Section One

Potentiometric Sensors and Voltammetry

Chapter One

Theoretical Background of Potentiometric Sensors

1.1.1. Introduction

Analytical chemistry is an important field of science and is responsible for the understanding and control of many processes throughout industry, research, medicine and environmental fields. The analysis of heavy metals in environment has become extremely important due to their potential toxicity to both animal and plant life. Developments in the analytical field are interested because of the need for instruments with high accuracy, low limits of detection, reduction of analysis times, cheap purchase and lower operating costs and ease of use. Ion-selective electrodes (ISEs) have a long history and the potential to fill many of the above mentioned requirements.

1.1.2. Ion Selective Electrodes

An ion-selective electrode (ISE) is a electrochemical sensor whose output potential, when measured against a suitable reference electrode, is logarithmically proportional to the activity of the selected ion in the test solution [1,2]. The differences in EMF are idealistically a direct result of activity changes of a targeted ion, with no interference from other species in a sample solution. ISEs have several valuable advantages that make them superior to other analytical techniques. Ion-Selective Electrodes compared to many other analytical techniques, are relatively inexpensive, measurements are simple, often rapid, nondestructive, and applicable to a wide range of concentrations. Many analyses can be performed directly without the need for time-consuming sample preparation, such as centrifugation and filtration. Solution color or turbidity does not affect results. ISEs are unresponsive to oxidation–reduction couples in the test solution. Portability enables them to be used in field work. However, ISEs have some major disadvantages. The classical ion-selective membranes cannot be used at high temperature or pressure and must be used in a straight position. ISEs also have the advantage of analyzing the free ion concentration, as opposed to the total ion concentration determined by techniques such as inductively coupled plasma-mass spectrometry (ICP-MS) and atomic absorption spectrometry (AAS).

ISEs have been known for almost a century with Cremer discovering in 1906 that a thin glass membrane was responsive towards the hydrogen ion [3]. With further researchs in the 1930's a pH electrode was developed and is still one of the most widely used analytical tools in modern chemistry. In the late 1930's, Tendeloo, Kolthoff and Sanders discovered that materials other than glass could selectively measure ions in aqueous solutions [4-7].

The ISE field was relatively quiet until the early sixties when Pungor and Hollos-Rokosinyi developed a sensor based on AgI and paraffin for the determination of Ag^+ and I^- in solutions [8]. Over the past years, research was conducted on a broad range of materials from single crystal LaF_3 to liquid ion-exchanger and neutral carrier membranes [9-18]. One very important discovery was the excellent selectivity demonstrated by the antibiotic valinomycin towards potassium ions [19,20].

ISEs can be characterized according to the ion-sensing matrix responsible for the sensor response and selectivity. The membranes in ISEs can be 1) crystalline in nature eg. a homogeneous mixture of LaF_3 or a heterogeneous mix of an electroactive species like CuS powder in an inert matrix of graphite, 2) non-crystalline in nature, with charged or neutral ion carriers distributed within a inert matrix eg. valinomycin in poly-vinyl chloride, 3) or as sensitised electrodes eg. an enzyme substrate electrode, or alternatively, a gas sensor electrode whereby a gas permeable membrane separates the sample solution from a solution containing an ISE [21].

At present the most widely used and researched matricies are those of liquid membranes with a rigid polymer support. The liquid or plasticizer and the supporting polymer, house the lipophilic ion and lipophilic ligand (ionophore), which is important to the selective and potentiometric response. The former is responsible for the membrane's permselectivity and Nernstian response while the latter is the membrane's ion recognition element capable of selectively binding the target ion species.

1.1.2.1. Components of Polymeric Ion-Selective Electrodes

Ion-selective electrodes consist of a range of components, with each contributing to the overall potential of the system. The primary component is the ion-sensing membrane, which contains several key elements needed for the production of potential differentials with selectivity. The vital components that make up an ion-sensing membrane are; polymer matrix, ionophore, plasticizer, lipophilic ion-exchanger and lipophilic salts. Each component is discussed in the following sections.

