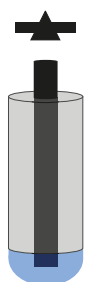


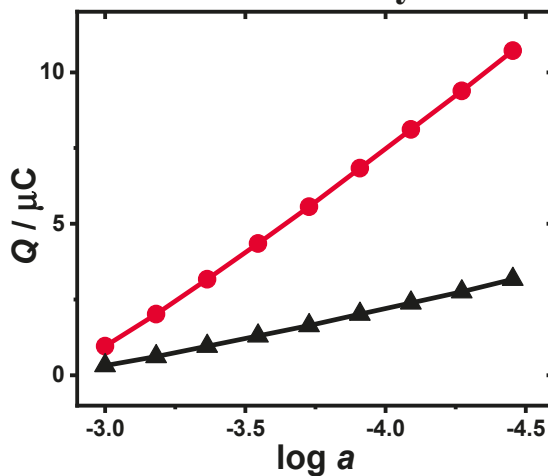
Tingting Han

# Coulometric Transduction Method for Solid-Contact Ion-Selective Electrodes

Coulometry



1 mC



5 mC



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# Coulometric Transduction Method for Solid-Contact Ion-Selective Electrodes

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To Tao, Ailin and Haoyu



## Preface

This doctoral thesis work was mainly carried out at the Analytical Chemistry Group of Laboratory of Molecular Science and Engineering at Åbo Akademi University under the supervision of Prof. Johan Bobacka, Dr. Ulriika Mattinen and Docent Zekra Mousavi during the years 2016-2021. Part of the work was done in cooperation with University of Geneva. Funding from Academy of Finland, Stiftelsens för Åbo Akademi Forskningsinstitut, Rector scholarship of Åbo Akademi University, grant from Molecular Process and Molecular Technology (MPMT) profiling area, and Johan Gadolin Process Chemistry Centre (PCC) is gratefully acknowledged. I would like to acknowledge financial support from Harry Elvings legat for exchange studies and research visits.

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Finally, I wish to express my gratitude to my parents for their love and encouragement. Thank my husband Tao for his endless support, understanding, love and care through all those years during my good and bad times. Deep love to my two angels, Ailin and Haoyu, thank you for bringing joyful to my life, teaching me to take responsibilities and growing to be a mom. I could not come to this far without you all. Thank you!!!

Åbo, October 2020

Tingting Han

## Abstract

As one of the pioneering works in the field of solid-contact ion-selective electrodes (SCISEs), a new coulometric transduction method was proposed by Bobacka's group from Åbo Akademi University. This thesis work was carried out to deepen the understanding of the coulometric transduction method for SCISEs.

In this thesis, cation-selective SCISEs ( $K^+$ ,  $H^+$ ,  $Ca^{2+}$  and  $Pb^{2+}$ ) and anion-sensitive SCISEs ( $Cl^-$ ,  $NO_3^-$ ,  $ClO_4^-$  and  $SO_4^{2-}$ ) were studied utilizing chronoamperometry, coulometry, and electrochemical impedance spectroscopy (EIS). The conducting polymer poly(3,4-ethylenedioxythiophene) PEDOT was used as ion-to-electron transducer in the fabrication of SCISEs. Cyclic voltammetry was performed for characterizing PEDOT-based films. In the coulometric transduction method, instead of measuring the potential between the SCISE and reference electrode, the potential is held constant and the current between the SCISE and counter electrode is measured. A transient current is obtained whenever the primary ion activity changes in the solution. Integration of the current-time curve results in the cumulated charge that is used as the analytical signal. The cumulated charge is linearly proportional to the logarithmic activity of the primary ion, and inversely proportional to the charge of the detected ion. The current and cumulated charge responses of cation-selective SCISEs and anion-sensitive SCISEs are of opposite sign under the same experimental protocol, in analogy with potentiometry. A thicker solid-contact film, *i.e.* larger redox capacitance of conducting polymer, leads to amplification of the cumulated charge, at the price of a longer response time.

The amperometric and coulometric response can be improved by increasing the geometrical area of the SCISE surface and by applying a thinner ion-selective membrane (ISM) deposited using a spin-coating technique. A larger electrode area and a thinner ISM lower the resistance of the ISM to facilitate the ion transport through the SCISE, *i.e.* the ISM and solid-contact film. Under optimized conditions, the high sensitivity of the coulometric method for the  $K^+$ -selective SCISE made it possible to detect 5  $\mu M$  concentration changes at the starting solution with 5 mM concentration, *i.e.* 0.1% change in activity was detectable. Theoretical modeling of the coulometric method was done with  $Cl^-$ -sensitive SCISEs. A 0.2% change in activity was detectable in  $Cl^-$ -sensitive SCISEs utilizing the coulometric method. The coulometric method was also applied for detecting pH changes in seawater and concentration changes of  $K^+$  ions in control serum samples.

Some interesting features were observed from coulometric results of divalent cation ( $\text{Pb}^{2+}$ - and  $\text{Ca}^{2+}$ -) SCISEs. The coulometric response of the  $\text{Pb}^{2+}$ -SCISEs was mainly limited by ion transport in the poly(3,4-ethylenedioxythiophene) poly(styrene sulfonate) PEDOT(PSS) solid-contact layer, while the coulometric response of  $\text{Ca}^{2+}$ -SCISEs was mainly dependent on the ion transport through the ISM. These results are in qualitative agreement with the obtained electrochemical impedance spectra.

Furthermore, anion sensors based on PEDOT doped with different counterions were studied using the coulometric transduction method and cyclic voltammetry. The obtained results indicate that the counter ions in the electrolyte solution used during electropolymerization play a role in the formation of the PEDOT solid-contact film, as well as influence the cyclic voltammograms when cycling in the electrolyte solution. This may be related to anion affinity following the Hofmeister series and the size (hydrated radius) of the anions. For a given polymerization charge, the nitrate counterion was found to give a higher yield of PEDOT, compared to chloride.

Keywords: Coulometric transduction method, Solid-contact ion-selective electrodes (SCISEs), PEDOT, Electrochemical impedance spectroscopy, Chronoamperometry, Coulometry,  $\text{K}^+$ -selective SCISEs,  $\text{Ca}^{2+}$ -selective SCISEs,  $\text{Pb}^{2+}$ -selective SCISEs,  $\text{H}^+$ -selective SCISEs, Anion-sensitive SCISEs

## Svensk sammanfattning

Som ett banbrytande arbete inom området jonselektiva elektroder med fast kontakt (SCISE), föreslogs en ny coulometrisk transduktionsmetod av Bobackas grupp från Åbo Akademi. Detta avhandlingsarbete utfördes för att fördjupa förståelsen för den coulometriska transduktionsmetoden baserad på SCISE.

I denna avhandling studerades katjonselektiva SCISEs ( $K^+$ ,  $H^+$ ,  $Ca^{2+}$  och  $Pb^{2+}$ ) och anjonkänsliga SCISE ( $Cl^-$ ,  $NO_3^-$ ,  $ClO_4^-$  och  $SO_4^{2-}$ ) med kronoamperometri, koulometri och elektrokemisk impedansspektroskopi (EIS). Den ledande polymeren poly (3,4-etylendioxietiofen) PEDOT användes som jon-till-elektron-omvandlare vid tillverkning av SCISE. Cyklisk voltammetri utfördes för att karakterisera PEDOT-baserade filmer. Med den koulometriska metoden hålls potentialen konstant i stället för att mäta potentialen mellan SCISE och referenselektroden och strömmen mellan SCISE och motelektroden mäts. En övergående ström erhålls närhelst den primära jonaktiviteten i lösningen ändras. Integrering av ström-tidskurvan resulterar i den kumulerade laddningen som används som analysignal. Den kumulerade laddningen är linjärt proportionell mot den logaritmiska aktiviteten för den primära jonen och omvänt proportionell mot laddningen för den detekterade jonen. De aktuella och kumulerade laddningarna för katjon-selektiva SCISE och anjonkänsliga SCISE är av motsatt tecken under samma experimentella protokoll, i analogi med potentiometri. En tjockare film med fast kontakt, dvs. större redoxkapacitans hos ledande polymer, leder till förstärkning av den kumulerade laddningen till priset av en längre responstid.

Den amperometriska och koulometriska responsen kan förbättras genom att öka ytan på SCISE och genom att använda en tunnare jonselektiv membran (ISM) framställd med en spinnbeläggningsteknik. En större elektrodyta och en tunnare ISM sänker ISM: s motstånd för att underlätta jontransporten genom SCISE, dvs. ISM och film med fast kontakt. Under optimerade förhållanden gjorde den höga känsligheten hos den koulometriska metoden för  $K^+$ -selektiv SCISE det möjligt att detektera  $5 \mu M$  koncentrationsförändringar i en startlösning med  $5 mM$  koncentration, dvs  $0.1\%$  förändring i aktivitet var detekterbar. Teoretisk modellering av den koulometriska metoden gjordes med  $Cl^-$ -känsliga SCISE.  $0.2\%$  förändring i aktivitet kunde detekteras i  $Cl^-$ -känsliga SCISE med användning av den koulometriska metoden. Den koulometriska metoden användes också för att detektera pH-förändringar i havsvatten och koncentrationsförändringar av  $K^+$ -joner i kontrollserumprover.

Några intressanta attribut observerades från koulometriska resultat för SCISE som var selektiva för divalenta katjoner ( $\text{Pb}^{2+}$  och  $\text{Ca}^{2+}$ ). Den koulometriska signalen för  $\text{Pb}^{2+}$ -SCISEs begränsades huvudsakligen av jontransport i poly(3,4-etylendioxietiofen) poly(styrensulfonat) PEDOT(PSS) skiktet, medan den koulometriska signalen för  $\text{Ca}^{2+}$ -SCISEs huvudsakligen var beroende av jontransporten genom ISM. Dessa resultat överensstämmer kvalitativt med erhållna elektrokemiska impedansspektra.

Dessutom studerades anjon-sensorer baserade på PEDOT (dopad med olika motjoner) med den koulometriska metoden och cyklisk voltammetri. Resultaten indikerar att motjonerna i elektrolytlösningen under elektropolymerisation spelar en roll i bildandet av PEDOT-fastkontaktfilmen, liksom påverkar de cykliska voltammogrammen vid cykling i elektrolytlösningen. Detta kan relateras till anjonaffinitet enligt Hofmeister-serien och storleken (hydratiserad radie) på anjonerna. För en given polymerisationsladdning visade sig nitratmotjonen ge ett högre utbyte av PEDOT jämfört med klorid.

Nyckelord: Koulometrisk transduktionsmetod, jonselektiva elektroder (SCISE) med fast kontakt, PEDOT, spektroskopi med elektrokemisk impedans, kronoamperometri, Koulometri,  $\text{K}^+$ -selektiva SCISE,  $\text{Ca}^{2+}$ -selektiva SCISE,  $\text{Pb}^{2+}$ -selektiva SCISE,  $\text{H}^+$ -selektiva SCISE, anjon-känsliga SCISE



## List of publications

This thesis is based on the following published papers, which are referred to in the text by their Roman numerals. The original publications are appended at the end of the thesis.

- I. T. Han, U. Vanamo, J. Bobacka, *Influence of electrode geometry on the response of solid-contact ion-selective electrodes when utilizing a new coulometric signal readout method*, **ChemElectroChem**. 3 (2016) 2071-2077
- II. Z. Jarolímová, T. Han, U. Mattinen, J. Bobacka, E. Bakker, *Capacitive model for coulometric readout of ion-selective electrodes*, **Anal. Chem.** 90 (2018) 8700–8707
- III. T. Han, U. Mattinen, J. Bobacka, *Improving the sensitivity of solid-contact ion-selective electrodes by using coulometric signal transduction*, **ACS sensors** 4 (2019) 900-906
- IV. T. Han, Z. Mousavi, U. Mattinen, J. Bobacka, *Coulometric response characteristics of solid-contact ion-selective electrodes for divalent cations*, **J. Solid State Electrochem.** 24 (2020) 2975-2983.
- V. T. Han, U. Mattinen, Z. Mousavi, J. Bobacka, *Coulometric response of solid-contact anion-sensitive electrodes*, **Electrochimica Acta**, 367 (2021) 137566.

## Contributions of the Author:

Paper I. The author did all the experimental work, evaluated the results, wrote the first draft of the manuscript, and finalized it in collaboration with the co-authors

Paper II. The author contributed to the plan and partially participated in the experimental work.

Paper III, IV and V. The author did all the experimental work, wrote the first draft of the manuscript, and finalized it in collaboration with the co-authors.

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## Abbreviations

CWE = coated-wire electrode

CP-ISE = conducting polymer-based ion-selective electrode

DOS = bis(2-ethylhexyl)sebacate

EDOT = 3,4-ethylenedioxythiophene

EIS = electrochemical impedance spectroscopy

ETH-500 = tetradodecylammonium tetrakis(4-chlorophenyl)borate

GC = glassy carbon

ISE = ion-selective electrode

ISM = ion-selective membrane

KTpCIPB = potassium tetrakis(4-chlorophenyl)borate

KTFPB = potassium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate

o-NPOE = ortho-nitrophenyl octyl ether

PEDOT = poly(3,4-ethylenedioxythiophene)

PEDOT(Cl) = poly(3,4-ethylenedioxythiophene) doped with chloride counterion

PEDOT(ClO<sub>4</sub>) = poly(3,4-ethylenedioxythiophene) doped with perchlorate counterion

PEDOT(NO<sub>3</sub>) = poly(3,4-ethylenedioxythiophene) doped with nitrate counterion

PEDOT(PSS) = poly(3,4-ethylenedioxythiophene) doped with poly(styrene sulfonate)

PEDOT(SO<sub>4</sub>) = poly(3,4-ethylenedioxythiophene) doped with sulfate counterion

PVC = poly(vinyl chloride)

SCISE = solid-contact ion-selective electrode

SP-ISE = single-piece ion-selective electrode

TDMACl = tridodecylmethylammonium chloride

## Symbols

$a_i$  = activity of primary ion

$C_{CP}$  = redox capacitance of conducting polymer

$C_{dl}$  = double layer capacitance

$C_i$  = concentration of respective ion  $i$

$E_{cell}$  = cell potential

$E_{cell}^0$  = standard potential

$E_{const}$  = sample-independent potential

$E_D$  = diffusion potential inside the membrane

$E_j$  = liquid junction potential

$E_{PB}$  = phase boundary potential

$E(\omega)$  = frequency dependent voltage

$i_p$  = peak current

$I(\omega)$  = frequency dependent current

$F$  = Faraday constant (96485 C/mol)

$f$  = frequency ( $[f] = \text{Hz} = \text{s}^{-1}$ )

$f_i$  = activity coefficient of ion  $i$

$I$  = ionic strength

$j = \sqrt{-1}$

$j$  = interfering ion  $j$

$K_{ij}$  = selectivity coefficient for primary ion  $i$  over interfering ion  $j$

$Q$  = cumulated charge

$R$  = universal gas constant (8.314 J/(mol×K))

$RC$  = resistor-capacitor in series

$R_{cell}$  = resistance of electrochemical cell

$R_{ct}$  = charge transfer resistance

$R_s$  = solution resistance

$T$  = absolute temperature (K), 0 K = -273.15 °C

$u_i$  = mobility of the respective ion  $i$

$Z$  = impedance of the system

$Z_d$  = finite-length diffusion impedance

$Z_w$  = Warburg impedance

$Z'$  = real impedance

$Z''$  = imaginary impedance

$z_i$  = charge number of primary ion  $i$

$z_+$  = charge number of cation

$z_-$  = charge number of anion

$\alpha$  = internal reference solution phase

$\beta$  = sample solution phase

$\omega$  = angular frequency

$\varphi$  = phase shift (phase angle)

$\varnothing_{GC}$  = diameter of glassy carbon electrode

## 1. Introduction

Electrochemical sensors are important analytical tools that provide information about the chemical composition of a sample in real time and they are widely used in a variety of fields related to our daily life [1–4]. The potentiometric ion sensors are among the oldest electrochemical sensors with origins dating back to the twentieth century, and have a very large number of applications, including the determination of ion concentrations in environmental and clinical analysis [5–8]. Potentiometric ion sensors can provide the possibility to detect chemical species with reasonable selectivity and low detection limit [9–12]. Replacing the internal filling solution of conventional ion-selective electrodes (ISEs) with solid-state ion-to-electron transducers resulted in solid-contact ion-selective electrodes (SCISEs). This made ISEs more durable and their miniaturization more facile and convenient for different applications [13]. The improved potential stability of SCISEs was realized by introducing a conducting polymer, with high redox-capacitance and mixed ion-electron conductivity, as ion-to-electron transducer between the ion-selective membrane (ISM) and the electrical conductor [1,6,12,14–17]. Additionally, there are also other factors determining the potential stability of SCISEs, such as interferences from  $O_2/CO_2$  and the possible presence of a water layer between solid contact and membrane [18,19]. Furthermore, the potential of SCISEs with conducting polymer as solid contact can be shifted by applying either a potential which deviates from the open-circuit potential of the electrode or by applying current pulses [20,21].

Traditionally, the response of potentiometric ion sensors are determined by the Nernst equation, where the potential is dependent on and also linearly proportional to the logarithm of activity of the primary ion detected in solution [22]. Recently, a new coulometric transduction method was presented by Bobacka's group, as a new innovative measuring technique in the field of SCISEs [23,24]. This transduction method is termed constant potential coulometry and can be used for SCISEs with high potential stability and large redox capacitance of the ion-to-electron transducers. The coulometric transduction method utilizes a three-electrode cell (ISE as working electrode, counter electrode and reference electrode) instead of the conventional two-electrode system (ISE as indicator electrode and reference electrode) used in potentiometry. Instead of measuring the potential between the ISE and reference electrode as it is done in traditional potentiometry, the potential of the ISE is kept constant using a potentiostat. As the activity of primary ion changes in the solution, the phase boundary potential of the

membrane|solution interface will change. Since the potential between the ISE and reference electrode remains constant, this will shift the oxidation/reduction state, and thus the potential, of the solid-contact film to compensate for the change of the phase boundary potential. The current will flow between the ISE and the counter electrode until the potential change of the solid contact film matches the change of the phase boundary potential. Integration of the response current with time results in the cumulated charge. The cumulated charge is linearly proportional to the change in the logarithmic activity of the primary ion. The advantage of the coulometric method is that the analytical response (cumulated charge) can be amplified by increasing the redox capacitance of the conducting polymers [23].

