
\text{Do[cia[m,\tau]]} = 10^{-7}, \{\tau,4 \, \text{tperiod}+1,5 \, \text{tperiod}\}\]
\text{Do[cia[m,\tau]]} = 10^{-6.5}, \{\tau,5 \, \text{tperiod}+1,6 \, \text{tperiod}\}\]
\text{Do[cia[m,\tau]]} = 10^{-6}, \{\tau,6 \, \text{tperiod}+1,7 \, \text{tperiod}\}\]
\text{Do[cia[m,\tau]]} = 10^{-5.5}, \{\tau,7 \, \text{tperiod}+1,8 \, \text{tperiod}\}\]
\text{Do[cia[m,\tau]]} = 10^{-5}, \{\tau,8 \, \text{tperiod}+1,9 \, \text{tperiod}\}\]
\text{Do[cia[m,\tau]]} = 10^{-4.5}, \{\tau,9 \, \text{tperiod}+1,10 \, \text{tperiod}\}\]
tmax = 10 \, \text{tperiod}

Inner side boundary membrane concentrations

\text{Do[cim[n,\tau]]} = 0.0009, \{\tau,0,\text{tmax}\}\]

Evolutions

For [\tau = 1, \tau < \text{tmax},

\{ \text{Do[cia[x, \tau]]} = \text{cia[x, \tau-1]} + p \, q \, (\text{cia[x-1, \tau-1]}-\text{2cia[x, \tau-1]}+\text{cia[x+1, \tau-1]}) \Delta \tau, \{x,1,m-1\}\},

\text{Do[cim[x, \tau]]} = \text{cim[x, \tau-1]}+(\text{cim[x-1, \tau-1]}-\text{2cim[x, \tau-1]}+\text{cim[x+1, \tau-1]}) \Delta \tau, \{x,1,n-1\}\},

\lambda = p \, q(\text{cia[1, \tau-1]}-\text{cia[0, \tau-1]}) \Delta \tau - q(\text{cim[0, \tau-1]}-\text{cim[1, \tau-1]}) \Delta \tau,
\[
\text{cia}[0, \tau] = \frac{1}{2} (\lambda - q \ \text{xtot} + q \ \text{cim}[0, \tau - 1] - kij \ cj + \text{cia}[0, \tau - 1]) + \\
\frac{1}{2} \sqrt{(\lambda - q \ \text{xtot} + q \ \text{cim}[0, \tau - 1] - kij \ cj + \text{cia}[0, \tau - 1])^2 + 4(kij \ cj + kij \ cj \ q \ \text{cim}[0, \tau - 1] + kij \ cj \ \text{cia}[0, \tau - 1])}
\]

\[
\text{cim}[0, \tau] = \text{xtot} \ \text{cia}[0, \tau] / (\text{cia}[0, \tau] + kij \ cj)
\]

\[
\tau ++\]

Outputs

Potential trace

ListLinePlot[
Table[{\tau \Delta t, -59.2 \ \text{Log}[10, kij \ cj/\text{xtot}] + 59.2 \ \text{Log}[10, \text{cia}[0, \tau]/\text{cim}[0, \tau]]}, \{\tau, 0, \text{tmax} - 1, 100\}], Frame -> True, PlotRange -> \{\{-100, 3100\}, \{-30, 350\}\}, BaseStyle -> \{16, FontFamily -> "Helvetica"\}, FrameLabel -> \{"TIME / s", "EMF CHANGE / mV"\}, LabelStyle -> \{FontFamily -> "Helvetica"\}, AxesOrigin -> \{-1000, -1000\}, AspectRatio -> 1, PlotStyle -> \{Thick, Red\}, FrameStyle -> \{Thick, Thick\}, FrameTicks -> \{\{Table[u, \{u, 0, 300, 50\}], None\}, \{Table[u, \{u, 0, 300, 60\}], None\}\}]

6.2.3.5 Calculation for Figure S1b

Parameters, initial concentrations as well as boundary concentrations and outputs are the same as Figure 3

Evolutions

The programs are same as in Figure 1.