1.1.2.1.1. Polymer Matrix

Liquid ISE membranes were originally prepared by soaking porous materials with a solution of a water-immiscible, nonvolatile, viscous organic liquid that contained the solved ionophore [22]. The application of polymers as homogeneous membrane matrices was first suggested for use with charged carriers [23, 24]. In practice, typically ~33% (w/w) of PVC, as the polymeric matrix, ~66% of plasticizer for homogenizing the matrix, and ~1% of the ionophore are used to prepare a sensing membrane [24]. The first polymeric ISE membranes, in which the polymer was considered to provide the needed physical properties, like elasticity and mechanical stability, were prepared with valinomycin, as a neutral ion carrier, in silicone rubber [25], or PVC [26], without the addition of lipophilic ionic sites. However, it is now understood that the Nerstian response of these ISEs had been just because of the possible presence of ionic impurities in the used PVC [27,28], and also in the other components of the membrane. That is due to the experimental facts that, membranes having no ionic sites at all, because of the application of approximately totally pure membrane ingredients in their construction, do not respond to the concentration of target ions [29,30]. There seems to be no need to mention that, there are other polymers which can be used instead of PVC in membrane construction, and PVC is not the only suitable polymer for this purpose. It was shown by Fiedler and Ruzicka [26], in order for a polymer to be suitable for being used in a sensing membrane, and apart from its having the required solubility, the most important factor is that the glass transition temperature (*T*g) of the polymer must be below the room temperature. Having this property, the constructed membranes are fluid enough, under ambient conditions, to permit diffusion of membrane components, reasonable ionic conductivities, and they also have suitable mechanical properties for routine processing and handling. With polymers of high *T*gs (e.g., high molecular weight PVC: T_g~80°), application of plasticizers will be necessary. However, regarding what mentioned above, polymers of low *T*gs (e.g., soft polyurethanes with a low content of crystalline units [31], siliconerubber [25], poly(vinylidene chloride) [32], and polysiloxanes [33] can be used without plasricizers, thus avoiding the disadvantages of plasticizer leaching. The absence of the plasticizers, however, leads to another disadvantage of loosing the possibility to modify ion selectivities by changing the plasticizer. Although, the polymer has only a slight effect on the performance of ISEs, detailed investigations show that it is not just an inert matrix but that it may influence the various membrane properties. For example, the polarity of a membrane differs significantly from that of the plasticizer alone. Thus the widely used

plasticizers DOS and *o*-NPOE exhibit dielectric constants of 4.2 and 21, respectively, whereas the values for the corresponding membrane phase with 33% PVC are 4.8 and 14 [34]. As to the extent of ion-pair formation, it is much lower in a DOS-PVC membrane than in DOS alone. Several chemically modified forms of PVC containing hydroxy, amino, or carboxylate groups have been synthesized in order to improve the adhesion properties of the membranes on electrode surfaces [28, 36].

1.1.2.1.2. Ionophore

The key component of any potentiometric ion-selective sensor is its ionophore or ligand, or the recognition element, because if it can exchange only one type of ion between the two phases, the resulting potential difference formed between the phases, will then be governed only by the activities of this specific ion in these phases**.** Ions other than the primary ion (interfering, or secondary ions) form weak to no complexes with the ionophore, and in turn reduce ion-exchange between the interfering and targeted ion. The complex formation constant of the ionophore should be several orders of magnitude greater for the primary ion over interfering ones, but not too large as the sensor will not function properly. If the binding of the primary ion is too strong, due to the kinetically too slow rate of complexation/decomplexation process, slow response time and deviation in response slope can observed [37]. For example, cryptands, which form highly stable complexes with certain ions, are not suitable and rarely use as ionophores in ISE and many crown ethers which form weaker complexes are excellent carriers for ion-selective membrane electrodes [38].

In planning ionophores for ISEs the dynamic complex stability is more important than the thermodynamic constant; the kinetic of formation and decomposition of complexes should be considered:

$$L + (M^{+}) \leftrightarrow (LM^{+})$$

There are examples of ionophores such as benzo- and naphtho-15-crown-5 for which complex stability constants for Na and K are nearly equal even though they show high selectivity (potentiometrically determined) for only one of these ions, the potassium ion. In these cases the stoichiometry of the complex plays an important role. X-Ray study shows that benzo-15- crown-5 forms a crystalline complex with NaI of stoichiometry 1:1 and with KI of stoichiometry 2:1 (Li_2K) [39]. Benzo-15-crown-5 forms complexes of 1:1 stoichiometry with Na and K of similar stability ($\log K_{Na} = 2.78$ and $\log K_K = 2.73$) and a sandwich type of complex with K^+ ion as well of 2:1 stoichiometry ($\log K_K = 3.40$),

determined in acetone [39]. This ligand shows selectivity for K over Na, $\log K_{K,Na}^{pot} = -1.9$ [40].