The main objective of this work was to gain a deep and thorough understanding of the coulometric transduction method. To achieve this, the coulometric transduction method was investigated and discussed in detail. For example, the resistance of ISM was decreased by enlarging the surface contact area of SCISEs (*Paper I*) or by using spin-coating instead of drop-cast ISM to decrease the thickness of the ISM (*Papers II, III, IV, V*). The sensitivity of SCISEs was improved by enlarging the redox capacitance of conducting polymers that was covered with spin-coated ISM (*Papers II, III*). The continuation of the research work on divalent cation  $\text{Pb}^{2+}$ - and  $\text{Ca}^{2+}$ -SCISEs demonstrated some unique features of the coulometric transduction method used for  $\text{Pb}^{2+}$  and  $\text{Ca}^{2+}$  cation detection (*Paper IV*). Furthermore, the investigation of anion-sensitive SCISEs utilizing the coulometric method was done (*Paper V*). Anion sensors were also characterized with cyclic voltammetry.

This thesis consists of four chapters. In chapter one and two, the basic knowledge of potentiometric ion sensors is briefly introduced, and the theoretical background of techniques related to this work is outlined. In chapter three, the results obtained in this research work are described and discussed. In chapter four, the thesis is wrapped up with thorough conclusions. All the original publications are attached in the final part.

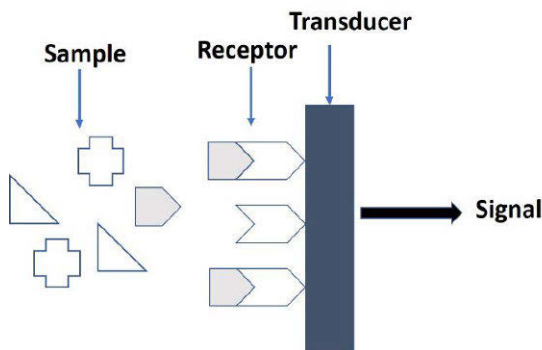
## 1.1 Electrochemical sensors

Electrochemical sensors are of high importance in our modern society due to the increased need to monitor various aspects related to our daily lives, such as monitoring fluoride in drinking water, blood health checking, heavy metal pollution in the environment *etc.* As shown in Figure 1, an electrochemical sensor consists of two parts: the recognition layer which acts as a receptor, and the transduction layer which converts information from the recognition process into a useful signal, such as voltage, current or resistance [25,26]. The transducer is often connected to a



signal amplifier during the recognition event, such as in enzyme-based biosensors [27]. Traditionally, electrochemical sensors can be divided into three main groups based on the measured signal: potentiometric sensors, amperometric sensors and conductometric sensors [27,28].

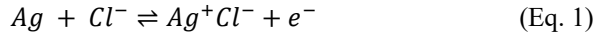
Potentiometric sensors are an important group of electrochemical sensors. They consist of two basic elements, *i.e.* ion recognition and signal transduction. A chemical recognition layer containing a receptor or ionophore performs the selective recognition of the target ion with respect to the interfering ions. The selectivity depends on the size, shape, polarity and binding strength of the target ion to the recognition layer. A transducer layer transforms the chemical information into a detectable signal, *i.e.* the electrical potential or electromotive force (emf). In the case of potentiometric ion sensors, a local equilibrium is established at the interphase between the membrane and the sample, and information about the composition of a sample is obtained from the potential difference between reference electrode and indicator electrode [29].



**Figure 1.** Signal transduction of electrochemical sensors

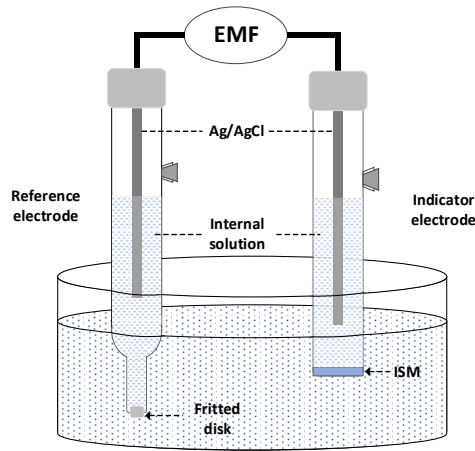
### 1.1.1 Potentiometric ion sensors

The signal that comes from potentiometric ion sensors is the potential difference between the reference electrode and the indicator electrode measured with a potentiometer under zero current conditions [13]. Figure 2 shows the set-up for a potentiometric measurement using a conventional ISE with an internal filling solution as indicator electrode and a Ag/AgCl/3 M KCl reference electrode. In this case, Ag/AgCl is immersed in an electrolyte solution (3 M KCl) containing a constant and high concentration of Cl<sup>-</sup> anions and separated from sample with a frit/junction. The ion-to-electron transduction with the reversible reaction of reference electrode can be expressed as follows,



The inner filling solution of conventional ISEs contains the primary ion for which the ISM is selective, and ions needed to stabilize the potential of the inner reference electrode ( $Cl^-$  in the case of a  $Ag/AgCl$  electrode). The reversible ionic equilibrium between the inner filling solution and ISM, as well as between ISM and sample solution leads to the stable cell potential of ISEs [22].

In contrast to a conventional ISEs, SCISEs are sensors where the internal filling solution and the internal reference element are substituted by an ion-to-electron transducing solid contact film [30].



**Figure 2.** Set-up for potentiometric ion sensors with a conventional ISE

The electrochemical cell can be considered as a galvanic cell, where the potential difference between the indicator electrode and the reference electrode ( $E_{cell}$ ) is the sum of all potential contributions from different interfaces. The magnitude of the resulting potential can be expressed as,

$$E_{cell} = E_{PB} + E_D + E_j + E_{const} \quad (\text{Eq. 2})$$

where  $E_{cell}$  is the cell potential,  $E_{PB}$  is the phase boundary potential at the ISM|solution interface,  $E_D$  is the diffusion potential inside the ISM,  $E_j$  is the liquid junction potential of the reference electrode, and  $E_{const}$  represents all the sample-independent potential contributions.

$E_{const}$  includes the phase boundary potential of the solid contact|membrane interface and inner ion-selective electrode solution|membrane interface as well as the potential of internal and external reference electrodes, which remain constant and independent of the sample solution. The diffusion potential inside the membrane ( $E_D$ ) is very small in comparison to the phase boundary potential ( $E_{PB}$ ) and can usually be neglected.

In the case of the reference electrode, the liquid-junction potential ( $E_j$ ) develops across the phase boundary of two dissimilar solutions, such as the internal filling solution of the reference electrode and the sample solution. Apart from the difference in ion concentration, the liquid-junction potential is also dependent on the ionic mobility, and is usually estimated by the Henderson equation,

$$E_j = \frac{RT}{F} \frac{\sum (|z_i|/z_i) u_i [C_i(\beta) - C_i(\alpha)]}{\sum |z_i| u_i [C_i(\beta) - C_i(\alpha)]} \ln \frac{\sum |z_i| u_i C_i(\alpha)}{\sum |z_i| u_i C_i(\beta)} \quad (\text{Eq. 3})$$

where  $z_i$  is the charge of the respective ion  $i$ ,  $u_i$  is the mobility of the respective ion  $i$ , and  $C_i$  is the concentration of the respective ion  $i$ ,  $\alpha$  and  $\beta$  are used to denominate the internal reference solution and the sample solution phases. The phase boundary potential can be stabilized by keeping a high (saturated) concentration of the internal reference electrolyte and choosing a salt with similar mobilities for the anion and the cation. As shown in Figure 2, Ag/AgCl/3 M KCl is used as the reference electrode. The charge transfer at the liquid junction is dominated by KCl, for which the mobility of the cation and anion is approximately the same, therefore minimizing the liquid junction potential.

The potentiometer measures the cell potential ( $E_{cell}$ ), the difference between the reference electrode and the indicator electrode in the solution. The potential changes are mainly dependent on the phase boundary potential ( $E_{PB}$ ) between ISM|solution interface, and is linearly proportional to the logarithm of the activity of the primary ion, according to the Nernst equation, as shown in Eq. 4 and Eq. 5 in two different forms,

$$E_{cell} = E_{cell}^0 + \frac{RT}{z_i F} \ln a_i \quad (\text{Eq. 4})$$

$$E_{cell} = E_{cell}^0 + \frac{2.303 RT}{z_i F} \log a_i \quad (\text{Eq. 5})$$

where  $E_{cell}$  is the cell potential,  $E_{cell}^0$  is the standard potential,  $R$  is the universal gas constant (8.314 J/(mol×K)),  $T$  is the absolute temperature (K),  $F$  is the Faraday constant (96485 C/mol),

$z_i$  is the charge of the primary ion  $i$ , and  $a_i$  is the activity of the primary ion  $i$ . The slope of the linear part in the plot of cell potential against logarithm of activity of the ion of interest would be  $59.2/z_i$  mV/decade at 25 °C, which is positive for cations and negative for anions [22].

According to the Nernst equation, the ISEs are responsive to the activity and not to the concentration of ions in the solution. Activity indicates the effective concentration of the ionic species in the solution and can be calculated from the concentrations using the following Eq. 6,

$$a_i = f_i C_i \quad (\text{Eq. 6})$$

where  $a_i$  is the activity,  $f_i$  is the activity coefficient, and  $C_i$  is the concentration of the respective ion  $i$ . The activity coefficient depends on the type of ions present in the solution and the total ionic strength of the solution. The activity coefficient (at 25°C) can be determined using the Debye-Hückel equation [22],

$$\log f_{\pm} = -\frac{Az_+z_-\sqrt{I}}{1+Bd_{\pm}\sqrt{I}} + CI \quad (\text{Eq. 7})$$

where  $A$  and  $B$  are conditional constants for each sample solution and depending on parameters like temperature, density and electric permittivity of the solvent.  $z_+$  and  $z_-$  are the charge numbers of the cation and anion, respectively.  $I$  is the ionic strength,  $d_{\pm}$  is the average of effective ion radius,  $d_+$  for cation,  $d_-$  for anion.  $C$  is an experimentally found coefficient which can be approximated by  $C = -0.1z_+z_-$ , for ionic strength up to 0.3 mol/dm<sup>3</sup>.

The ionic strength of the solution is defined by Eq. 8:

$$I = \frac{1}{2} \sum_i C_i z_i^2 \quad (\text{Eq. 8})$$

where  $C_i$  is the concentration and  $z_i$  is the charge of the respective ion  $i$  [22].

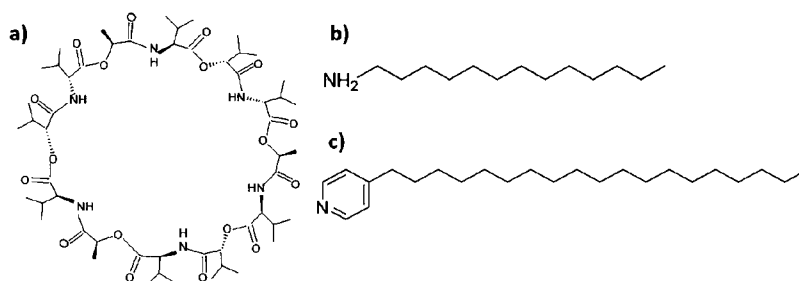
### 1.1.2 Ion-selective membrane

The ion-selective membrane (ISM) provides the selectivity of the ISEs to a specific ion. The selective solvent polymeric membrane is ideally a liquid of high viscosity containing the components as 30-33 wt% poly(vinyl chloride) (PVC), 60-66 wt% plasticizer, and 0.5-2 wt% ionophore plus the lipophilic salt. The molar ratio of the ionophore to the lipophilic salt should

be carefully optimized in order to keep and improve the selectivity of ISEs. All the membrane components are dissolved and well dispersed in a solvent which is usually tetrahydrofuran. The resulting mixture is referred to as the membrane cocktail. In this thesis, drop-casting and spin-coating techniques were used for applying the ISM on top of the solid contact layer of the SCISEs. Before measurement, the electrodes were left to dry overnight for spin-coated membranes and 1-2 days for drop-cast membranes, followed by conditioning in a corresponding and appropriate aqueous solution (*Papers I-V*).

### 1.1.2.1 Ionophore

The ionophore, or ion carrier, is the most important component in any polymeric membrane as it has the main influence on the selectivity and sensitivity of the sensor. The selectivity of ISE depends on the binding ability of the ionophore with the target ion, with respect to the interfering ions. An ionophore should bind the target ion with high affinity and good reversibility. Additionally, the ionophore structure must contain numerous lipophilic groups in order to minimize its leaching rate from the membrane to the sample phase. A well-known neutral ionophore for  $K^+$ -selective membranes is valinomycin, which consists of twelve alternating amino acids and esters that forms a macrocyclic molecule [31,32].



**Figure 3.** Example of the sensing ionophore: a) valinomycin (potassium ionophore I), b) tridecylamine (hydrogen ionophore I), c) 4-nonadecylpyridine (hydrogen ionophore II)

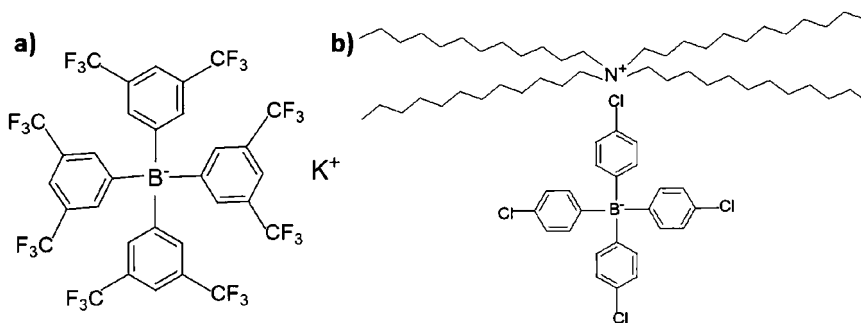
### 1.1.2.2 Lipophilic salt

Lipophilic salts are also known as ion exchangers. For a Nernstian response of the ISE, the prerequisite is trying to avoid the coextraction of counter ions together with the primary ion from the sample into the membrane phase. This means that the membrane is permeable only for ions with the same charge sign as that of the primary ion. Adding a known quantity of lipophilic salts into the membrane can greatly improve the ISEs' response time, stability,

reproducibility and selectivity. Thus, lipophilic salts are incorporated into the membrane to provide permselectivity, or the ability to prevent the interference from counter ions (Donnan exclusion) [33–35]. In the absence of ion exchanger in the membrane, the simultaneous coextraction of sample counterions may occur according to the following reaction:



Therefore, it is of importance to incorporate the ionic sites into the membrane to avoid and minimize coextraction processes of counterions. In addition, the amount of lipophilic salt in the membrane must be carefully controlled as an excessive amount may lead to selectivity failure of the ISEs. In this thesis, a small amount (1 wt%) of potassium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (KTFPB) and cannot be added in molar excess vs ionophore were used for  $K^{+}$ -selective membranes (in order to preserve the selectivity) [23]. As for  $K^{+}$ -selective electrode, the lipophilic ion  $TFPB^{-}$  anion would be kept in organic phase, while  $K^{+}$  cation can move freely between membrane and aqueous solution. For anion sensors, a rather high portion (15 wt%) of tridodecylmethylammoniumchloride (TDMACl) was incorporated in anion-sensitive membrane [36]. Besides, the addition of a lipophilic salt without ion-exchanger properties also reduces the electrical resistance of the membrane. For example, the resistance of a  $K^{+}$ -selective membrane was decreased further by addition of tetradodecylammonium tetrakis(4-chlorophenyl)borate (ETH-500) where both the anion and the cation are lipophilic, and both stay in the membrane phase, which means ETH-500 could increase the conductivity of the ISM [37].



**Figure 4.** Example of lipophilic salts: a) potassium tetrakis[3,5-bis(trifluoromethyl)phenyl] borate (KTFPB), b) tetradodecylammonium tetrakis(4-chlorophenyl)borate (ETH-500)

### 1.1.2.3 Polymeric matrix

The polymeric matrix provides mechanical stability and structural integrity to the membrane. It should be inert, as an inactive component and have no chemical interactions with the detected ions. Shatkay *et al* [38,39] was the first to use a polymer as a homogenous membrane matrix for an ISM and polymeric ISE membranes are commonly prepared with PVC.

### 1.1.2.4 Plasticizer

A plasticizer is added to increase the plasticity of the ISM. It can reduce the viscosity of a PVC membrane by lowering the glass-transition temperature and ensure a relatively high mobility of the membrane constituents. The plasticizer provides a homogeneous and miscible system of the organic membrane phase and it also plays a role in dissolving the other membrane components. Depending on its polarity and dielectric constant, a plasticizer can influence the ion-exchanger characteristics of the membrane and the selectivity can be affected, as a consequence. Leaching of the plasticizer should be taken into account, since the leaching of the plasticizer from the membrane will increase the loss of ionophore and lipophilic salts, thereby decreasing the lifetime and performance of ISEs [22]. Two commonly used plasticizers are bis(2-ethylhexyl) sebacate (DOS) or ortho-nitrophenyl octyl ether (o-NPOE) [40].