6.2.3.6 Calculation for Figure S4b and Figure S4c by using eq 1 or eq 9

Figure S4b

Parameters:

\[
\begin{align*}
kij \ cj &= 10^{-11.7} \\
xtot &= 0.0043 \\
\delta_m &= 200 \times 10^{-5} \ \text{dm} \\
\delta_{aq} &= 50 \times 10^{-5} \ \text{dm} \\
\delta &= 10 \times 10^{-5} \ \text{dm}
\end{align*}
\]
\[ \delta' = 10 \times 10^{-5} \text{dm} \]

\[ n = 20 \]

\[ m = 5 \]

\[ \text{Diaq} = 1.65 \times 10^{-7} \text{dm}^2 \text{s}^{-1} \]

\[ \text{Dim} = 1.1 \times 10^{-11} \text{dm}^2 \text{s}^{-1} \]

\[ \Delta t = 0.02 \text{ s} \]

\[ \Delta \tau = 0.000022 \]

\[ p = 1.5 \times 10^4 \]

\[ q = 1 \]

Initial concentrations

\[ c_{\text{initial}} = 10^{-7} \]

Do[cia[x, 1] = c_{\text{initial}}, \{x, 0, m\}]

Do[cim[x, 1] = 0.00, \{x, 0, n\}]

Boundary sample concentrations

\[ t_{\text{period1}} = \text{IntegerPart}[60/\Delta t] \]

\[ t_{\text{period2}} = \text{IntegerPart}[1.5 \times 60/\Delta t] + t_{\text{period1}} \]

\[ t_{\text{period3}} = \text{IntegerPart}[6.5 \times 60/\Delta t] + t_{\text{period2}} \]

\[ t_{\text{period4}} = \text{IntegerPart}[60/\Delta t] + t_{\text{period3}} \]

\[ t_{\text{period5}} = \text{IntegerPart}[5 \times 60/\Delta t] + t_{\text{period4}} \]

\[ t_{\text{period6}} = \text{IntegerPart}[60/\Delta t] + t_{\text{period5}} \]

\[ t_{\text{period7}} = \text{IntegerPart}[4 \times 60/\Delta t] + t_{\text{period6}} \]

\[ t_{\text{max}} = \text{IntegerPart}[20 \times 60/\Delta t] \]

Do[cia[m, \tau] = 10^{-7}, \{\tau, 1, t_{\text{period1}}\}];

Do[cia[m, \tau] = 10^{-5}, \{\tau, t_{\text{period1}} + 1, t_{\text{period2}}\}];

Do[cia[m, \tau] = 10^{-6}, \{\tau, t_{\text{period2}} + 1, t_{\text{period3}}\}];

Do[cia[m, \tau] = 10^{-5}, \{\tau, t_{\text{period3}} + 1, t_{\text{period4}}\}];

Do[cia[m, \tau] = 10^{-6}, \{\tau, t_{\text{period4}} + 1, t_{\text{period5}}\}];
\[
\text{Do[cia[m,τ]]} = 10^{-5}, \{\tau, \text{tperiod5}+1, \text{tperiod6}\};
\]
\[
\text{Do[cia[m,τ]]} = 10^{-6}, \{\tau, \text{tperiod6}+1, \text{tperiod7}\};
\]

Inner side boundary membrane concentrations

\[
\text{Do[cim[n,τ]]} = 0.00, \{\tau, 1, \text{tmax}\};
\]

Evolutions

The calculation programs are same as in Figure 1.

**Figure S4c**

Parameters:

\[
\delta = 2 \times 10^{-5} \text{ dm}
\]

\[
\delta' = 10 \times 10^{-5} \text{ dm}
\]

\[
n = 100
\]

\[
m = 5
\]

\[
\Delta t = 0.02 \text{ s}
\]

\[
\Delta \tau = 0.00055
\]

\[
p = 3 \times 10^3
\]

\[
q = 0.2
\]

Other parameters as well as the initial and boundary concentrations are the same as in Figure S4b

Evolutions

The calculation programs are same as Figure 2.
6.3 References

Conclusions and Outlooks

The first project of this thesis was centered on the fabrication of the robust potentiometric anion selective electrodes for environmental analysis. The motivation to accomplish this was fueled by incompetent conventional liquid-contact electrodes in regards to remaining resilient to harsh environmental conditions such as high water pressure, water velocity and broad temperature variation, causing distortion of the membrane and deterioration of the potential stability. With view of that, solid-contact ion selective electrodes came as an alternative configuration due to its intrinsic rigidity property.