Molecules utilised in ISEs should therefore consist of a balance between structural preorganisation and flexiblity, to minimize the overall free energy barrier between the complexed and Free states whilst still maintaining fast kinetics [37, 41].

Initially the membranes selectivity without ionophore is directly related to the sample ions hydration enthalpies [42]. Once the ionophore is incorporated into the membrane, its selectivity is directly related to the complex formation constant of the ionophore with various ions. Apart from the main binding site in the molecule the ionophore must also contain significantly large or numerous lipophilic groups in order to remain in the membrane phase and not leach out into the aqueous sample. Lipophilicity defined as the partition coefficient of the compound between water and n-octanol and can be express as a value (log *P*). It can be determined by TLC on reverse phase silica gel plates (C18) [43] or it can be calculated by the method of Hansch and coworkers [44]. Both methods are in rather good agreement. The required values of the ionophore lipophilicity for the measurements in aqueous solutions are mlog P_{TLC} = 4.8 but for more lipophilic media, such as blood or serum, log P_{TLC} should be about 11.3 for a sensor lifetime of 30 days (720 h) [45]. The relation between ligand lipophilicity and selectivity has been known for some time, however only structural studies can give the answer why and how lipophilicity of ionophores can affect selectivity of ISE.

Ionophores can be either charged or neutral ion binding molecules. Charged ionophores or ion-exchangers were first tested in 1967 by Ross for the construction of a Ca^{2+} selective membrane [46]. The first neutral ionophore incorporated into membranes is the well-known antibiotic, valinomycin, which forms a 1:1 complex with K^+ ions [20, 23]. Since the initial discovery of this naturally occurring ionophore, a great amount of research has been conducted into the synthesis of new and better ionophores for various elements.

A successful ionophore usually contains a hydrophilic cavity, which binds with the selected ion and a hydrophobic surrounding allowing it to be evenly dispersed within the polymer matix. This is often achieved through the addition of non-polar groups around the polar cavity therefore shielding the charged cavity from the non-polar membrane [47]. Valinomycin, shown in Fig. 1.1.1 (a), is able to wrap around the K^+ ion to form this cavity effect. The selectivity of ionophores is often closely related to the size of the hydrophobic cavity and its ability to exclude certain ions.