## 1.1.3 Selectivity of potentiometric ion sensors

The selectivity of ISEs is an important parameter for potentiometric ion sensors, and it represents the ability of an ISE to discriminate interfering ions from the target ion. The main functional component for selectivity of ion-selective membranes is the ionophore. Increasing the selectivity of ISEs requires the optimization of ionophore structures and membrane compositions [41]. For cation-selective ISMs, there are ionophores with good performance and high selectivity [31,42,43]. In addition to the ionophore, lipophilic salts, known as ion exchangers, also contribute to the selectivity of ISEs, as mentioned above. The selectivity of membranes that contain only ion exchanger (no ionophore) closely follows the Hofmeister series [44,45], which gives the cation's and anion's affinity to the aqueous phase based on their free hydration energy, shown as follows,

Large lipophilic anions  $> \text{ClO}_4^- > \text{SCN}^- > \text{I}^- > \text{NO}_3^- > \text{Br}^- > \text{Cl}^- > \text{HCO}_3^- > \text{SO}_4^{2-}$

Large lipophilic cations  $> \text{Cs}^+ > \text{K}^+ > \text{NH}_4^+ > \text{Na}^+ > \text{Li}^+ > \text{Sr}^{2+} > \text{Ca}^{2+} > \text{Mg}^{2+}$

The Nikolskii-Eisenman equation (Eq. 10) is used to evaluate the selectivity of ISEs [22]. In Eq.10,  $z_i$  is the charge of primary ion,  $z_j$  is the charge of interfering ion,  $a_i$  is the activity of primary ion,  $a_j$  is the activity of interfering ion, and  $K_{i,j}$  represents the selectivity coefficient of the electrode to the primary ion ( $i$ ) with respect to the interfering ion ( $j$ ).

$$E_{cell} = E_{cell}^0 + \frac{2.303 RT}{z_i F} \log(a_i + \sum_j K_{i,j} a_j^{\frac{z_i}{z_j}}) \quad (\text{Eq. 10})$$

It should be realized that the Nikolskii-Eiseman equation (Eq. 10) is valid for the primary ion and interfering ion with the same charge ( $z_i = z_j$ ). If  $z_i = z_j$ , then the term  $z_i/z_j = 1$  and the equation can be slightly simplified. In the case of different charges ( $z_i \neq z_j$ ), an extended version of the equation should be considered.

#### 1.1.4 Development of solid-contact ion sensors (SCISEs)

The development of ISEs with a solid contact transducer instead of an internal aqueous electrolyte has been a topic of research for many years [30]. Conventional ISEs with inner filling solution limited the applications of ISEs due to continuous maintenance needed, and that they should always be used in the vertical position. Elimination of the internal filling solution of conventional ISEs results in the so-called coated-wire electrodes which are more durable and easier to miniaturize [46]. Historically, the coated-wire electrode is a simple and robust design where the ISM is directly cast on the surface of a solid conductor. However, the interface between an electronic conductor and an ion-conducting membrane is a blocked interface without a well-defined ion-to-electron transduction mechanism, resulting in potential instability and drift.

With the research carried out on the SCISEs, it was found out that several prerequisites should be fully considered for good solid-contact layers [13,30]: First, the solid-contact transducer should provide a sufficiently fast and reversible transition from ionic to electronic conduction, at the same time have good stability and avoid any parallel side reactions. Second, a solid-contact transducer should possess a large redox/double-layer capacitance to protect against the limited current flow applied during potentiometry and have the ability to stabilize equilibrium if some external disturbances occur. Third, a potential stability between the solid-contact transducer and the ISM has to be maintained and the good reproducibility of standard potential between different SCISEs is also an important parameter. Fourth, the chemical stability of solid-contact functional materials is very essential, and minimizing the influence of light, gas, and



redox species on solid contact is also very important [18]. Sufficient hydrophobicity and low water absorption of solid-contact materials are required to prevent the formation of a water layer at the solid contact/ISM interface [47].

Electroactive conjugated polymers have emerged as one of the most promising ion-to-electron transducers for SCISEs. Conducting polymers, such as PEDOT [14,48,49], polypyrrole [17,50–53], poly(3-octylthiophene) POT [15,31] and polyaniline [54] have been used as ion-to-electron transducers. Among conducting polymers, polypyrrole was the first to be used in SCISEs [17]. Redox couples can also be used as solid contact, such as Prussian blue [55] and Ag/AgCl [56,57]. Furthermore, materials with a large surface area, such as carbon nanotubes [58,59], graphene [60,61], porous silicon [62] *etc.* have also been used as solid contacts where potential stability is obtained via a large double layer capacitance, instead of a redox capacitance.

### 1.1.5 Conducting polymers in potentiometric sensors

Conducting polymers are good candidates, applied as ion-to-electron transducer because of their mixed electronic and ionic conductivity, which ensures proper electronic and ionic conductivity. Conducting polymers show a high redox capacitance which is beneficial to maintain a high potential stability [14] and less side reactions [18]. Figure 5 shows different types of solid-state ISE based on conducting polymers: solid-contact ISE (SCISE), single-piece ISE (SP-ISE) [56,63,64], and conducting polymer ISE (CP-ISE) [67]. In solid-contact ISEs (SCISEs) the conducting polymer is used as ion-to-electron transducer. Alternatively, the conducting polymer was incorporated in the ISM resulting in single-piece ISE (SP-ISE). In these two forms of solid-state ISEs, the conducting polymer only act as an ion-to-electron transducer, while the selectivity of ISEs is mainly determined by the ionophore in the ISM. The one-step fabrication of SP-ISE is considered as an advantage regarding easy preparation in comparison to SCISE using conducting polymers as transducers [64,66]. However, since the conducting polymer is present in the ISM of the SP-ISE, redox species that are present in the sample solution may cause a redox interference [13]. In the so-called CP-ISE, ion-recognition sites are directly incorporated in the conducting polymer film during electrochemical deposition of the conducting polymer. The sensing mechanism is dependent on the interactions of the analyte with functional groups on the conducting polymer or the doping ions used for electropolymerization [67,68]. In this case, conducting polymers are responsible for both the ion recognition and the signal transduction. The application of CP-ISEs is limited due to the nonselective or limited ionic response of conducting polymers [13]. Thus, until now, conducting polymers were mostly used as ion-to-electron transducers in SCISEs. In this thesis (*Papers I-*

V), conducting polymer PEDOT-based films were used as the ion-to-electron transducers, while the ISM was responsible for the selectivity to the target ion.

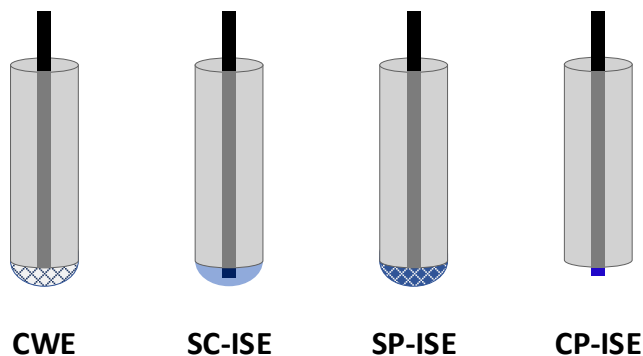


Figure 5. Various types of solid state ISEs: coated wire electrode (CWE), solid contact ISE (SCISE), single-piece ISE (SP-ISE), conducting polymer ISE (CP-ISE)

However, conducting polymers as ion-to-electron transducers still have difficulties to fulfill all requirements of an ideal solid-contact transducer. Depending on the polymer and the measuring conditions, conducting polymers can suffer from long term potential drift, irreproducibility of standard potential, light sensitivity and other redox process *etc*, that may happen during the measurement [13]. He *et al* [19,47,69] used hydrophobic conducting polymers as solid contact to improve the performance of SCISEs, such as increase the potential stability and the standard potential reproducibility. Vanamo *et al* [20,21] presented that the standard potential of SCISEs can be shifted by applying current with chronopotentiometry or short circuit SCISEs with a reference electrode. In addition, chronopotentiometry can also be used as a technique to verify the potential stability of SCISEs [14].

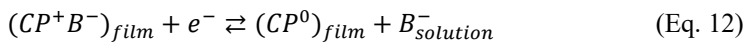
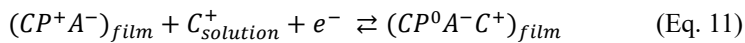
### 1.1.6 PEDOT as ion-to-electron transducers in SCISEs

Poly(3,4-ethylenedioxythiophene), often abbreviated as PEDOT, is an electrically conducting polymer with high stability, conductivity and transparency. Due to its unique properties, it has wide applications in capacitors, touch screens and potentiometric ion sensors [1,14,70]. A considerable amount of works have been published on utilizing PEDOT as solid contact in the fabrication of SCISEs for ion detection [71,72]. For example,  $K^+$ -selective SCISEs based on PEDOT showed higher electrochemical stability in the presence of  $O_2$  and  $CO_2$  compared to SCISEs based on polypyrrole [18]. The capacitance of PEDOT used in  $K^+$ -SCISEs can be increased depending on the dopants used. Mousavi *et al* showed that PEDOT doped with carbon

nanotubes, used as ion-to-electron transducer, gives a larger capacitive-like current than PEDOT(Cl) [73].

PEDOT can be synthesized in different ways: electrochemical polymerization, chemical polymerization, and photochemical polymerization. The electrochemical polymerization method is preferred because of its simplicity and reproducibility. In this work, the synthesis is done galvanostatically with the EDOT monomer dissolved in an aqueous electrolyte solution. The obtained polymer is in oxidized form, while simultaneously counter/doping ions are incorporated into the polymer film in order to compensate the charge created in the film during the polymerization process. The morphology and conductivity of the polymer are influenced by the chemical structure of the counter ion in the electrolyte solution [74,75].

The potential of the conducting polymer solid contact is related to the ratio of the reduced and oxidized forms of the conducting polymer and to the concentration of ions in the solution [13]. When the potential and redox state of the conducting polymer is changed, doping ions transfer between the solution and the conducting polymer to preserve overall electroneutrality in the conducting polymer film. When the conducting polymer is used as solid contact, *i.e.* coated with an ISM, then any change in the redox state of the conducting polymer involves transfer of ions between the conducting polymer and the ISM. Depending on the doping ions incorporated, the PEDOT layer will show either anionic or cationic response. As shown in Eq. 11 and Eq. 12, if the counter anion is bulky ( $A^-$ ), it is immobilized in the conducting polymer film and the negative charge can be compensated by small mobile cations ( $C^+$ ).  $C^+$  can move in and out of the polymer film when the conducting polymer is reduced or oxidized. Such cation movements (and cationic response) are observed for PEDOT doped with poly(styrenesulfonate)(PSS), *i.e.* PEDOT(PSS). If small counter ions ( $B^-$ ) were introduced into the polymer film during synthesis, this small and mobile anion ( $B^-$ ) can move freely in and out of the film during oxidation/reduction of the conducting polymer. This behavior is observed for PEDOT doped with chloride and other small anions.



## 1.2 Coulometric transduction method

Conventional ISEs and SCISEs have been used with potentiometry from the twentieth century.

Potentiometry is an accurate, and fast analysis technique, where the analytical response of ISEs is dependent on the logarithmic activity of the targeted ion. The logarithmic dependency has its advantages and disadvantages. A wide range of activities of ISEs can usually be detected with potentiometry, which counts in as an advantage. However, the sensitivity of potentiometry suffers from the fact that the measured potential is proportional to the logarithm of ion activity. Small changes of activity in the sample solution will result in even smaller change in potential that is measured after logarithmic calculation [76,77]. Thus, the disadvantage of potentiometry is determined already by the analytical performance of the sensors itself. For example, according to Nernst equation, a potential different of 1 mV needs a 4% change in ion activity for a monovalent ion and 8% change for divalent ion. A growing demand in clinical, forensic and environmental analyses calls for the development of in-situ, portable and selective sensors with high sensitivity, especially in clinical analysis, where the concentration intervals are extremely narrow [78].

In recent years, some non-zero current measurements protocols of ISEs have attracted considerable attention. These alternative measurement modes are chronopotentiometry [5,79], voltammetry [80–84], and constant potential coulometry [23,24,39] among others. Amemiya *et al* [83] reported the analysis of nanomolar concentrations of perchlorate in drinking water utilizing ion-transfer stripping voltammetry. Bakker's group [80] presented simultaneous detection of multiple ion activities using a thin-layer ionophore-based membrane and cyclic voltammetry. A new constant potential coulometric transduction method was proposed by Bobacka's group [23,24]. This method opened a new approach and is an important technique for SCISEs. The method is based on constant potential coulometry, utilizing a common three-electrode system instead of two-electrode cell with a constant potential being held between the working electrode (SCISE) and the reference electrode. The current flow between SCISE and the counter electrode is measured.

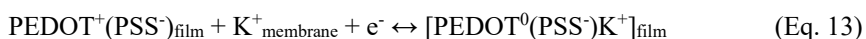
Importantly, the traditional selectivity of the membrane is maintained even though the coulometric transduction method is unconventional for ISEs. Although it is a coulometric method, it currently still needs at least a one-point calibration, because the transient current originally comes from potential changes at the interface between membrane and aqueous solution. The analytical signal of coulometric method is dependent on the oxidation/reduction of the solid contact film. Thus, the method is suitable for SCISEs. The coulometric transduction method can be also applied for coated-wire electrode but in this case the analytical cumulated charge is really limited due to the blocked interface, *i.e.* low double layer capacitance [23]. The analytical signal (cumulated charge) of the coulometric method is linearly proportional to the

change in the logarithm of primary ion activity and can be amplified by increasing the redox capacitance of the conducting polymer. This is an advantage of the coulometric method, *i.e.* to improve the sensitivity of ion detection, allowing measurements of very small ion activity changes in various fields of applications, including clinical analysis [3,78]. An amplified analytical signal (cumulated charge) also indicates a larger number of ion transport through the conducting polymer and ISM, which results in longer response times [23].

This thesis work (*Papers I-IV*) is a continuation of the investigation of the coulometric transduction method for SCISEs beyond the discoveries. Until now, the coulometric method was mainly investigated for SCISEs with PEDOT as solid contact, except of Na<sup>+</sup>-sensitive SCISEs using Prussian blue as solid contact (*Paper II*) and NO<sub>3</sub><sup>-</sup>-selective SCISEs using an ordered mesoporous carbon [85].

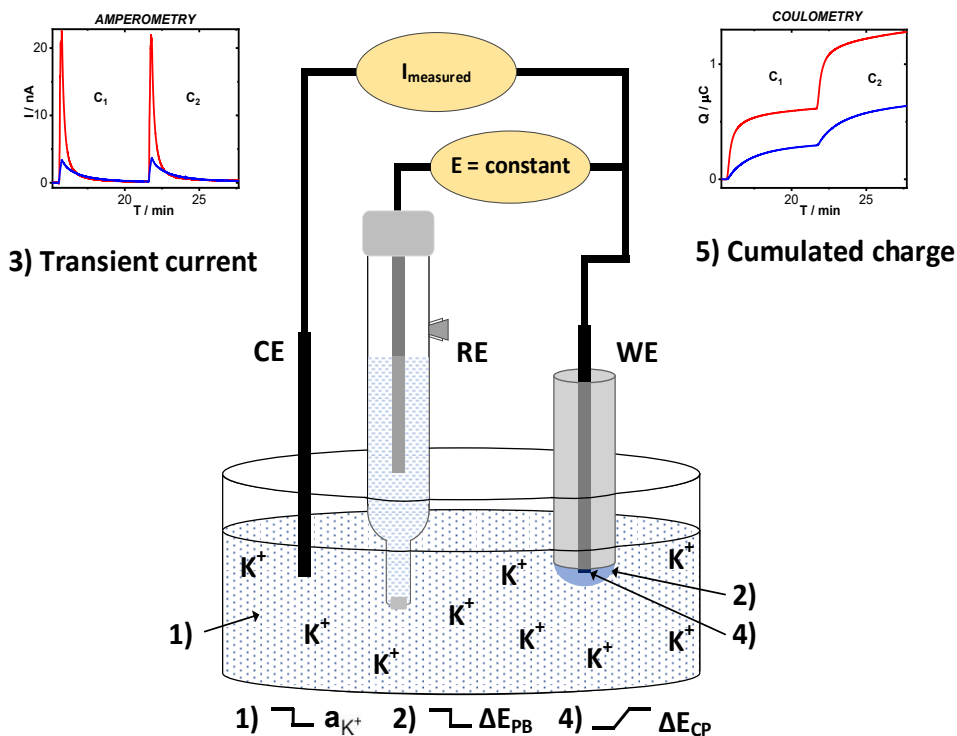
### 1.2.1 Principles of the coulometric method for cation-selective SCISEs

In a recent proof of concept for the coulometric transduction method, the novel signal transduction principle for SCISEs is demonstrated thoroughly using K<sup>+</sup>-selective SCISEs based on PEDOT(PSS) conducting polymer as solid contact [23,24]. In this case, the reaction taking place between PEDOT(PSS) and the ISM is shown in Eq. 13,



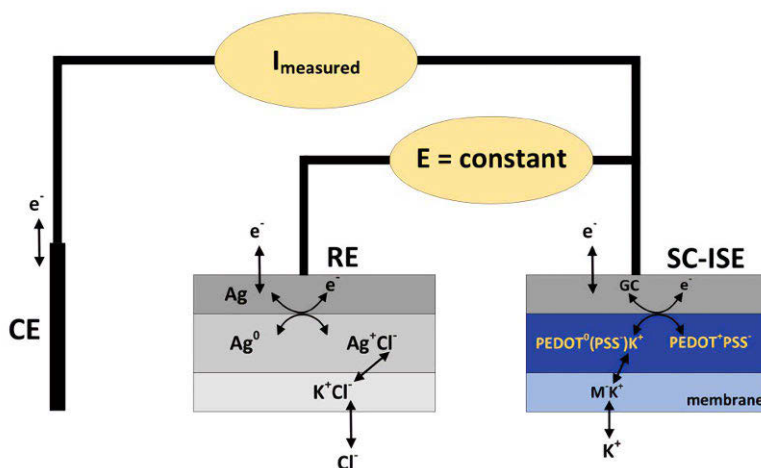
As shown in Figure 6, at the beginning, the three-electrode cell was stabilized at an applied potential. The value of the applied potential is dependent on the potential of the reference electrode, the potential stability window of PEDOT and the activity of primary ion in solution. Applying a potential that is close to the open circuit potential of the SCISE is expected to give the shortest initial equilibration time. The applied potential at the SCISE is maintained constant vs the reference electrode by the use of a potentiostat. A potential change at the sample|membrane interface originating from the activity alteration of the primary ion (1) will result in a potential change between SCISEs and reference electrode (2). Since the potential between SCISEs and reference electrode is forced to remain constant by a potentiostat, a transient current (3) will pass through SCISEs and counter electrode. The oxidation/reduction current generated by the potential change at the sample|membrane interface will cease when the potential change of the conducting polymer exactly compensates for the potential difference at the membrane|solution interface ( $\Delta E_{CP} = -\Delta E_{PB}$ )(4). The cumulated charge is obtained as the integral of current over time ( $Q = \int idt$ )(5). The logarithm of the activity (change) shows

a linear relationship to the total cumulated charge, and the slope of the curve depends on the redox capacitance of the solid contact. A theoretical description of the coulometric response is given below in Equations 15-20 [23].