Conducting polymers (CPs) have long been exploited for inner ion-to-electron transducers for these electrodes due to their high capacitance, good homogeneity and lipophilicity. However, CPs are photosensitive, as demonstrated by the POT test, which limits their environmental application. In addition, CPs are not suitable for transducers of anion selective electrodes as CPs favor lipophilic cation exchanger as dopant and potential stabilizer, which is usually absent in anion selective membranes. Thus, multi-walled carbon nanotubes (MWCNTs) modified with ODA group were explored as a viable alternative. The modification performed prior to use endowed them with higher lipophilicity, making them more soluble in an organic solvent (e.g., THF). A rubber mask was used to confine the effective zone on the glassy carbon or gold electrode surface. The MWCNT cocktail was then drop cast onto the confined surface area to ensure homogeneity of the transducing layer. This was followed by the deposition of the ion selective membrane cocktails. The as-prepared solid-contact electrodes were successfully applied for detection of anions such as carbonate, nitrate, nitrite and dihydrogen phosphate. Fortunately, the water layer test confirmed that no obvious water layer formed between solid contact and ion selective membrane. Moreover, a light sensitivity test showed that the MWCNT based transducer was insensitive to light irradiation. The electrodes based on MWCNTs exhibited a good medium-term potential stability and were utilized in further work in our lab for many in-situ and on-line applications in lake and sea water samples.

Despite of the prowess of the MWCNT solid contact mentioned above, there is still room possibly for improvement. The first critical factor that would benefit from further research is the homogeneity of the MWCNT transducing layer, a factor that prevents the water layer formation and affects the electrode long-term potential stability. Due to the residual charged impurities on the carbon nanotube surface, MWCNTs were prone to aggregation in the course of THF evaporation, resulting in a lower homogeneity. These impurities were difficult to completely remove. A strategy could be to look for other organic solvent (instead of THF) that
could lower the MWCNTs’ tendency to aggregate. Moreover, the manual drop cast method used for the MWCNT transducer preparation could be replaced by an inkjet printing method which could ensure better homogeneity. Another issue to overcome is the tedious calibration step prior to measurement. The latter was necessary to counteract the formal potential variation between different electrodes. The MWCNT transducer functioned as an electron capacitor with no constant electrode potential. Reducing the formal potential variations and achieving the goal of calibration-free sensors (Chapter 2) could be achieved by doping the MWCNTs with a specified amount of redox couples. All of these elements present themselves as future work for the optimization of the transducer layer but the search for an element to enhance the robustness of potentiometric anion selective electrodes was beautifully met by MWCNTs.

The second project of the thesis focalized on the voltammetric study of thin-layer solid contact ion selective electrodes. While traditional SC-ISE usually used a membrane thickness of several hundred micrometers for potentiometric application, thin layer SC-ISE reduced the membrane thickness only to several hundred nanometers. As the size diminished, the electrochemical property naturally changed. For instance, a Gaussian-shaped voltammetric peak now became very distinct due to the minimization of membrane resistance and thickness. Earlier work indicated that the voltammetric signal was diffusion controlled at low analyte concentration but showed no diffusion control at high analyte concentration. However, the two case scenarios had never been thoroughly investigated in a combined general case and thus no comprehensive theory was proposed to analyze these two regimes.

For this purpose, the voltammetric experiment conducted in this thesis used the silver ionophore as a model since it exhibits high selectivity for silver (Ag) over a sodium (Na) background, resulting in two distinctive peaks. The voltammetric analysis showed two regimes as predicted: one, where the Ag peak current increased linearly with increasing Ag concentration; and another, where the Ag peak potential showed a Nernst-pattern shift with increasing Ag concentration. Based on the new experimental data, a comprehensive model incorporated with the diffusion term was proposed. This new model was capable of simulating all the main electrochemical evidence observed, including varying sample concentrations, different potential scan rates, and electrode rotating speeds. (Chapter 3). However, the model with numerical simulations was not straightforward for experimental guidance. Simplified theory closely related with experimental parameters could bring a quick insight into experimental data. Two key parameters, $\alpha$ and $\beta$, respectively referring to the saturation level of ion selective membrane and perturbation extent of interfacial aqueous Ag concentrations, were thereby defined. The introduction of $\alpha$ and $\beta$ together with relevant calculation equations, supplied convenience to predict transition between thin layer regime and diffusion
regime. The equations for the calculation of $\alpha$ and $\beta$, as well as limit of detection in the potentiometric mode, were validated both by theoretical modeling and comparison to experimental data. The semi-empirical treatment proposed here should be a predictive approach for other solid contact cation selective membranes (Chapter 4).