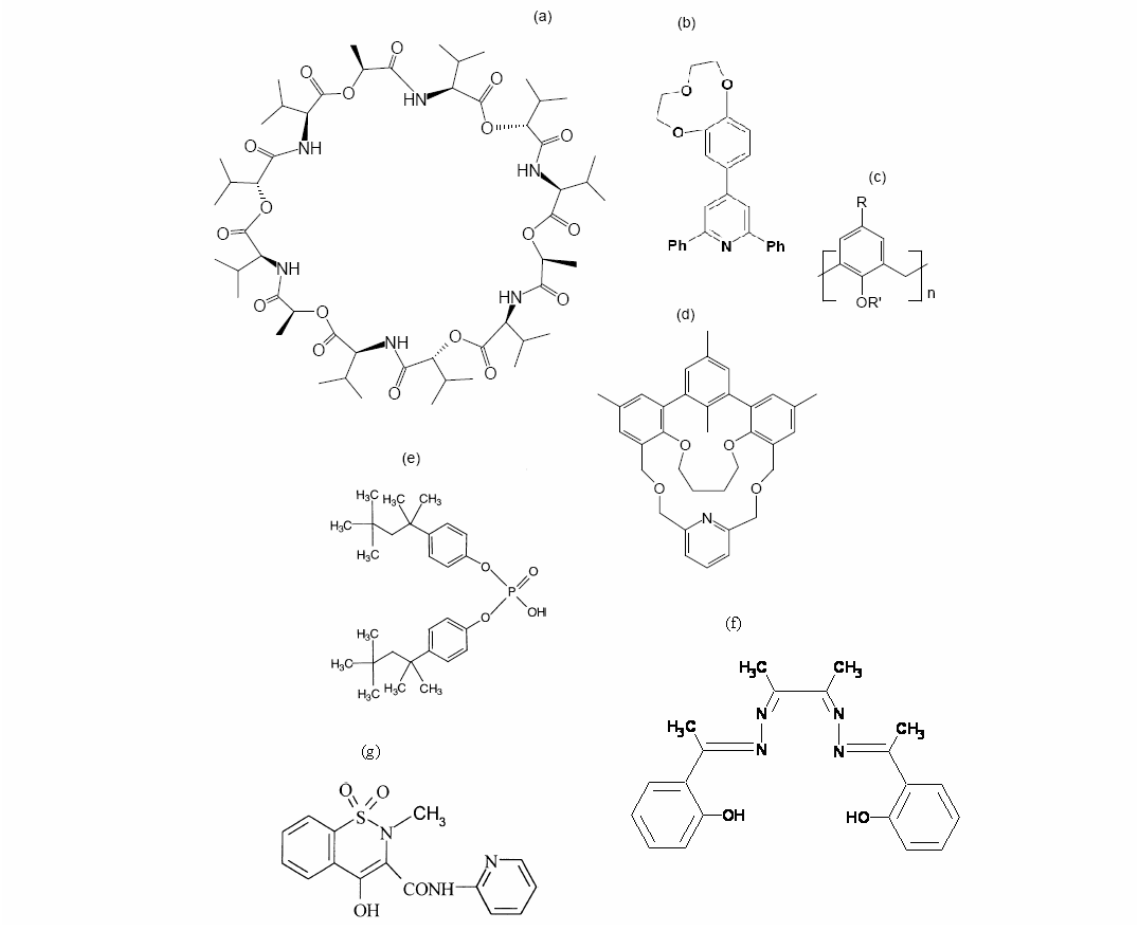


Fig. 1.1.1. Molecular structures of some common ionophores: (a-d) cavity forming molecules, (e-g) acyclic molecules; a) Valinomycin, K^+-selective [48]; b) typical crown ether, Benzo-9-crown-3, Be^{2+}-selective [13]; c) calix[n]arene with various attached functionalities [49]; d) hemispherand, Na^+-selective [37]; e) bis[4-(1,1,3,3-tetramethylbutyl)-phenyl]phosphoric acid, Ca^{2+}-selective [50]; f) Bis(2-hydroxyacetophenone)butane-2,3-dihydrazone, Cu^{2+}-selective [14]; g) Piroxicam, Pb^{2+}-selective [51].

The most highly selective ionophores are usually the ones with cavities of minimal size variations, allowing only ions of a particular size to complex with the binding site. Ions larger than the cavity will be excluded from binding, whilst ions of small size will complex less readily as the distance between the binding sites and the ion is increased and the repulsion forces and energy required to bring the binding atoms closer together will be too great.

Crown ethers, Fig. 1.1.1 (b), were perfect candidates for ionophores due to their numerous binding atoms and cavity forming ability. The large number of hard donor atoms

improved the selectivity for alkali and alkaline earth metals over other ions. The selectivity could be tuned towards specific ions, by varying the macrocyclic ring size and/or the incorporation of different donor atoms like nitrogen and sulphur [13, 52-55].

Acyclic ionophores (Fig. 1.1.1 (e-g)) have also shown good to moderate selectivity in ISEs. The structure of these molecules enhances complexation by minimizing the free energy of the free-to-complexed ionophore transition [37]. Similar to macrocyclic ionophores, additional functionalities can be added to enhance the binding characteristics, such as lipophilic tails and electron-density-withdrawing/donating groups [37]. Even though these ionophores are less rigid than most of the macrocycles, their flexibility allows the binding sites to be brought into an optimized binding conformation with minimal energy [37, 60]. As is the case with macrocycles, the selectivity of acyclic ligands is dictated by the nature of the binding atoms. Both the macrocyclic and chelate effect are desirable in ionophores as they would help to stabilise the host-guest system whilst still maintaining fast exchange kinetics.

Schiff base also have become one of the most utilized series of compounds incorporated into sensors as neutral ionophores [14, 16, 56-59]. Their benefits in ionophore development are discussed further in the following chapters.

1.1.2.1.3. Plasticiser

Solvent polymeric membranes used in ion sensors are usually based on matrix containing about 30–33 %(w/w) of PVC and 60–66% of a membrane solvent. Films with such a high amount of plasticizer show optimum physical properties and ensure relatively high mobilities of their constituents [61]. In order to give a homogeneous organic phase, the membrane solvent must be physically compatible with the polymer, i.e., have plasticizer properties. For various reasons, it also has an influence on the selectivity behavior. For a ligand-free ISE membrane based on an ion exchanger that is incapable of specific interactions, the selectivities are determined by the difference between the standard free energies of the ions in the aqueous and organic phases, which is only influenced by the plasticizer. The selectivity sequence obtained with such membranes is always the same as the Hofmeister series. The sequences obtained for some cations and anions were later shown to agree with those of the free energies of hydration of the ions [62,63]. On the other hand, selectivities of carrier-based ISEs are highly influenced by the membrane solvent. For example, the change in plasticizer from the polar *o*-NPOEto the apolar dibutyl phthalate (DBP) reduced the Cu^{2+}-selectivity of the ISE with the ionophore