**Figure 6.** Schematic illustration of the coulometric transduction method. In this system, the potential between SCISE and reference electrode is forced to be constant. The alteration of activity of the primary ion in the solution (1), which causes the potential changes at the sample|ISM interface (2), gives rise an oxidation/reduction current (3) until the potential change of solid contact is totally compensated with potential change at the sample|ISM interface (4). The cumulated charge is obtained by integrating the current with time (5). Amperometric (3) and coulometric (5) response of  $K^+$ -SCISEs ( $\Phi_{GC} = 3$  and  $10$  mm) covered with  $1$  mC PEDOT(PSS) and drop-cast membrane. The starting solution is  $0.1$  M KCl with  $0.1$  M NaCl as constant ionic background and the dilution step is  $\Delta \log a_{K^+} = 0.18$  decades.

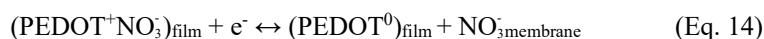
Simultaneously, the ion and electron transfer processes as well as the redox reaction of PEDOT(PSS) involved in the ion-to-electron transduction are clearly shown in Figure 7, and corresponds to the transduction principle of the coulometric method shown in Figure 6.



**Figure 7.** Schematic illustration of the ion and electron transfer processes as well as the redox reactions involved in the ion-to-electron transduction

### 1.2.2 Principles of the coulometric method for anion-sensitive SCISEs

In the case of the coulometric method for anion-sensitive SCISEs, the oxidation/reduction of PEDOT-based solid contact for  $\text{NO}_3^-$ -sensitive SCISE with PEDOT(Cl) solid contact after conditioning in  $\text{NO}_3^-$  aqueous solution, is shown as follows,



The working principle of the coulometric transduction method has been clearly and thoroughly demonstrated utilizing  $\text{K}^+$ -selective SCISE. According to Nernst equation, the potential of anion-sensitive SCISE increases, while that of cation-selective SCISEs decreases, when the concentration (activity) of the primary ion decreases. As a consequence of potentiometric measurement, the amperometric and coulometric responses of anion-sensitive SCISEs should give an opposite analytical signal from the response of cation-selective SCISEs, when the same sample solution dilution protocol is employed. Thus, the obtained current and cumulated charge of anion-sensitive and cation-selective SCISEs are of opposite sign, while the absolute magnitude of the obtained cumulated charge is the same.

### 1.2.3 Theoretical model for the coulometric transduction method

The theoretical modelling of the coulometric transduction method based on SCISEs was performed using  $\text{Cl}^-$ -SCISEs (*Paper II*). Before starting the coulometric measurement, the

system was allowed to reach equilibrium at the applied potential. An activity change at time  $t_0$  results in a potential change at the membrane|sample interface, which is shown as follows, according to the Nernst equation:

$$\Delta E_{PB}(\text{sample}) = \frac{0.0592}{z_i} \log \frac{a_i(\text{final})}{a_i(\text{initial})} \quad (\text{Eq. 15})$$

where  $z_i$  is the charge of the analyte ion,  $E_{PB}$  is the phase boundary potential,  $a_i$  is the activity of primary ion. Since the imposed potential remains constant, the potential change at the conducting polymers should be exactly opposite this value with same amount.

$$\Delta E_{PB}(\text{inner side}) = \frac{0.0592}{z_i} \log \frac{a_i(\text{initial})}{a_i(\text{final})} \quad (\text{Eq. 16})$$

As Bobacka *et al* pointed out, SCISEs can be modelled by a series resistor-capacitor ( $RC$ ) equivalent circuit, where the resistance of the electrochemical cell  $R_{cell}$  was attributed primarily to the bulk resistance of the ISM, and the capacitance  $C_{CP}$  was attributed to the bulk redox capacitance of the conducting polymer acting as ion-to-electron transducer [86]. At low frequencies the impedance response of conducting polymer is close to a capacitor arising from the reversible redox process of the conducting polymer. The capacitances relating to the ISM are very small and they mainly contribute to the high frequency response. At low frequencies, the equivalent circuit of the ISM reduces to a resistance  $R$  in series with the Warburg diffusion impedance. In the absence of Warburg diffusion, the total equivalent circuit of the SCISEs can be approximated by a series  $RC$  model.

The resulting current response of the SCISE when utilizing the coulometric method can thus be written as

$$i(t) = \frac{\Delta E_{PB}(\text{inner side})}{R_{cell}} e^{t-t_0/C_{CP}R_{cell}} \quad (\text{Eq. 17})$$

where  $C_{CP}$  is the capacitance of the conducting polymer and  $R_{cell}$  is the resistance of the electrochemical cell. Combining Eq. 16 with Eq. 17 results in the relationship between transient current and activity change in the sample as follows:

$$i(t) = \frac{0.0592}{z_i R_{cell}} \log \left( \frac{a_i(\text{initial})}{a_i(\text{final})} \right) e^{t-t_0/C_{CP}R_{cell}} \quad (\text{Eq. 18})$$



This transient current describes a current peak at time  $t_o$  that decays with a time constant  $RC$  which is a function of the capacitance of the conducting polymer and the cell resistance. Larger resistance of ISM leads to larger time constants. The time response of the current transient is dependent on the mass transport through the membrane. Thus, spin-coated thin-layer membrane (ca. 1-4  $\mu\text{m}$ ) can improve the coulometric signal, as expected (*Papers II, III*).

The peak current is found at  $t_o$  as

$$i_p = \frac{0.0592}{z_i R_{cell}} \log \left( \frac{a_i(\text{initial})}{a_i(\text{final})} \right) \quad (\text{Eq. 19})$$

It is evident that the magnitude of the peak current depends both on the Nernst function and cell resistance. The peak current should be larger with spin-coated ISM in comparison to drop-cast membrane, which is in good agreement with the obtained results (*Papers II, III*).

The cumulated charge  $Q$  was obtained as the integral of current over time and results in cumulated charge that is independent of the resistance.

$$Q = C_{CP} \frac{0.0592}{z_i} \log \left( \frac{a_i(\text{initial})}{a_i(\text{final})} \right) \quad (\text{Eq. 20})$$

The cumulated charge should be linearly proportional to logarithmic activity change in the sample. In the case of  $\text{K}^+$ -SCISEs with dilution experiments, the cumulated charge gives a positive slope of  $C_{CP}(0.0592/z_i)$  for cations and negative sign for anions, which is opposite to the Nernst slope. Increasing the redox capacitance of solid contact leads to larger cumulated charge, but at the price of a larger time constant, thus longer equilibration time (response time). This theoretical calculation of coulometric transduction method is closely correlated with the obtained results during this thesis work (*Papers I-V*). Mikhelson *et al* also presented a modified theoretical model of the amperometric and coulometric response of  $\text{K}^+$ -SCISEs that takes into consideration the concentration polarization in the ISE membrane [39].

## 2. Electrochemical measurements

This chapter describes the experimental techniques used for the synthesis and characterization of the SCISEs based on conducting polymers. The main goal of this chapter is to provide background information for understanding the results.

### 2.1 Potentiometry

The potentiometric measurements are performed in a two-electrode system: the indicator electrode and the reference electrode. The potential-measuring device (potentiometer, mV-meter) should have high input impedance. In this case, the current flow is kept as low as possible (in the order of magnitude of pA-fA). For ISE measurement, the potential of the ISE as indicator electrode is related to the activity of the primary ion, while the reference electrode should provide a quantitatively stable potential. The working principles and detailed description of this method was more thoroughly discussed in section 1.1.

In this work, potentiometric measurements were conducted to verify the proper function of the SCISEs (*Papers I-V*), *i.e.* to confirm that the SCISEs studied showed a Nernstian response where the response of potential against activity has a slope larger than 55 mV/decade for monovalent ion and larger than 25 mV/decade for divalent ion. For comparing potentiometry with chronoamperometry and coulometry, potentiometry was employed in the standard addition or dilution experiments in aqueous solution sensitivity test, as well as in control serum and seawater sample measurements (*Papers II, III*).

### 2.2 Chronoamperometry and coulometry

Chronoamperometry is an electrochemical method that is widely used in electroanalysis. It is based on measuring the current in a three-electrode setup but at a constant potential (or sudden changes in potential) for a certain amount of time. The transient current produced from the potential is recorded until it reaches equilibrium. The chronoamperometric measurements performed in the work described here were done using a three-electrode cell, consisting of a working electrode, a reference electrode and a counter electrode. The potential of the working electrode against the reference electrode was maintained constant by a potentiostat and the current flow between the counter electrode and the working electrode was measured. The

coulometric transduction method is an integration of the chronoamperometric current with time recorded at a constant applied potential, and can thus be called constant potential coulometry. This technique was conducted in all the five publications (*Papers I-V*), performed using an IVIUMSTAT (IviumStat.h standard, Ivium Technologies, Netherlands). The amperometric and coulometric response of SCISEs was mainly characterized by stepwise dilution protocol experiments.

### **2.3 Electropolymerization**

As mentioned earlier, the synthesis of conducting polymers can be done electrochemically, chemically, or photochemically [87]. Galvanostatic electropolymerization was used in this work and performed using a three-electrode cell. A constant current was applied on the working electrode, where the polymerization and deposition of the PEDOT film occurred. During the galvanostatic polymerization, the potential was measured as a function of time between working electrode and reference electrode by employing chronopotentiometry. The main conducting polymer studied in this thesis (*Papers I-V*), was prepared by electrochemical polymerization of EDOT monomer in aqueous solution. The PEDOT film was synthesized and doped with the counter ions, *i.e.* PSS<sup>-</sup>, Cl<sup>-</sup>, or NO<sub>3</sub><sup>-</sup> and the PEDOT films were thus obtained in the conducting p-doped state. During electropolymerization, the PEDOT film morphology is strongly influenced by the polymerization solution and especially by the counter ions incorporated into the film [75]. After the electrosynthesis of the PEDOT film, the oxidative state can be easily changed electrochemically, accompanied by movement of counter-ions in or out of film.

In this work, different thicknesses of PEDOT film were galvanostatically prepared and performed with Autolab General Purpose Electrochemical System (AUT30.FRA2-Autolab, Eco Chemie, B.V., The Netherlands).

### **2.4 Electrochemical impedance spectroscopy**

Electrochemical impedance spectroscopy (EIS) is an excellent technique to be used for characterizing the electrical properties of materials and interfaces of both solid and liquid systems [88–90]. The EIS measurement is done in a three-electrode system consisting of working electrode, counter electrode and reference electrode. When a constant (*dc*) potential is applied to the system, the potential/current ratio is known as the resistance of this system. In EIS, when a small, sinusoidally changing potential is applied to the electrochemical cell, it will

result in a sinusoidal alternating current recorded with an appropriate phase shift or phase angle between the applied potential and the resulting current response. The applied potential and the measured current are shown in Eq. 21 and Eq. 22, where  $\omega=2\pi f$  is the angular frequency, and  $\varphi$  is the phase angle between the applied potential and the resulting current. The potential is typically set to oscillate around the equilibrium potential with a very small amplitude, around 5-10 mV. A phase shift of  $0^\circ$  corresponds to a pure resistor,  $45^\circ$  occurs with a Warburg impedance (further described below) because of diffusion limitation and  $90^\circ$  means a pure capacitor, as shown in Figure 8.

$$E(\omega) = E \sin(\omega t) \quad (\text{Eq. 21})$$

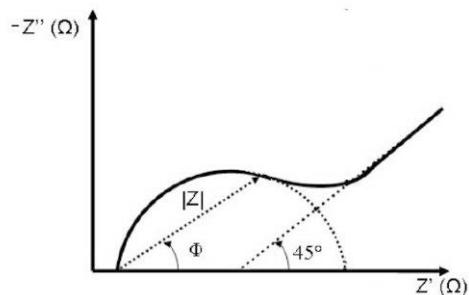
$$I(\omega) = I \sin(\omega t + \varphi) \quad (\text{Eq. 22})$$

The impedance  $Z$  of the system is given by Eq. 23, where  $E(\omega)$  and  $I(\omega)$  are the frequency dependent voltage and current, respectively. The impedance  $Z$  of a system is a vector quantity, given in Eq. 24. The real  $Z'$ , and the imaginary  $Z''$  components represent the resistive and the reactive part of the impedance, and  $j = \sqrt{-1}$  is the imaginary number.

$$Z(\omega) = E(\omega)/I(\omega) \quad (\text{Eq. 23})$$

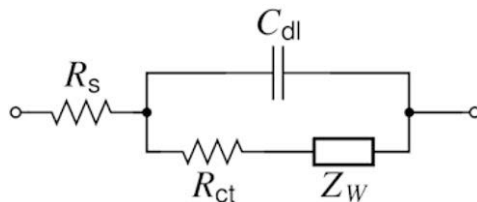
$$Z(\omega) = (Z') - j(Z'') \quad (\text{Eq. 24})$$

As shown in Figure 8, the real  $Z'$  impedance component is on x-axis and the imaginary  $Z''$  impedance component is on y-axis. The obtained vector is plotted into the so-called “Nyquist plot” with the  $Z'$  and  $-Z''$  as the vector components at each frequency. A Nyquist plot, as shown in Figure 8, is a plot of the imaginary impedance component vs the real impedance component, with no information about the value of the applied alternating current frequency to which the points in the plot corresponds. The shape of the Nyquist plot as well as the numerical values for the real ( $Z'$ ) and imaginary ( $-Z''$ ) impedances help in explaining the electrochemical process occurring at the electrode|electrolyte interface.



**Figure 8.** “Nyquist plot” of the impedance ( $Z$ )

The EIS response of electrode|electrolyte systems can be modelled as an equivalent circuit. As shown in Figure 9, the simplest circuit for a faradaic reaction is called the Randles circuit, which consists of electrolyte solution resistance ( $R_s$ ) connected in series with a double-layer capacitor ( $C_{dl}$ ) in parallel with a charge transfer resistor ( $R_{ct}$ ) and a Warburg element ( $Z_w$ ). Warburg impedance results from the diffusion of redox species from the bulk electrolyte to the electrode interface. When studying the properties of potentiometric ion sensors, EIS is used to characterize the charge transport in the conducting polymer films and ISM, as well as the charge transfer kinetics and double-layer contributions from the ISM|solution interface [86]. When studying the redox processes of conducting polymer in their conducting state, the redox centers are located throughout the polymer film and the counterions will diffuse into the polymer matrix. This process can be modeled by replacing the classical Warburg impedance with a finite-length diffusion impedance that accounts for the ion diffusion inside the polymer film. Under ideal conditions for a conducting polymer in the doped form, the redox reaction is diffusion controlled with a phase angle shift at  $45^\circ$  at intermediate frequencies. At low frequencies, it will display a capacitive-like behavior with phase angle at  $90^\circ$  as the conducting polymer is fully charge saturated and acts as a pure capacitor. At high frequencies, the redox reaction can be kinetically controlled and modeled by the parallel combination of the double-layer charging and charge transfer at the polymer|solution interface. In practical situations, under real measuring systems, the equivalent circuit can be complicated depending on the mechanism of the electrochemical processes and the interfaces involved [91].

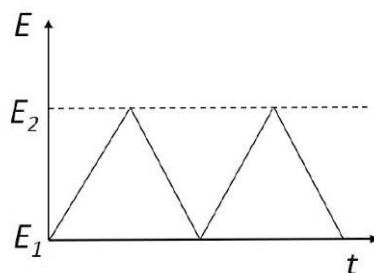


**Figure 9.** The Randles equivalent circuit where  $R_s$  is the solution resistance,  $R_{ct}$  is the charge transfer resistance,  $C_{dl}$  is the double layer capacitance and  $Z_w$  is the Warburg impedance.

In *Papers I-V*, EIS for the SCISEs was measured in the corresponding aqueous solution at open circuit potential with 10 mV as the excitation amplitude. EIS was used to characterize the electrochemical behavior of the SCISEs in order to further understand the mechanism of the coulometric transduction method.

## 2.5 Cyclic voltammetry

Cyclic voltammetry is one of the most versatile and widely used electrochemical techniques. Typically, cyclic voltammetry is measured in a three-electrode system, containing a working electrode, a counter electrode, and a reference electrode. The potential between the working electrode and the reference electrode is varied (scanned) linearly with time (Figure 10) under simultaneous measurement of the current flowing between the working and the counter electrode. Measurements are usually performed in unstirred solutions. The potential range and the scan rate can be adapted to the required investigated reactions. This technique is very frequently used for synthesis and characterization of conducting polymers to obtain qualitative information about the electrochemical reactions taking place at the conducting polymer-coated electrode in contact with an electrolyte solution. In this case, cyclic voltammograms are studied in a monomer free solution, with supporting electrolyte and solvent. Thus, as the potential is scanned there is an electron transfer at the electrode|polymer interface with a concurrent counterion transfer at the polymer|solution interface in order to maintain electroneutrality during the doping-dedoping reactions [92–94].



**Figure 10.** Potential vs time plot in cyclic voltammetry measurements

In this thesis (*Paper V*), cyclic voltammetry was used for the characterization of the redox capacitance of solid contact films, together with the coulometric method to demonstrate the influence of counter ions in the electrolyte solutions on the formation of the PEDOT film used as solid contact.