The third work of the thesis continued the research of thin layer SC-ISE, focusing on ion-ionophore complexation within the membrane. Voltammetric scans trigger the ion transfer between the membrane/water interface, resulting in a simultaneous association or dissociation for the ion-ionophore complexations. Voltammetry based on this thin layer electrode setup is in some respects advantageous to the well-known ion transfer experiment at interface between two immiscible electrolyte solutions (ITIES). For instance, mass transport could be neglected by choosing proper experimental conditions (e.g., low scan rates and high analyte concentration), which extensively simplifies mathematical treatment. Nonetheless, the potential to transfer the ion at the interface and the potential for oxidizing (or reducing) POT should be clearly identified in a double thin layer configuration (thin layer membrane and POT). The electrochemical potential of POT was described with a pseudo-Nernst equation where satisfactory results were acquired in the prediction of investigated experimental phenomena. However, the simulated peak was relatively narrower than the experimental one, reflecting the incompleteness of the Nernst assumption. The POT electrochemical property was claimed as an overlap of many redox processes, similar to that of semiconductor. Yet, there was still no all-agreeable potential-charge formula for this process, especially in the solid contact form in our electrode configuration.

The method to obtain the potential-charge curve for POT in this work was to not rely on a full bottom-up built theory. Instead, a chemically inert reference ion tetrabutylammonium (TBA$^+$) was introduced, whose ion transfer curve was semi-empirically calculated and later utilized to extract the POT potential as a function of charge (the charge is proportional to the amount of cation exchanger inside the membrane). The empirically obtained potential-charge function was then subtracted from the total applied potential to isolate pure ion transfer curve for the membrane with ionophore. Valinomycin was selected for the proof-of-concept validation of the new method. The complex stoichiometry, complex formation constant and selectivity coefficient were successfully determined for potassium (K) and Na by fitting the experimental potential-charge function, which in turn corroborated the correctness of the POT treatment. The method, however, is still limited to only a few neutral ionophores for cations. Electrically charged ionophores were found to deteriorate the electrochemical signal, masking the useful information of the ion transfer. Stable and repeatable cyclic voltammograms for anions are so far not observed, possibly due to the decomposition of POT by its exposure to small hydrophilic
anions (e.g., Cl\(^-\)). The search of other robust conducting polymers (CPs) or their replacement with other redox species may be a promising work for extending this technique for anion-ionophore reactions (Chapter 5).

The final section of the thesis aimed to clear a long-time-standing fog around the calculation of boundary elements in the computer simulation process of polymeric ion selective electrode behavior by finite difference method. Computer simulations are a very strong tool for analyzing and predicting the electrochemical response of ion selective electrodes. Nonetheless, fault calculations may result in incorrect conclusions and even misguide experimental practices. The proper boundary elements calculation is sometimes the most important and also the most difficult part. The diffusion layer model assuming a thermodynamic equilibrium at the membrane/solution interface had been frequently used to simulate ion transport in the membrane and aqueous phase. In this model, Morf had initially proposed a formula for boundary elements, but since it was derived improperly from mathematical derivation, it was found to bring many unstable and oscillating results. Alarmingly, this formula is still being frequently used. Thereby, a clarification of this misuse and a substituted correction formula was necessary. The novel formula was derived by the method of introducing the concept of “thin-layer” space element and by considering the mass balance conservation in each element. The “thin layer” element definition was analogous to the “box” definition described in the introduction part of the thesis (Chapter 1). The new provided formula was verified and was shown to be more robust than Morf’s at various conditions, thereby being suggested as a replacement for computer simulations in future work (Chapter 6).
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