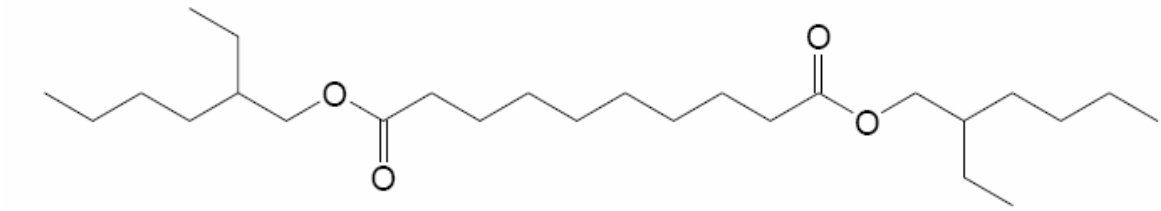
bis(2-hydroxyacetophenone)butane-2,3-dihydrazone [14]. It has been assumed that this influence is due to the polarity of the plasticizer, which can be estimated from the interaction of charged species with a continuum of given dielectric constant (Born model) [64]. With more polar solvents, divalent ions are preferred than the monovalent ones, this effect being especially pronounced with thin ligand layers [53,65]. The nature of the plasticizer strongly influences the measuring range (i.e., the upper and lower detection limits) of ion-selective sensors, too.

Another factor, highly influenced by the membrane solvent, is the formation of ion-pairs. The ion-pairs formed between complexed ions and lipophilic counterions seem to be negligible in polar membranes, but are relevant in nonpolar ones. Formation of ion-pairs may influence the slope of the response function. If, for example, divalent cations M^{2+} form associates with a monovalent anion X^{-}, so that predominantly monovalent species MX^{+} take part in the phase transfer equilibrium [66] and/or occur in the membrane, a slope characteristic for monovalent ions can be obtained [66, 67]. Furthermore, ion association may influence the selectivity factors as well. The formation of ion-pairs in the membrane decreases the concentration of the free ions and has thus a similar effect as an increase of the complex formation constant. However, this influence is likely to be nonspecific, i.e., similar for primary and interfering ions, and therefore, degenerates the selectivity. Such a loss in selectivity is expected to be especially significant for sterically unhindered ionic sites (such as sulfonates) and for ionophores forming weaker complexes.

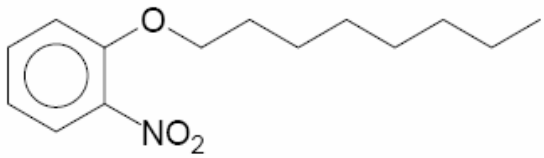
The choice of the plasticizer also depends on what purpose the ISE is used for. During measurements in blood or serum, deposits of charged species (mainly proteins) on the membrane surface give rise to potential drifts. These effects are more severe with polar solvents. Therefore, in some cases, the preparation of Ca^{2+}-selective membranes with low polarity solvents, and hence, reduced selectivities toward monovalent ions, has been proposed [68]. Another concern is that, at least to some extent, even highly lipophilic solvents leach from the membrane phase and thereby cause inflammation if applied in living organisms [31]. This can be avoided by using a plasticizer of high molecular weight [69] or by photopolymerizing it after membrane preparation [70].

The plasticiser is essential to increase the mobility of the membrane components if the glass transition temperature of the polymer is greater than room temperature [42]. The plasticiser reduces the viscosity of the membrane whilst still maintaining mechanical strength and allows the membrane components to be homogenously distributed within the polymer matrix. The chemical structures of two common plasticisers are shown in Figure 1.1.2 The

structures of the plasticisers often contain highly lipophilic alkyl chains, aromatic rings, and adamantyl groups, which help prevent loss to the sample solution through leaching and also allow for high mobility and solubility.