### 3. Results and discussions

The research work carried out using the coulometric transduction method in recent years was briefly introduced in section 1.2. The principles and the modelling calculations of the coulometric transduction method were also discussed. This chapter describes the main results obtained in this work regarding the amperometric and coulometric responses of SCISEs with PEDOT-based films as ion-to-electron transducers (*Papers I-V*). The investigation of the coulometric transduction method on cation-selective and anion-sensitive SCISEs with drop-cast ISM is described in chapter 3.1 (*Papers I, IV, V*). In chapter 3.2, the amperometric and coulometric response improvements of SCISEs by increasing surface area and using spin-coated thin-layer ISM are discussed (*Papers I-V*). Some interesting responses of  $\text{Pb}^{2+}$ - and  $\text{Ca}^{2+}$ -SCISEs with PEDOT(PSS) as solid contact utilizing the coulometric method (*Paper IV*) are presented in chapter 3.3. In chapter 3.4, the influence of doping counterions in the electrolyte solution on the PEDOT-based films is described. (*Paper V*).

In this work, one-step calibration of all the fabricated SCISEs using potentiometry was done prior to coulometric measurement. The slope of the potential vs logarithm of activity of primary ion for each electrode was checked to verify that the SCISEs show a near-Nernstian response. The same dilution protocol was used in both potentiometric and coulometric measurements. The starting sample solution with a volume of 100 ml at a given concentration of primary ion was diluted by removing 34.2 ml of sample solution and replaced with an equivalent amount of deionized water or 0.1 M NaCl aqueous solution as constant ionic background. The magnitude of the alteration of activity per each dilution is 0.18 decades. Of course, the activity change of primary ion can be altered by varying the removing volume of the sample solution, according to each experiment requirements.

#### 3.1 Coulometric response of SCISEs with drop-cast thick ISM

Before starting the coulometric transduction method, it is crucial to wait for the SCISEs to reach equilibrium state under the applied potential. This was done in order to reduce the background drift and to minimize its influence on the analytical signal of the coulometric method. Open circuit potential of the SCISEs at a given ion concentration of the sample solution is expected to give the shortest initial equilibrium time and was selected as the applied potential for each SCISE in this work.

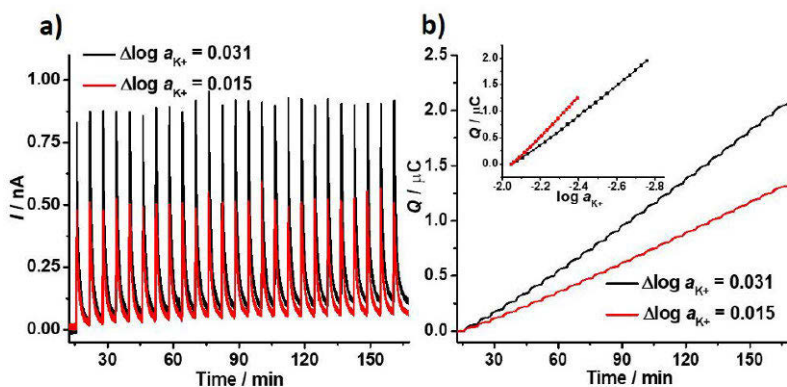


### 3.1.1 Cation-selective SCISEs

#### 3.1.1.1 $K^+$ -selective SCISEs

Figure 11a shows the chronoamperometric responses of the  $K^+$ -selective SCISEs during 25 successive dilution steps with  $\Delta \log a_{K^+} = 0.031$  and  $0.015$  decades/step utilizing the coulometric method.  $K^+$ -selective SCISEs were based on 1 mC PEDOT(PSS) solid contacts covered with drop-cast thick ISM (*ca* 100  $\mu\text{m}$ ). From Figure 11a, it can be seen that the current peaks originating from the activity decrease of the primary ion ( $K^+$ ) are rather reproducible, in presence of 0.1 M NaCl as a constant background electrolyte during the whole dilution sequence. This also indicates that the selectivity of the ISM is maintained when utilizing the coulometric transduction method. Even a small change of  $\Delta \log a_{K^+} = 0.015$  decades/step is clearly detected, and the chronoamperometric response is reproducible.

The cumulated charge  $Q$  vs time is shown in Figure 11b and the cumulated charge  $Q$  vs  $\log a_{K^+}$  is given as an inset in Figure 11b. According to the theoretical model of the coulometric method (*Paper II*), the cumulated charge should be linearly proportional to the activity change of the primary ion at a given capacitance of the solid contact. The slope of the cumulated charge  $Q$  vs  $\log a_{K^+}$  of the inset shown in Figure 11b for 0.031 and 0.015 decades/step should be the same. The deviation of the cumulated charge lines can be due to the insufficient dilution interval time at the given activity changes, especially for 0.031 decades steps with the drop-cast thick membrane having a large resistance. Thus, the slope of the cumulated charge is suppressed. This phenomenon can also be seen from the drifting baseline for larger activity changes at 0.031 decades/step, shown in Figure 11a. Thus, the importance of reaching equilibrium after each dilution step to obtain the full charge should be considered when utilizing the coulometric method.



**Figure 11.** Chronoamperometric (a) and coulometric response (b) of  $K^+$ -SCISEs with 1 mC PEDOT(PSS) and drop-cast thick ISM for two dilution protocols:  $\Delta \log a_{K^+} = 0.031$  or 0.015 decades/step. Cumulated charge  $Q$  vs  $\log a_{K^+}$  is shown in the inset of Figure 11b. (revised from Figure 2 in *Paper I*)

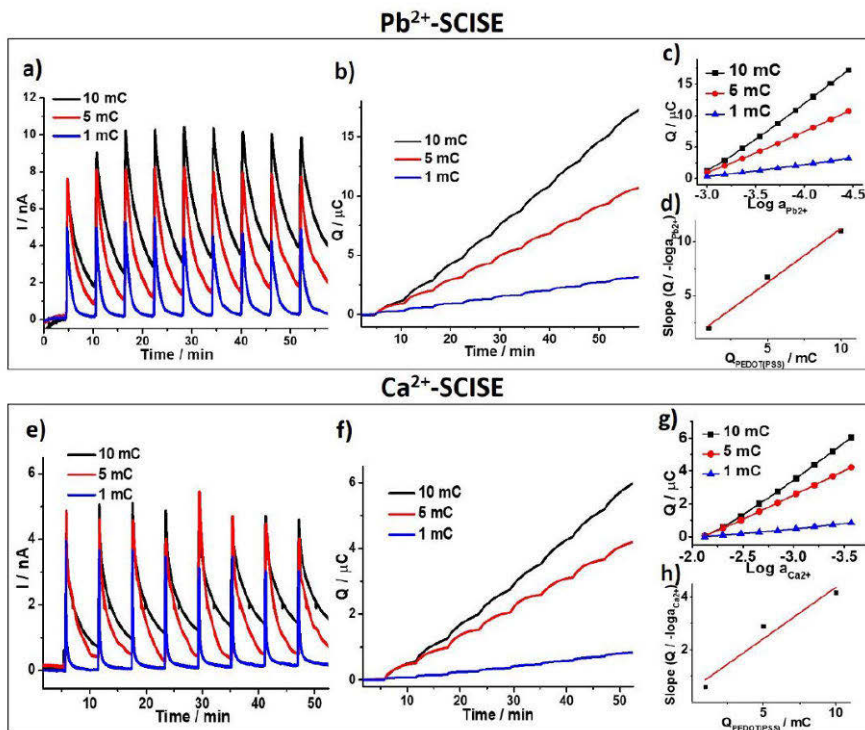
### 3.1.1.2 $Pb^{2+}$ - and $Ca^{2+}$ -selective SCISEs

Besides investigation on  $K^+$ -selective SCISEs, the coulometric transduction method was further performed using  $Pb^{2+}$ - and  $Ca^{2+}$ -selective SCISEs (*Paper IV*). The amperometric and coulometric responses of the  $Pb^{2+}$ - and  $Ca^{2+}$ -SCISEs with 1, 5, and 10 mC PEDOT(PSS) solid contacts covered with drop-cast thick ISM, are shown in Figure 12. The dilution step is  $\Delta \log a_{Ca^{2+}}$  and  $\Delta \log a_{Pb^{2+}} = 0.18$  decades. Figure 12 shows that a higher PEDOT(PSS) loading (higher redox capacitance) in the SCISEs means a larger amount of PEDOT(PSS) to be oxidized/reduced, leading to larger cumulated charge and longer equilibration time needed, at a given activity change in the sample solution.

The amperometric response of  $Pb^{2+}$ - and  $Ca^{2+}$ -SCISEs with drop-cast thick ISM and with 1, 5, and 10 mC PEDOT(PSS) as solid contact is shown Figure 12a, d. It is clearly seen that 5 min equilibration time between each dilution is relatively adequate for  $Pb^{2+}$ - and  $Ca^{2+}$ -SCISEs with 1 mC PEDOT(PSS) solid contact, but not for the SCISEs with 5 mC and 10 mC PEDOT(PSS). The cumulated charge is linearly dependent on  $\log a_{Pb^{2+}}$  (Figure 12c and 12g), and the cumulated charge is amplified by increasing the thickness (redox capacitance) of the solid contact (Figure 12b and 12f). These results are in good agreement with previous results reported by Vanamo *et al* using  $K^+$ -SCISEs with drop-cast thick ISM [23].

The slope of  $Q / (\log a_{Pb^{2+}}$  or  $\log a_{Ca^{2+}})$  is not linearly proportional to the polymerization charge

of PEDOT(PSS) for both  $\text{Pb}^{2+}$ - and  $\text{Ca}^{2+}$ -SCISEs (Figure 12d and 12h). This is because the total charge for larger redox capacitance of the solid contact, *i.e.* 5 and 10 mC PEDOT(PSS) with drop-cast thick ISM cannot be fully utilized and is limited by the time (5 min) between each dilution. This again calls for the importance of reaching equilibrium after each activity change to obtain the total charge in the coulometric transduction method.

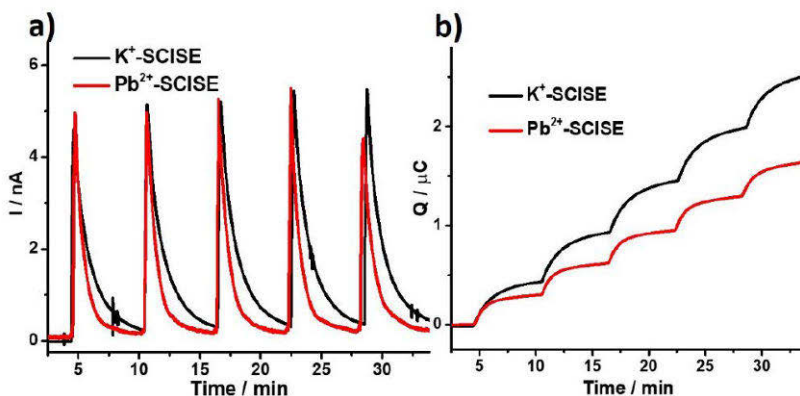


**Figure 12.** Chronoamperometric (a, e), coulometric response (b, f), cumulated charge  $Q$  vs  $\log a_{\text{Pb}^{2+}}$  or  $\log a_{\text{Ca}^{2+}}$  (c, g) and the slope of the cumulated charge  $Q$  vs the polymerization charge of PEDOT(PSS) solid contact (d, h) of  $\text{Pb}^{2+}$ -SCISEs and  $\text{Ca}^{2+}$ -SCISEs loading with 1, 5 and 10 mC PEDOT(PSS) as solid contact covered with drop-cast thick ISM. (Figure 1 in *Paper IV*)

### 3.1.1.3 Comparison of coulometric response of $\text{K}^{+}$ -selective SCISEs and $\text{Pb}^{2+}$ -selective SCISEs

A comparison of amperometric and coulometric response of  $\text{K}^{+}$ -SCISE and  $\text{Pb}^{2+}$ -SCISE prepared using 1 mC PEDOT(PSS) as solid contact and drop-cast thick ISM where  $\Delta \log a_{\text{K}^{+}}$  and  $\Delta \log a_{\text{Pb}^{2+}} = 0.18$  decades/dilution step is shown in Figure 13 (*Paper IV*). In the case of SCISEs with drop-cast thick membranes, the peak current is mainly dependent on the bulk resistance of the drop-cast membrane. According to the Nernst equation ( $E_{\text{cell}} = E_{\text{cell}}^0 +$

$\frac{2.303 RT}{z_i F} \log a_i$ ), and  $\text{Pb}^{2+}$  is divalent cation ( $z_i=2$ ) while  $\text{K}^+$  is a monovalent cation ( $z_i=1$ ), the potential change of the monovalent  $\text{K}^+$ -SCISE should be twice that of the divalent  $\text{Pb}^{2+}$ -SCISE for a given dilution step, here  $\Delta \log a_{\text{K}^+}$  and  $\Delta \log a_{\text{Pb}^{2+}} = 0.18$  decades. In analogy with potentiometry, the cumulated charge  $Q$  vs time should be twice as large for the  $\text{K}^+$ -SCISE compared to that of the  $\text{Pb}^{2+}$ -SCISE, under the same experimental conditions. However, the difference in charge  $Q$  is smaller than expected, as shown in Figure 13b. This phenomenon may be related to the differences in the redox capacitance of PEDOT(PSS) in the presence of  $\text{Pb}^{2+}$  in comparison to  $\text{K}^+$  or ion transfer limitation within the SCISEs. Figure 13a shows a faster amperometric response of  $\text{Pb}^{2+}$ -SCISE than  $\text{K}^+$ -SCISEs at  $\Delta \log a_{\text{K}^+}$  and  $\Delta \log a_{\text{Pb}^{2+}} = 0.18$  decades/dilution step. The cumulated charge value of  $\text{Pb}^{2+}$ -SCISEs is closer to equilibrium value in comparison to  $\text{K}^+$ -SCISEs with 5 min dilution interval time.



**Figure 13.** Chronoamperometric (a) and coulometric response (b) of  $\text{K}^+$ -SCISE and  $\text{Pb}^{2+}$ -SCISEs with 1 mM PEDOT(PSS) solid contact covered with drop-cast thick ISM.

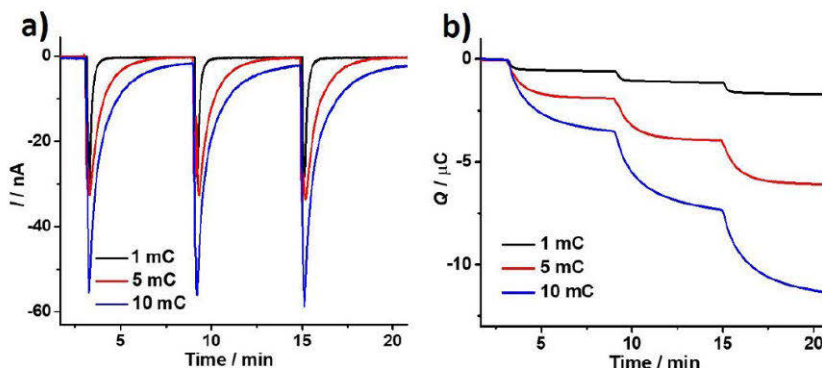
### 3.1.2 Anion-sensitive SCISEs

#### 3.1.2.1 $\text{NO}_3^-$ -sensitive SCISEs

The chronoamperometric and coulometric response recorded for the  $\text{NO}_3^-$ -sensitive SCISEs with 1, 5, and 10 mM PEDOT doped with nitrate counterion (PEDOT( $\text{NO}_3$ )) as solid contact and covered with drop-cast thick ISM is shown in Figure 14. As expected, the amperometric and coulometric responses of  $\text{NO}_3^-$ -sensitive SCISEs give an opposite analytical signal to the response of  $\text{K}^+$ -selective SCISEs, according to Nernst equation, when the same sample dilution protocol was employed. The obtained cumulated charge of  $\text{NO}_3^-$ -sensitive SCISEs is therefore

opposite to that of  $K^+$ -selective SCISEs under the same experimental conditions.

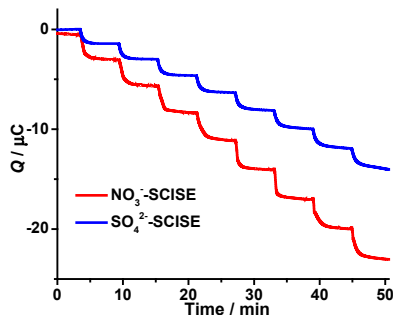
The starting solution of 0.1 M  $NaNO_3$  is diluted with water in  $\Delta \log a_{NO_3} = 0.18$  decades/dilution steps. A thicker film of conducting polymer PEDOT( $NO_3$ ) covered with drop-cast thick ISM leads to amplification of the cumulated charge (larger amount of PEDOT involved) with the price of longer equilibrium time at a given activity change of primary ion in the solution. The cumulated charge is proportional to the thickness (polymerization charge) of PEDOT film.



**Figure 14.** Chronoamperometric (a) and coulometric response (b) of  $NO_3^-$ -sensitive SCISEs with 1, 5, and 10 mC PEDOT( $NO_3$ ) and drop-cast thick ISM. (Revised from Figure 4 in *Paper IV*)

### 3.1.2.2 Comparison of coulometric response of $NO_3^-$ -sensitive SCISEs and $SO_4^{2-}$ -sensitive SCISEs

A comparison of the cumulated charge  $Q$  vs time curve of  $NO_3^-$ - and  $SO_4^{2-}$ -sensitive SCISEs is shown in Figure 15. According to the Nernst equation, the linear slope curve of potential vs logarithm of activity change of divalent anion is half of the monovalent anion. Since the analytical signal (cumulated charge) is induced by potential changes at the interface between the membrane and the sample solution, it is expected to show matching response upon the same dilution protocol. In Figure 15, the results presented for  $NO_3^-$ - and  $SO_4^{2-}$ -sensitive SCISEs are as expected and the coulometric response for  $NO_3^-$ -sensitive SCISE is approximately double that of the  $SO_4^{2-}$ -sensitive SCISE, in analogy with potentiometric measurement. This is in good agreement with the Nernst equation ( $z_i = -2$  for sulfate and  $z_i = -1$  for nitrate).



**Figure 15.** Coulometric response of  $\text{NO}_3^-$ - and  $\text{SO}_4^{2-}$ -sensitive SCISEs with 10 mC PEDOT(Cl) solid contact covered with spin-coated ISM during sequential dilution steps ( $\Delta \log a_{\text{NO}_3^-}$  or  $\Delta \log a_{\text{SO}_4^{2-}} = 0.18$  decades/step). (Revised from Figure 10 in *Paper V*)

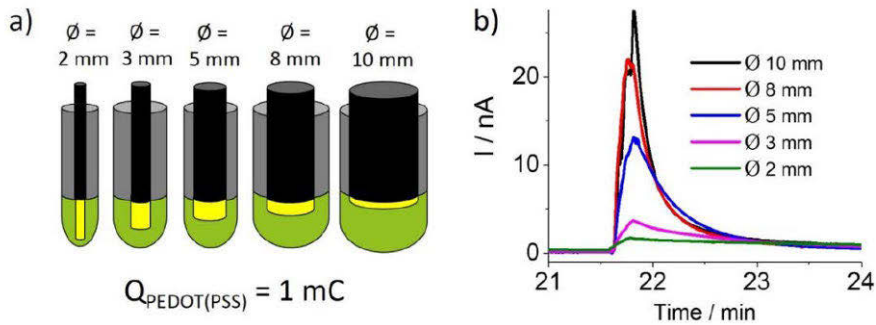
Application of the coulometric method for cation-selective SCISEs and anion-sensitive SCISEs is feasible. The chronoamperometric response of SCISEs showed good reproducibility, even in the case with 0.015 decades/step for  $\text{K}^+$ -selective SCISEs, as shown in Figure 11. The amperometric and coulometric signal of cation-selective and anion-sensitive SCISEs are opposite, when utilizing the same dilution protocol. The analytical cumulated charge signal is linearly proportional to the logarithm of activity of the primary ion. A thicker solid contact leads to amplification of the cumulated charge (larger amount of oxidation/reduction of PEDOT is involved), meaning that a larger amount of charging/discharging reaction occurs at the price of longer equilibrium (response) time. The cumulated charge slope of divalent ion is half of the monovalent ion.

### 3.2 Improvements of the coulometric transduction method for SCISEs

The coulometric transduction method is relevant when applied to SCISEs with drop-cast thick membranes. However, the drawbacks of SCISEs with drop-cast thick membranes for the coulometric method are obvious, *i.e.* the relatively small and slow current response requires a long equilibration time, which is visible as background current drift if the measurement time is not long enough. Improving the coulometric current response and shortening the equilibration time is of importance to obtain the full accumulated charge between each dilution step. Two approaches were studied for SCISEs to lower the electrode resistance and thus to shorten the coulometric response time: increasing the surface geometry area to increase the contact area and decrease the thickness of PEDOT for a given redox capacitance (*Paper I*) and using spin-coated ISM instead of drop-cast ISM to facilitate the mass transport through the ISM (*Papers II-V*).

### 3.2.1 Influence of the electrode geometry on the coulometric response

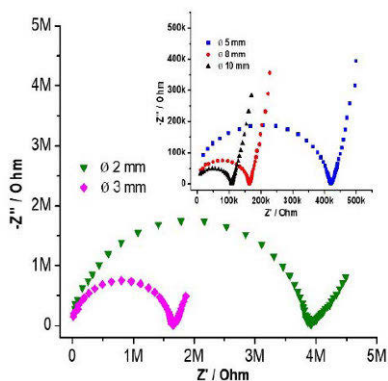
In *Paper I*, the influence of the electrode geometry on the response time of SCISEs, used in the coulometric transduction method was studied and characterized with the support of EIS. The fabrication of SCISEs was done by electropolymerizing 1 mC PEDOT(PSS) as solid contact on the surface of glassy carbon (GC) electrodes with different diameters ( $\varnothing_{GC} = 2, 3, 5, 8,$  and 10 mm). The thickness of the ISM was kept constant for all the electrodes (Figure 16a). The amperometric responses of SCISEs, with 1 mC PEDOT(PSS) and different surface area of GC electrode during one step dilution with  $\Delta \log a_{K^+} = 0.18$  decades, are shown in Figure 16b. The response time of the SCISE decreases with increasing surface area, while the magnitude of the current peak increases with enlarging the surface area. As shown in Figure 16b, SCISE ( $\varnothing_{GC} = 10$  mm) gives the shortest response time and highest current peak, while SCISE ( $\varnothing_{GC} = 2$  mm) shows the longest response time and lowest current peak. Within the 5 min timeframe, the cumulated charge of SCISE ( $\varnothing_{GC} = 10$  mm) is largest due to the facilitated ion transport with enlarging the surface area, while for SCISE ( $\varnothing_{GC} = 2$  mm) the cumulated charge is smallest because of inability to reach equilibrium completely at a given primary activity change ( $\Delta \log a_{K^+} = 0.18$  decades), as shown in Figure 3 in *Paper I*.



**Figure 16.** Schematic illustration of  $K^+$ -SCISEs with constant 1 mC PEDOT(PSS) solid contact electropolymerized on different geometrical surface areas and covered with drop-cast ISM (a), and chronoamperometric response of  $K^+$ -SCISEs with one dilution step at  $\Delta \log a_{K^+} = 0.18$  decades (b). (Figure 1 in *Paper I*)

Results from the EIS measurements performed at open circuit potential of all SCISEs with different diameters are shown in Figure 17. The bulk resistance of the ISM, decreases with increasing electrode diameter, as expected, due to the bigger surface area.

The imaginary impedance ( $Z''$ ) at the lowest frequency (10 mHz) can be used to roughly estimate the redox capacitance of PEDOT(PSS) when coated with drop-cast ISM. The low frequency capacitance of SCISE ( $\varnothing_{GC} = 10$  mm) gives the highest value indicating that the PEDOT(PSS) solid contact is most accessible due to the largest surface area and lowest bulk resistance of ISM, among all the SCISEs ( $\varnothing_{GC} = 2, 3, 5, 8,$  and 10 mm). In contrary, the low-frequency line of SCISE ( $\varnothing_{GC} = 2$  mm) is clearly tilted (*ca*  $50^\circ$ ), corresponding to a diffusion process. This implies that ion diffusion through the SCISE plays a significant role in the case of SCISE ( $\varnothing_{GC} = 2$  mm) with the smallest surface area and highest bulk membrane resistance. Thus, when utilizing the coulometric transduction method, mass-transport limitations can certainly result in the longer equilibrium time for smaller diameter electrodes, which is in good agreement with chronoamperometric results in Figure 16b. Thus, increasing the electrode area to reduce the bulk resistance of ISM can give a faster response, shorter equilibration time and larger current peaks, which make it a good way to improve the analytical signal of the coulometric transduction method. The disadvantage of this method is the increasingly large surface area of SCISEs which may limits the applications of SCISEs using coulometric method in practical measurements in very small sample volumes.



**Figure 17.** Electrochemical impedance spectrum recorded for  $K^+$ -SCISEs with 1 mM PEDOT(PSS) and drop-cast thick ISM on different size of glassy carbon electrodes ( $\varnothing_{GC} = 2, 3, 5, 8, 10$  mm). (revised from Figure 5 in *Paper I*)

### 3.2.2 SCISEs with drop-cast thick ISM and spin-coated thin ISM

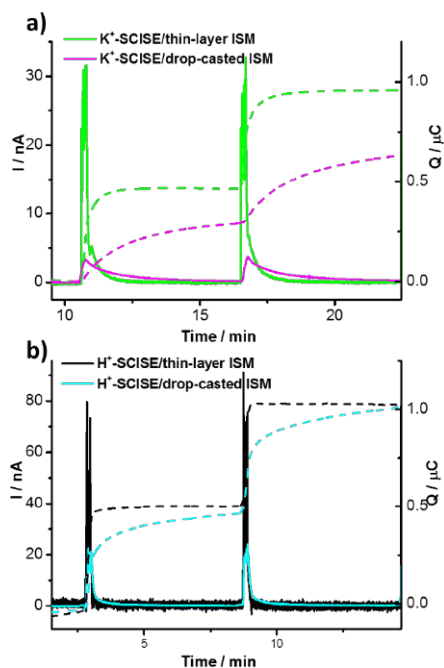
In addition to improving the coulometric response by increasing the surface area, another way to facilitate the ion transfer and improve the coulometric response for SCISEs is to decrease the bulk resistance of the ISM by using a spin-coated thin-layer ISM. The amperometric and coulometric response of SCISEs with spin-coated ISM was investigated and furthermore



characterized using EIS. The coulometric response comparison of SCISEs covered with spin-coated thin ISM and drop-cast thick ISM are discussed in this section.

### 3.2.2.1 $K^+$ -selective SCISEs and $H^+$ -selective SCISEs

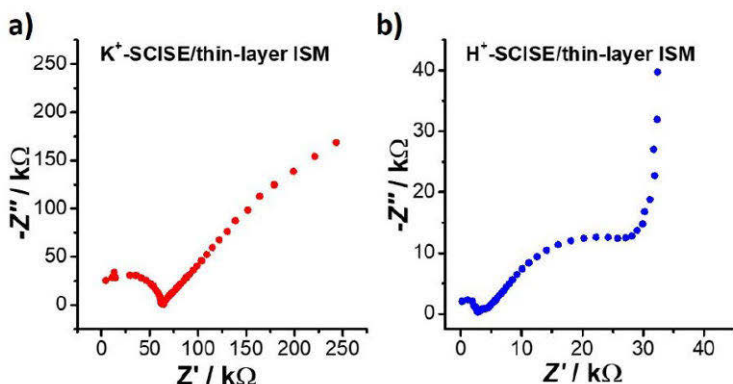
The amperometric and coulometric response of  $K^+$ -SCISEs and  $H^+$ -SCISEs with 1 mC PEDOT(PSS), covered with drop-cast thick and spin-coated thin ISMs, are shown in Figure 18. The coulometric response of  $K^+$ -SCISEs and  $H^+$ -SCISEs with a spin-coated thin-layer membrane results in higher current peaks and faster response (shorter equilibration time) than the drop-cast membrane. When comparing  $K^+$ -SCISEs with  $H^+$ -SCISEs, there are some interesting features when utilizing the coulometric transduction method.  $H^+$ -SCISEs show a much faster amperometric and coulometric response (Figure 18b) than the corresponding  $K^+$ -SCISEs (Figure 18a). The cumulated charge obtained by integration of the current with time are shown as dashed lines in Figure 18. Relatively equal amount of charge was obtained for  $H^+$ -SCISEs with both drop-cast thick and spin-coated thin-layer ISMs (Figure 18b), whereas  $K^+$ -SCISEs with a spin-coated thin-layer ISM showed comparatively larger amount of charge than that for  $K^+$ -SCISEs with a drop-cast thick membrane (Figure 18b). These results indicate that the transport of  $H^+$  in the  $H^+$ -SCISEs is faster than the transport of  $K^+$  in the  $K^+$ -SCISEs. The high mobility of protons in the  $H^+$ -SCISE is interesting when considering that the selective ion transport in ISMs is assumed to take place in the form of ion-ionophore complexes and thus should not be dramatically faster for  $H^+$  in comparison to  $K^+$  [95]. In addition to ion transport in the ISM, ion transport in PEDOT(PSS) and an additional ion-transfer resistance at the PEDOT(PSS)/ISM interface also play a role [96]. Thus, the charge transfer process through SCISEs includes the charging/discharging reaction of PEDOT(PSS) associated with both ion and electron transport in PEDOT(PSS), compensating ion transfer through the ISM, ion-transfer at the ISM|solution interface, ion transfer at the PEDOT(PSS)|ISM interface as well as electron transfer at the PEDOT(PSS)|electrode conductor interface, all these processes can contribute to the coulometric response.



**Figure 18.** Chronoamperometric (solid line) and coulometric response (dashed line) of  $K^+$ -SCISEs (a) and  $H^+$ -SCISEs (b) with 1 mC PEDOT(PSS) solid contact covered with spin-coated thin-layer and drop-cast thick ISM. (Figure 3 in *Paper III*)

EIS measurements were performed for  $K^+$ - and  $H^+$ -SCISEs with 10 mC PEDOT(PSS) as solid contact covered with spin-coated thin-layer ISMs (Figure 19). The semicircle of the electrochemical impedance spectrum represents the bulk resistance of the ISM in parallel with the geometric capacitance of the ISM. The low frequency of the electrochemical impedance spectrum represents the bulk capacitance of the solid contact [91]. The bulk resistance of  $K^+$ -SCISEs with spin-coated thin-layer membrane (65 k $\Omega$ ) is much smaller compared to that with drop-cast membrane (1.7 M $\Omega$ , as shown in Figure 15 for  $K^+$ -SCISE ( $\varnothing_{GC}=3$  mm)). The low-frequency line (ca 45 $^\circ$ ) of the impedance spectrum of  $K^+$ -SCISEs indicates that the ion transfer of  $K^+$  in  $K^+$ -SCISEs is diffusion controlled. On the contrary, for  $H^+$ -SCISE, the low-frequency line is an almost vertical capacitive line indicating fast ion transfer of  $H^+$  in  $H^+$ -SCISEs. These results are in good agreement with the coulometric response. The EIS results demonstrate that the ion transfer limitations of  $K^+$  leads to longer equilibration time for  $K^+$ -SCISE in comparison to  $H^+$ -SCISE. The imaginary impedance ( $Z''$ ) at the lowest frequency (10 mHz) can be used to estimate the low frequency capacitance of PEDOT(PSS) when coated with the thin-layer ISM. In the case of  $H^+$ -SCISEs with 10 mC PEDOT(PSS) and spin-coated thin-layer ISM, the

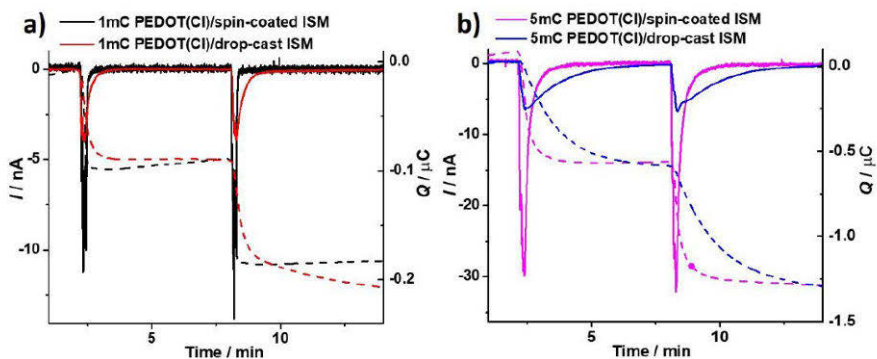
calculated low frequency capacitance is *ca* 400  $\mu\text{F}$ , which is nearly equal to the capacitance of a bare PEDOT(PSS) without membrane [91]. Results from both EIS and coulometry indicate fast ion transfer of  $\text{H}^+$  through SCISEs, in a way that the redox capacitance of PEDOT(PSS) can be effectively utilized. The overall resistance of the  $\text{H}^+$ -SCISE is significantly lower than that of the  $\text{K}^+$ -SCISE, which corresponds to the faster coulometric response of the  $\text{H}^+$ -SCISE. Overall, the behavior of  $\text{K}^+$  and  $\text{H}^+$ -SCISEs shown by EIS is in quantitative agreement with the obtained coulometric results discussed in Figure 18.



**Figure 19.** Electrochemical impedance spectrum recorded for  $\text{K}^+$ -SCISE (a) and  $\text{H}^+$ -SCISE (b) with spin-coated thin-layer ISM in 0.1 M KCl and 0.1 M HCl, respectively. (Figure 5 in *Paper III*)

### 3.2.2.2 $\text{SO}_4^{2-}$ -sensitive SCISEs

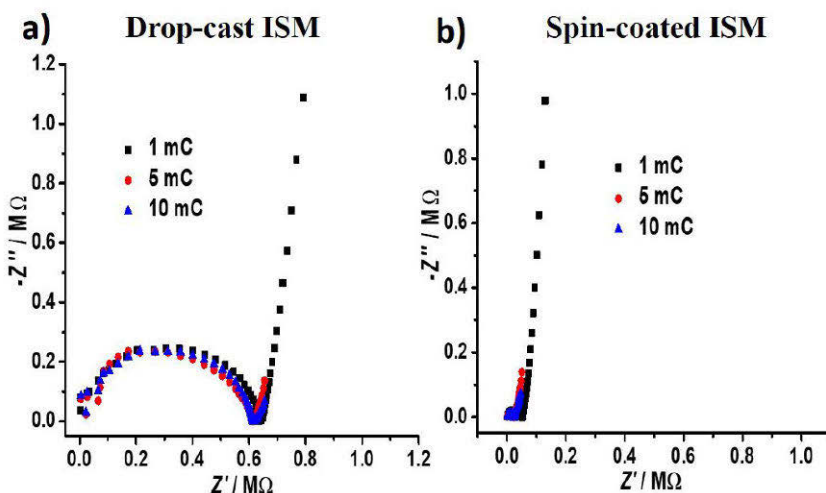
In Figure 20, the amperometric and coulometric response of  $\text{SO}_4^{2-}$ -sensitive SCISEs with 1 and 5 mC PEDOT(Cl) covered with drop-cast thick membrane and spin-coated thin membrane are compared. During experimental process, GC/PEDOT(Cl) was not conditioned in  $\text{SO}_4^{2-}$  solution before applying the corresponding membrane. A thicker film of PEDOT(Cl) in  $\text{SO}_4^{2-}$ -sensitive SCISEs covered with drop-cast thick and spin-coated thin membrane resulted in larger cumulated charge at a given activity change for both cases. The  $\text{SO}_4^{2-}$ -sensitive SCISEs with spin-coated thin membrane results in higher current peaks and faster response (shorter equilibrium time) than that of drop-cast thick membrane with the same loading of the solid contact.



**Figure 20.** Chronoamperometric (solid line) and coulometric response (dash line) of  $\text{SO}_4^{2-}$ -sensitive SCISEs with 1 mC (a) and 5 mC (b) PEDOT(Cl) solid contact covered with drop-cast thick and spin-coated thin-layer ISM. (Figure 7 in *Paper V*)

A comparison of the impedance spectra for  $\text{SO}_4^{2-}$ -sensitive SCISEs with 1, 5, and 10 mC PEDOT(Cl) solid contact covered with drop-cast thick- and spin-coated thin-ISM is shown in Figure 21. The diameter of the high-frequency semicircle represents the bulk resistance of the anion-sensitive membrane, which decreases with reducing the thickness of the membrane. The bulk resistance of the ISM of  $\text{SO}_4^{2-}$ -sensitive SCISEs is much smaller in the case of spin-coated thin-layer membrane, compared to the drop-cast thick membrane. The resistance of the PEDOT solid contact is only in the range of hundreds of ohms and its influence on the overall cell resistance of the SCISEs (*ca* 0.6 M $\Omega$  (drop-cast thick membrane) and *ca* 40 k $\Omega$  (spin-coated thin-layer membrane)) can be neglected. The overall cell resistance is mainly dependent on the bulk resistance of the ISM.

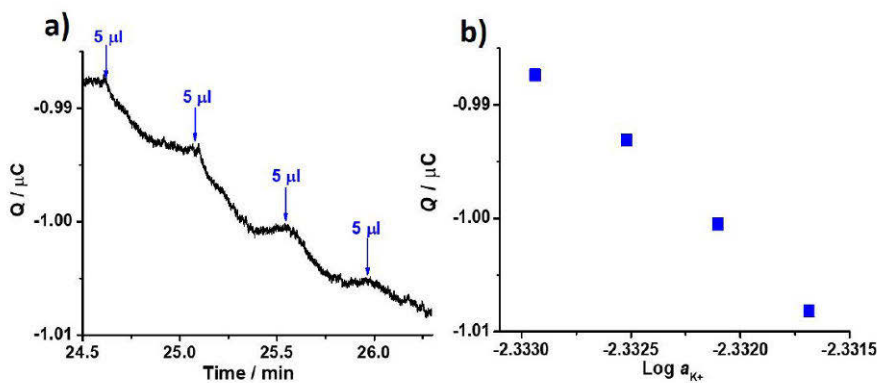
The imaginary impedance ( $Z''$ ) at the lowest frequency (10 mHz) can be used to estimate the low frequency capacitance of PEDOT(Cl) of  $\text{SO}_4^{2-}$ -sensitive SCISEs with both drop-cast and spin-coated ISM [91]. The estimated redox capacitance ( $C_{CP}$ ) values for  $\text{SO}_4^{2-}$ -sensitive SCISEs with drop-cast and spin-coated thin-layer ISM are roughly the same, indicate that the redox capacitance of  $\text{SO}_4^{2-}$ -sensitive SCISEs is independent of the thickness of the ISM. As clearly shown in Figure 3 in *Paper V*, the redox capacitance ( $C_{CP}$ ) of SCISEs at the low frequency point is linearly proportional to the polymerization charge (thickness) of PEDOT(Cl) solid contact in a predictable manner, which is also in quantitative agreement with results obtained from the coulometric measurements.



**Figure 21.** Electrochemical impedance spectrum recorded for  $\text{SO}_4^{2-}$ -sensitive SCISEs with 1, 5, and 10 mC PEDOT(Cl) solid contact covered with drop-cast ISM (a) and spin-coated thin-layer ISM (b) in 0.1 M  $\text{Na}_2\text{SO}_4$ . (Figure 2 in *Paper V*)

### 3.2.3 Sensitivity improvement with spin-coated thin-layer ISM

The output signal of the coulometric transduction mode can be amplified by increasing the redox capacitance of the solid-contact film in the SCISEs. With this unique property, coulometry is potentially a very attractive method for monitoring small changes in concentration in, for example, clinical analysis and personal health monitoring. To explore the possibilities for the detection with improved sensitivity,  $\text{K}^+$ -SCISEs ( $\varnothing_{\text{GC}} = 10$  mm) with a 100 mC PEDOT(PSS) covered with a spin-coated thin-layer ISM were fabricated. As shown in Figure 22, a small volume (5  $\mu\text{l}$ ) of 0.1 M KCl (0.1 M NaCl as constant ionic background) was repeatedly added into the 100 ml 5 mM KCl (0.1 M NaCl as constant ionic background) sample solution. The concentration change for each addition was thus only 5  $\mu\text{M}$  at a 5 mM concentration level of the sample solution, *i.e.* 0.1% change in activity of  $\text{K}^+$  in the sample solution. This can be detected based on  $\text{K}^+$ -SCISEs with 100 mC PEDOT(PSS) covered with spin-coated thin-layer ISM utilizing the coulometric method. In potentiometric measurement, a 0.1% change in activity results in a potential change of 0.025 mV, which is very challenging to measure in practice. The results shown in Figure 22 indicate that the coulometric signal transduction method can improve the sensitivity of ion detection with SCISEs under optimized conditions (*Paper III*). In the case of  $\text{Cl}^-$ -sensitive SCISEs, with 10 mC PEDOT(Cl) ( $\varnothing_{\text{GC}} = 3$  mm) that is covered with spin-coated thin-layer ISM, a small concentration change of 20  $\mu\text{M}$  decrease at a 10 mM level in solution, *i.e.* 0.2% change in activity, was still measurable with the coulometric transduction method (*Paper II*).

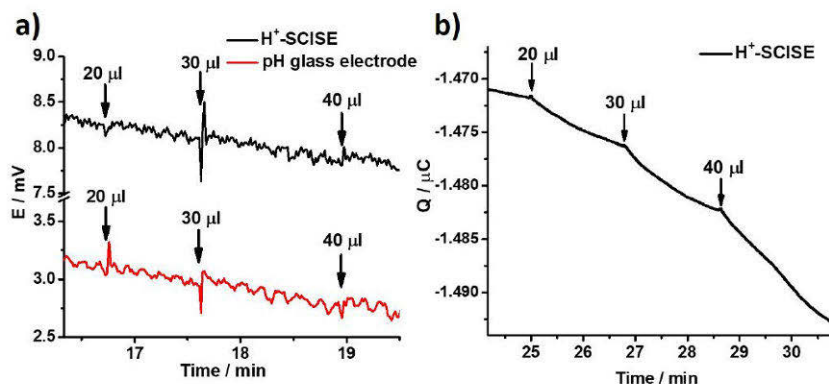


**Figure 22.** Cumulated charge  $Q$  vs time response (a) and cumulated charge  $Q$  vs  $\text{log } a_{\text{K}^+}$  (b) of a large-area  $\text{K}^+$ -SCISE ( $\varnothing_{\text{GC}} = 10$  mm) with 100 mC PEDOT(PSS) as solid contact and a spin-coated thin-layer ISM. (revised from Figure 6 in *Paper III*)

### 3.2.4 Sensitivity test of the coulometric method in seawater sample

The measurement of pH is of enormous importance in most chemical and environmental processes [97]. In order to understand the influence of seawater pH on the marine life, it is necessary to increase the accuracy of seawater pH measurement at an adequate measurement frequency. The sensitivity of the coulometric transduction method was compared with the potentiometric measurement by measuring small pH concentration changes in a seawater sample (Figure 23). The seawater sample was collected by the coast of the Baltic Sea (Ruissalo, Turku, Finland). Small pH changes were induced with standard additions of acid/base solutions. The potentiometric response is relatively noisy and the small potential change due to the change in pH is not visible for both glass pH and  $\text{H}^+$ -SCISEs. However, the coulometric response of the same  $\text{H}^+$ -SCISEs shows a relatively clear signal for such small pH changes. Any potential drift in the measuring system will influence both the potentiometric measurement and the coulometric response to decrease the accuracy of the measurements. Thus, it is of importance to have a high potential stability of SCISEs and reference electrode for coulometric method as well. Possible factors that influence the stability and accuracy of the potentiometric and coulometric measurements include side reactions that influence the redox state of PEDOT(PSS) solid contact (e.g.  $\text{O}_2$ ), slow pH changes in the seawater sample due to the standard addition mode or  $\text{CO}_2$  from air, and water layer formed between solid contact and ISM [19]. The comparison of potentiometry with coulometry shows that the coulometric transduction method can improve the quality of the signal from the  $\text{H}^+$ -SCISEs in seawater sample, but minimizing the potential drift of SCISEs is still crucial for both potentiometric and coulometric transduction methods.

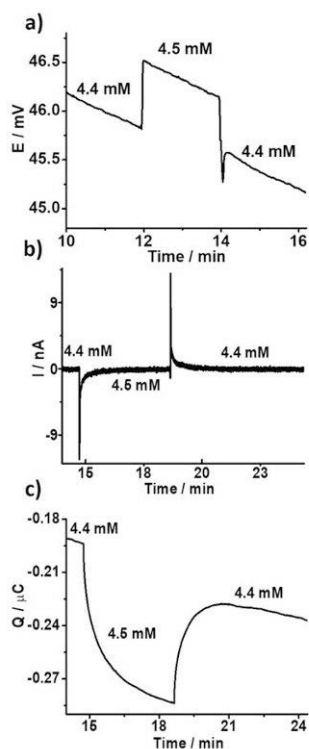
In a similar way, Bakker's group [98] presented pH measurements in seawater using constant potential coulometry in a flow cell by adding a capacitor as charging/discharging transducer in combination with a conventional pH sensor in the setup instead of SCISEs. It was demonstrated that pH changes down to 0.001 pH units are easily distinguished in buffer and seawater samples, orders of magnitude better than what is possible with potentiometric pH probes.



**Figure 23.** Potentiometric response of pH-selective glass electrode (Metrohm) and H<sup>+</sup>-SCISE (a) and coulometric response of H<sup>+</sup>-SCISE (b). Standard additions were done by stepwise adding of 0.1 mM HCl with volume 20, 30, 40 μl to a seawater sample (50 ml) under constant stirring. (Figure 7 in *Paper III*)

### 3.2.5 Applications of the coulometric method in control serum sample

The feasibility of potentiometric, chronoamperometric and coulometric measurement modes was tested in a control serum sample using a K<sup>+</sup>-SCISE with 4 mC PEDOT(PSS) solid contact which is covered with spin-coated thin-layer ISM. As shown in Figure 24, the potentiometric response is fast and reversible but shows an obvious potential drift. The amperometric response is also reversible with clearly visible current spikes due to the oxidation/reduction of the PEDOT(PSS) solid contact induced by the standard additions which change the activity of the primary ion K<sup>+</sup> in the sample. However, the current response is relatively noisy and there is a slight deviation from the zero-current baseline, which could be due to the potential drift of SCISEs. The coulometric signal is also reversible but distorted due to the background current originating from the potential drift. These results show that coulometric method can be used for a real sample with a complicated composition, such as control serum sample. It is of importance to minimize or even eliminate the potential drift from SCISEs and reference electrodes in order to achieve the signal amplification advantage of coulometric transduction method.



**Figure 24.** Potentiometric (a), chronoamperometric (b) and coulometric response (c) of  $K^+$ -SCISE with 4 mC PEDOT(PSS) and spin-coated thin-layer ISM measured in a control serum sample with  $K^+$  concentrations varied from 4.4 mM to 4.5 mM and back to 4.4 mM. (Figure 8 in *Paper III*)

The coulometric response of SCISEs can be improved by decreasing the bulk resistance of the ISM to facilitate the ion transfer process by increasing the geometric surface area of SCISEs (*Paper I*) and by using spin-coated thin-layer ISMs (*Papers II-V*). SCISEs with spin-coated thin-layer ISMs give shorter equilibration time and faster coulometric response than drop-cast thick ISM. The sensitivity of the coulometric method can be increased by increasing the redox capacitance of the conducting polymer and by using spin-coated membranes. Under optimized conditions, small activity changes of only 0.1% are detectable with the coulometric method for  $K^+$ -SCISEs. Applications of the coulometric method in a seawater sample and a control serum sample is demonstrated. Potential drift of SCISEs disturbing the potentiometric measurement mode is also a problem when utilizing the coulometric method.

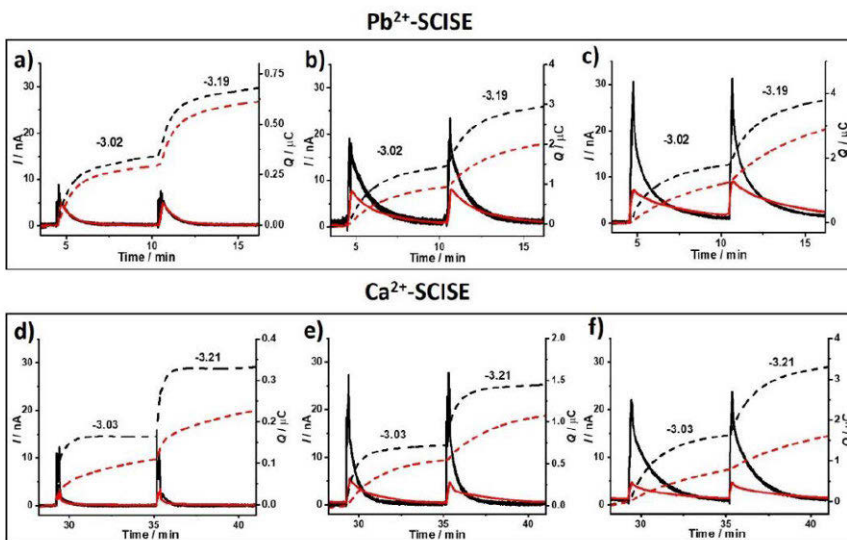


### 3.3 Unique features of the coulometric response for $\text{Pb}^{2+}$ -SCISEs and $\text{Ca}^{2+}$ -SCISEs

As it was mentioned in section 1.2, the cumulated charge signal of the coulometric transduction is based on a current transient involving a change in the redox state of the conducting polymer requiring transport of charge-compensating ions through the ISM and the conducting polymer. The amperometric and coulometric response can therefore be influenced by any transfer process of the charge-compensating ions, *i.e.* ion transport through the bulk of the ISM or PEDOT, or by ion transfer at the PEDOT|ISM or ISM|solution interfaces. The unique charge transfer properties of  $\text{Pb}^{2+}$  and  $\text{Ca}^{2+}$  in SCISEs when used for divalent cation detections was further studied by coulometry and EIS (*Paper IV*).

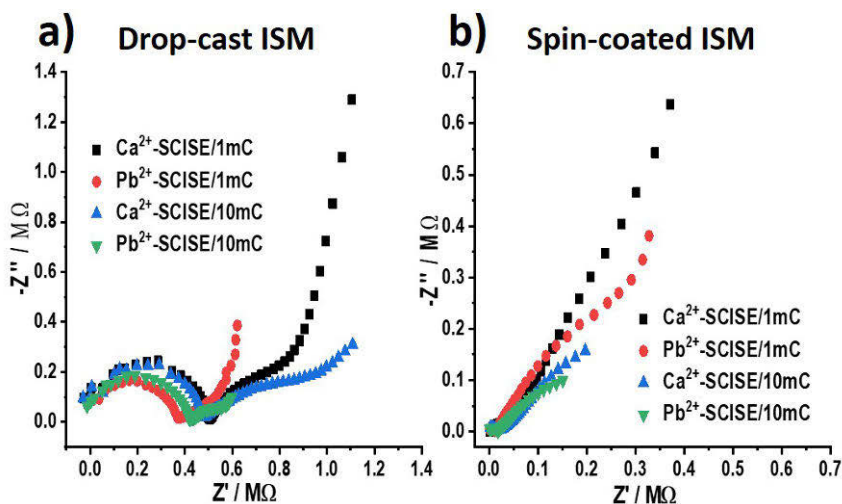
Current vs time and the corresponding cumulated charge  $Q$  vs time of  $\text{Pb}^{2+}$  and  $\text{Ca}^{2+}$ -SCISEs with spin-coated thin-layer and drop-cast thick ISMs at the given primary ion activity change are shown in Figure 25. Results from the amperometric and coulometric responses of  $\text{Pb}^{2+}$  and  $\text{Ca}^{2+}$ -SCISEs also showed that a spin-coated thin-layer ISM gives a faster coulometric response than drop-cast thick ISM. An increase in the thickness (redox capacitance) of the PEDOT solid contact leads to larger coulometric signal (cumulated charge), which is in agreement with earlier results [23].

Interestingly, Figure 25 illustrate some unique features of divalent cation-selective SCISEs when utilizing the coulometric method. In the comparison of  $\text{Pb}^{2+}$  and  $\text{Ca}^{2+}$ -SCISEs with 1 mC PEDOT(PSS) as solid contact, the amperometric and coulometric response of  $\text{Pb}^{2+}$ -SCISEs with 1 mC PEDOT(PSS) are almost independent of the ISM thickness showing almost equal response, as shown in Figure 25a. However, for  $\text{Ca}^{2+}$ -SCISEs, both current response and the resulting cumulated charge are strongly dependent on the ISM thickness. The response of the  $\text{Ca}^{2+}$ -SCISE is improved by reducing the membrane resistance with spin-coated thin-layer ISM compared to drop-cast ISM (Figure 25d). The cumulated charge of  $\text{Ca}^{2+}$ -SCISEs is only half of the  $\text{Pb}^{2+}$ -SCISEs for both drop-cast thick and spin-coated thin ISM (Figure 25a and 25d). In the case of spin-coated thin-layer membrane, the amperometric and coulometric response of  $\text{Pb}^{2+}$ -SCISEs is slower compared to  $\text{Ca}^{2+}$ -SCISEs (Figure 25a and 25d). These results demonstrated that the coulometric response of  $\text{Pb}^{2+}$ -SCISEs is mainly limited by the charge transfer through PEDOT(PSS) solid contact, while for  $\text{Ca}^{2+}$ -SCISE the transfer of the charge-compensating ions through membrane plays a role.



**Figure 25.** Chronoamperometric (solid line) and coulometric response (dash line) of  $\text{Pb}^{2+}$ - and  $\text{Ca}^{2+}$ -SCISEs with 1 mC (a, d), 5 mC (b, e), and 10 mC (c, f) PEDOT(PSS) solid contact covered with spin-coated thin-layer (black) or drop-cast (red) ISM, respectively. (Figure 5 in *Paper IV*)

Electrochemical impedance spectra recorded for  $\text{Pb}^{2+}$  and  $\text{Ca}^{2+}$ -SCISEs with 1 and 10 mC PEDOT(PSS) as solid contact covered with drop-cast thick and spin-coated thin-layer membrane are shown in Figure 26. The high frequency semi-circle for both  $\text{Pb}^{2+}$ - and  $\text{Ca}^{2+}$ -SCISEs with spin-coated membrane is not visible due to low bulk resistance of the membrane (Figure 26b).



**Figure 26.** Electrochemical impedance spectrum recorded for  $\text{Pb}^{2+}$  and  $\text{Ca}^{2+}$ -SCISEs with 1 and 10 mC PEDOT(PSS) solid contact covered with drop-cast ISM (a) or spin-coated thin-layer ISM (b), measured in 0.1 M  $\text{Pb}(\text{NO}_3)_2$  and 0.1 M  $\text{CaCl}_2$ , respectively. (Figure 5 in *Paper IV*)

The low-frequency capacitance ( $C_{CP}$ ) values for  $\text{Pb}^{2+}$ - and  $\text{Ca}^{2+}$ -SCISEs estimated from the impedance spectra in Figure 26, are shown in Table 1. The low frequency capacitance for both  $\text{Pb}^{2+}$ - and  $\text{Ca}^{2+}$ -SCISEs increased with increasing thickness of PEDOT(PSS). The low frequency capacitance of  $\text{Pb}^{2+}$ -SCISEs shows relatively equivalent values with drop-cast and spin-coated membranes. This indicates that the  $\text{Pb}^{2+}$ -SCISEs is independent of the thickness of ISM.  $\text{Pb}^{2+}$  transfer through  $\text{Pb}^{2+}$ -SCISEs is mainly limited by charge transfer through PEDOT(PSS). In the case for  $\text{Ca}^{2+}$ -SCISEs with spin-coated membrane, the lowest frequency  $C_{CP}$  is twice that of drop-cast membrane. This indicates that the response of the  $\text{Ca}^{2+}$ -SCISEs is mainly limited by the mass diffusion through the membrane. These impedance results are in qualitative agreement with the obtained coulometric responses from both  $\text{Pb}^{2+}$  and  $\text{Ca}^{2+}$ -SCISEs (Figure 25).

Two reasons for the unique coulometric performance of  $\text{Pb}^{2+}$  and  $\text{Ca}^{2+}$ -SCISEs can be considered. The first one is the affinity difference between  $\text{Pb}^{2+}$  and  $\text{Ca}^{2+}$  towards PEDOT(PSS). The affinity between various cations and  $\text{PSS}^-$  was reported to decrease in the following order:  $\text{Ba}^{2+} > \text{Pb}^{2+} > \text{Sr}^{2+} > \text{Ca}^{2+} > \text{Cu}^{2+} > \text{Co}^{2+} > \text{Ni}^{2+} > \text{Mg}^{2+} > \text{H}^+ > \text{K}^+ > \text{Na}^+ > \text{Li}^+$ . Hence, the interaction of  $\text{Pb}^{2+}$  with PEDOT(PSS) is stronger than that with  $\text{Ca}^{2+}$  [72]. Secondly, the HSAB theory states that soft acids react faster and form stronger bonds with soft bases, when all other factors are equal [99]. In this case, “soft” refers to species which are big, have low charge states

and are strongly polarizable [100]. This was also realized in the research work by Vazquez *et al* [101] that showed significant interactions between the “soft”  $\text{Ag}^+$  cation and poly(3-octylthiophene). In this case,  $\text{Pb}^{2+}$  being a “soft” cation may interact with sulphur atoms in PEDOT. Thus, the transfer of  $\text{Pb}^{2+}$  through PEDOT(PSS) could be retarded.

**Table 1** Low-frequency capacitance ( $C_{CP}$ ) values for  $\text{Pb}^{2+}$ -SCISEs and  $\text{Ca}^{2+}$ -SCISEs calculated from the impedance spectrum in Figure 26. (Data from Table 1 in *Paper IV*)

Electrode	Polymerization charge of PEDOT(PSS) / mC	ISM	$C_{CP}$ / $\mu\text{F}$
$\text{Pb}^{2+}$ -SCISE	1	Spin-coated	42
$\text{Pb}^{2+}$ -SCISE	1	Drop-cast	41
$\text{Pb}^{2+}$ -SCISE	10	Spin-coated	160
$\text{Pb}^{2+}$ -SCISE	10	Drop-cast	160
$\text{Ca}^{2+}$ -SCISE	1	Spin-coated	25
$\text{Ca}^{2+}$ -SCISE	1	Drop-cast	12
$\text{Ca}^{2+}$ -SCISE	10	Spin-coated	101
$\text{Ca}^{2+}$ -SCISE	10	Drop-cast	51

### 3.4 Influence of the PEDOT counter ions on the coulometric response of anion-sensitive SCISEs

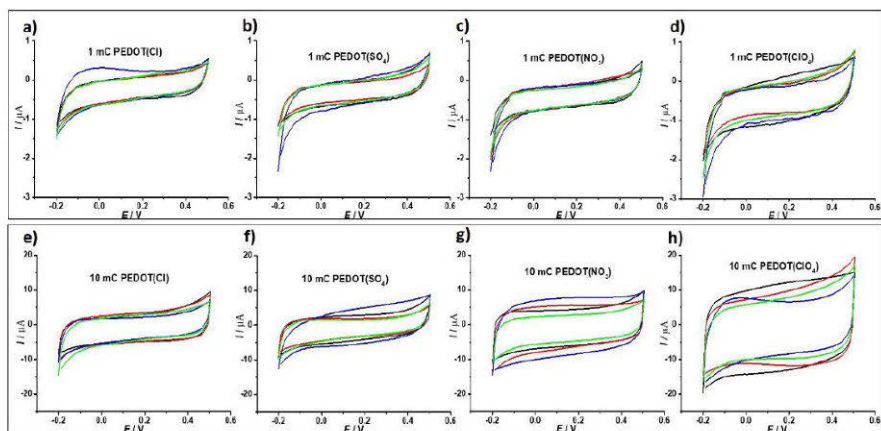
The response of anion-sensitive SCISEs was further investigated using the coulometric transduction method. The influence of the counter ions on the electrochemical properties of PEDOT was studied using the coulometric transduction method, together with cyclic voltammetry. PEDOT(Cl) and PEDOT( $\text{NO}_3$ ) solid contacts were used for the fabrication of SCISEs (*Paper V*).

#### 3.4.1 Cyclic voltammograms of PEDOT-based films

The cyclic voltammograms of PEDOT doped with chloride (PEDOT(Cl)), PEDOT doped with nitrate (PEDOT( $\text{NO}_3$ )), PEDOT doped with sulfate (PEDOT( $\text{SO}_4$ )), and PEDOT doped with perchlorate (PEDOT( $\text{ClO}_4$ )) films cycled in various electrolyte solutions are shown in Figure 27. The capacitive-like current behavior of PEDOT cyclic voltammograms was observed in the potential range -0.2 V to 0.5 V. PEDOT as ion-to-electron transducer provides high redox

capacitance and good ionic conductivity for SCISEs [14]. The capacitive-like current of the PEDOT solid contact is of importance for the coulometric method. The reason is that the analytical signal (cumulated charge) of the coulometric method derives from the charging/discharging of the PEDOT solid contact.

The cyclic voltammetric current of 1 mC PEDOT-based films cycled in various electrolyte solutions are compared in Figure 27a-d. The capacitive-like current responses were relatively identical in the case of KCl, NaNO<sub>3</sub>, and Na<sub>2</sub>SO<sub>4</sub> electrolytes, while slightly higher current values were obtained in KClO<sub>4</sub> solution. As the loading of the PEDOT-based film was increased to 10 mC (Figure 27e-h), the current differences become obvious. The largest capacitive-like current response was observed for the 10 mC PEDOT(ClO<sub>4</sub>) film in various electrolyte solutions, while the smallest current response was seen for the 10 mC PEDOT(Cl) film. The capacitive-like currents of 10 mC PEDOT films roughly follow this sequence: PEDOT(ClO<sub>4</sub>) > PEDOT(NO<sub>3</sub>) > PEDOT(SO<sub>4</sub>) ≈ PEDOT(Cl). This phenomenon follows the Hofmeister series, indicating that the anion affinity may influence the electrosynthesis of PEDOT as well as its capacitive-like current in the cyclic voltammograms. This phenomenon may also be influenced by the hydrated radius of the anions, so that the counter ions in the electrolyte will affect the film thickness and morphology of the solid contact [73,102]. Thus, for a certain polymerization charge, the PEDOT film thickness is influenced by the counterions used as the supporting electrolyte in the electrochemical polymerization of the film. The supporting electrolyte used during cyclic voltammetry also influences the resulting current response. This indicates that for a given polymerization charge, a higher yield is obtained for PEDOT(ClO<sub>4</sub>) and PEDOT(NO<sub>3</sub>) in comparison to PEDOT(Cl).

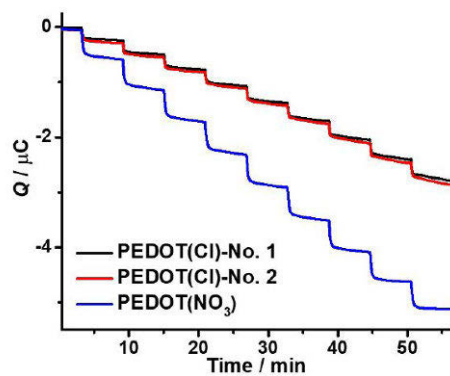


**Figure 27.** Cyclic voltammograms of 1 and 10 mC of PEDOT(Cl) (a, e), PEDOT(SO<sub>4</sub>) (b, f), PEDOT(NO<sub>3</sub>) (c, g) and PEDOT(ClO<sub>4</sub>) (d, h) films measured in 0.1 M NaNO<sub>3</sub> (black), 0.1 M KClO<sub>4</sub> (red), 0.1 M Na<sub>2</sub>SO<sub>4</sub> (blue), 0.1 M KCl (green) with 50 mV/s scan rate. (Figure 1 in *Paper V*)

### 3.4.2 Coulometric response of NO<sub>3</sub><sup>-</sup>-sensitive SCISEs based on PEDOT(NO<sub>3</sub>) and PEDOT(Cl)

As shown in Figure 27, the counter ions in electrolyte solutions used for electropolymerization of PEDOT influence the PEDOT thicknesses (electroactivity) and the electrolyte used in cyclic voltammetry measurement affect the current response as well. A comparison of the cumulated charge  $Q$  vs time of NO<sub>3</sub><sup>-</sup>-sensitive SCISEs with 1 mC PEDOT(Cl) or PEDOT(NO<sub>3</sub>) solid contact and drop-cast membranes when  $\Delta \log a_{\text{NO}_3^-} = 0.18$  decades/dilution steps is shown in Figure 28. The two replicates of electrodes with PEDOT(Cl) solid contact show good electrode-to-electrode reproducibility in the coulometric measurement mode.

The cumulated charge  $Q$  vs time curve of the electrode with PEDOT(NO<sub>3</sub>) solid contact is significantly larger than that of the SCISEs with PEDOT(Cl), even with the equivalent polymerization charge of the 1 mC PEDOT solid contacts. Larger cumulated charge  $Q$  means larger portion of reduction/oxidation reactions are involved. This implies a higher yield of electropolymerization when using NaNO<sub>3</sub> as electrolyte due to the larger hydrated nitrate ion in comparison to chloride ion. The higher affinity of nitrate with respect to chloride ion could also play a role. These coulometric results are in good agreement with cyclic voltammograms shown in Figure 27.



**Figure 28.** Cumulated charge  $Q$  vs time for  $\text{NO}_3^-$ -sensitive SCISEs based on 1 mM PEDOT(Cl) and PEDOT( $\text{NO}_3$ ) solid contact covered with drop-cast ISM. (Figure 6 in *Paper V*)

## 4. Conclusions

A novel coulometric signal transduction method for SCISEs was studied and discussed in this work. The chronoamperometric and coulometric responses of SCISEs were studied, and factors influencing the analytical signal of the coulometric method were also investigated using electrochemical impedance spectroscopy and cyclic voltammetry methods.

The conducting polymer PEDOT(PSS) was used as ion-to-electron transducer for cation-selective SCISEs ( $K^+$ ,  $H^+$ ,  $Ca^{2+}$  and  $Pb^{2+}$ ), while PEDOT(Cl) and PEDOT( $NO_3$ ) were used as solid contact for anion-sensitive SCISEs ( $Cl^-$ ,  $NO_3^-$ ,  $ClO_4^-$  and  $SO_4^{2-}$ ). SCISEs with drop-cast thick- and spin-coated thin- membranes were fabricated. Results from the chronoamperometric and coulometric responses of SCISEs showed that the cumulated charge of the coulometric method is linearly proportional to the logarithm of the activity of the primary ion, and inversely proportional to the charge of the ion detected. The current and cumulated charge behavior of cation and anion SCISEs are totally opposite under same experimental protocol, as expected based on the Nernst equation. A thicker solid contact film, *i.e.* larger redox capacitance of conducting polymer leads to amplification of the cumulated charge signal, at the price of longer equilibrium (response) time.

It was shown that the amperometric and coulometric response of the SCISE can be improved by lowering the resistance of the ISM to facilitate the ion transfer process. This was done by enlarging the surface geometrical area of the SCISE and using spin-coated thin ISM instead of drop-cast thick ISM to decrease the mass transport resistance through the ISM.

In *Paper I*, it was shown that the chronoamperometric response of the SCISE has high reproducibility. The equilibration time can be significantly shortened by increasing the surface area of the electrode, *i.e.* improving the accessibility of the PEDOT(PSS), while the magnitude of the current peaks can be significantly increased as well. Ion transfer in SCISEs with different surface areas were characterized with the coulometric method and EIS. Results indicate that SCISEs with larger surface area (lower bulk resistance of ISM) facilitate the ion transfer through SCISEs, resulting in a faster coulometric response and shorter response time.

In *Paper II*, model calculations of the coulometric transduction method were done using a  $Cl^-$ -SCISEs with spin-coated ISM as an example. The modeling calculation is supportive and in



quantitative agreement with our obtained results. The coulometric method exhibits high sensitivity and reproducibility with a relatively quick response time in the case of SCISEs covered with spin-coated thin-layer ISM. SCISEs with spin-coated thin-layer ISM show faster response time and lower electrode resistance than SCISEs with drop-cast thick ISM.

In *Paper III*, coulometric and impedance measurements show that the ion transfer process in  $K^+$ -SCISEs was diffusion controlled even with spin-coated thin-layer ISM, while  $H^+$ -SCISEs showed a low impedance and a fast coulometric response even with drop-cast thick ISM. This was due to the rapid transport of  $H^+$  in the ISM and PEDOT(PSS) solid contact. Small changes in activity (0.1%) were detectable in the case of  $K^+$ -SCISEs utilizing the coulometric transduction method, which is relatively challenging when using the classical potentiometric method. Furthermore, it was possible to apply the coulometric method in real sample analysis, e.g. to detect small pH changes in seawater and to measure  $K^+$  concentration in a control serum sample. Minimizing the potential drift is also of importance for the coulometric method.

In *Paper IV*, solid-contact ion-selective electrodes for divalent cations ( $Pb^{2+}$  and  $Ca^{2+}$ -SCISEs) were studied with chronoamperometry, coulometry and EIS methods. Divalent cations and the respective SC-ISEs revealed interesting features from the coulometric method. The coulometric response of  $Pb^{2+}$ -SCISEs is mainly limited by the ion transport through PEDOT(PSS), while the coulometric response of  $Ca^{2+}$ -SCISEs is mainly dependent on the ion transport through the ISM. The obtained results from EIS measurements are in good agreement with coulometric responses of SCISEs. The limited transport of  $Pb^{2+}$  in PEDOT(PSS) was attributed to the interactions between  $Pb^{2+}$  and PEDOT(PSS).

In *Paper V*, the coulometric transduction method was further investigated for anion-sensitive SCISEs, together with cyclic voltammetry and EIS methods. Results obtained by cyclic voltammetry showed that the electrolyte solution used in the electrodeposition of the conducting polymer-based solid contact film and in the cyclic voltammetric measurements affects the current responses. This is correlated with the size of hydrated doping anions. Electropolymerization of the solid contact film at a given polymerization charge showed that the yield of PEDOT is significantly larger when using nitrate as counter ion, compared to chloride. The cumulated charge is also larger for  $NO_3^-$ -sensitive SCISE with PEDOT( $NO_3$ ) as solid contact compared to PEDOT(Cl) solid contact. Results from EIS measurements carried out for  $SO_4^{2-}$ -sensitive SCISEs clearly indicate that the high-frequency semicircle originates from the ISM. The low frequency capacitance at the lowest frequency (10 mHz) of  $SO_4^{2-}$ -sensitive SCISEs showed to be independent of the ISM thickness. Electrode-to-electrode

reproducibility of SCISEs when utilizing the coulometric method is an essential parameter as well.

The results presented in this work demonstrate that the coulometric transduction method is appropriate and applicable for SCISEs in ion detection applications. In comparison with traditional potentiometry, the high sensitivity of the coulometric method makes it proper and useful in practical applications where minute concentration changes need to be monitored. However, when utilizing the coulometric method in real samples, there are still some practical issues that need to be addressed, such as minimizing the potential drift of SCISEs. Actually, a low potential drift of SCISEs as well as a good reproducibility are required both for potentiometry and coulometry methods.

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