DOS



o-NOPE

Figure 1.1.2. Chemical structures of some common plasticisers: Bis-(2-ethylhexyl) sebacate (DOS), (apolar, ε_t ~ 3.9), 2-nitrophenyl octyl ether (o-NOPE) (polar, ε_t ~ 23.9)

1.1.2.1.4. Ionic Additives

The lipophilic ion-exchanger is a large salt that is incorporated into the neutral membrane to ensure its permselectivity, or Donan exclusion, which means that no significant amount of counter ions may enter the membrane phase. To achieve this so-called Donnan exclusion with electrically neutral carriers, counter ions (ionic sites) limited to the membrane must be present. Although neutral-carrier-based ISE membranes may work properly even when they contain only a very small amount of ionic sites, the addition of a salt of a lipophilic ion is advisable and beneficial for various other reasons as well. The original reason for adding a tetraphenyl borate salt to the membrane of a cation-selective electrode is to reduce the anionic interference observed in the presence of lipophilic anions like thiocyanate or perchlorate [71]. At the same time, the electrical resistance of the membrane is lowered, which is especially important with microelectrodes [72]. Ionic additives are ion exchangers, which themselves induce a selective response if no or only an insufficient amount of ionophore is present. Therefore, their concentration must be adjusted carefully. The electrical resistance may also be lowered by adding a salt of two lipophilic ions [73, 74]. Such a salt has no ionexchanging properties, and can be applied in excess amounts relative to those of the ionophore.

Ionic sites, moreover, have a selectivity-modifying influence as their amount in the membrane determines the exchangeable ions of opposite charge. Hence, by adjusting the molar ratio of the ionic sites to ionophore, so that the latter is present in excess with respect to the primary ion but in deficiency regarding the interfering ions, the selectivity behavior of ISEs can be improved.

The names of the most important salts used as lipophilic additives are given in Table 1.1.2 [75]. Various tetraphenyl borate derivatives are currently used as anionic additives. Unfortunately their chemical stability is limited, especially in the presence of acids, oxidants, and light. The decomposition is due to an attack of H^+ ions on the phenyl substituents [76]. The stability could be increased by introducing electron withdrawing substituents [77, 78]. Because of their chemical stability and lipophilicity, sodium tetrakis-[3,5-bis(1,1,1,3,3,3-hexafluoro-2-methoxy-2-propyl)- phenyl]borate trihydrate (NaHFPB) and potassium tetrakis[3,5-bis(trifluoromethyl) phenyl]borate (KTFPB), oleic acid (OA) and potassium tetrakis [*p*-chlorophenyl]-borate (KTPCPB) are the best anionic additives available.

Table 1.1.1. The names of the most important salts used as lipophilic cationic additives [75].

Cationic additives
Potassium tetrakis [3,5-bis(trifluoro methyl) phenyl] borate (KTFPB)
Potassium tetrakis (4-chloro-phenyl-borate) (KTK)
Potassium tetrakis (p- chlorophenyl) borate (KTPCPB)
Sodium tetrakis-[3,5-bis(1,1,1,3,3,3-hexafluoro-2-methoxy-2-propyl)-phenyl] borate (NaHTPB)
Sodium tetraphenyl borate (NaTPB)
Anionic additives
Hexadecyl pyridinium bromide (HDPB)
Hexadecyl trimethyl ammonium bromide (HTAB)
Hexadecyl trioctadecyl ammonium bromide (HDTODAB)
Tetradodecyl ammonium bromide (TDDAB)
Tetroctyl ammonium bromide (TOABr)
Tridodecyl methyl ammonium chloride (TDDMACl)
Trioctyldodecyl ammonium bromide (TODAB)

Recently the first use of a fatty acid such as oleic acid, as a very suitable lipophilic additive for inducing permselectivity to some PVC membrane selective electrodes was reported by Ganjali et al. [79, 80].

Lipophilic tetraalkylammonium salts such as tridodecyl methylammonium chloride (TDDMACl), hexadecyl trimethylammonium bromide (HDTMAB) are suitable cationic additives. The hydrophilic counter ions of these lipophilic additives are exchanged with the primary ion as soon as the ISE is conditioned in the respective solutions. Leaching of ionic sites may be avoided by bonding them covalently to the polymer matrix as, for example, in sulfonated PVC [81]. Such a polymer may however show modified selectivity behaviors, because of direct interaction of the sulfonate group with cations [81]. The names of the most important salts used as lipophilic cationic additives are given in Table 1.1.1.

1.1.2.2. Response Mechanism of Ion-Selective Electrodes

The basic setup of an ion-selective electrode measuring station is presented in Figure 1.1.3, and consists of two galvanic half-cells that are connected to a potential measuring device [21]. One of the half cells consists of a reference electrode maintained in a reference electrolyte; the other is that of the ion-selective electrode. The ion selective electrode can consist of either an ion-selective membrane with an internal reference system (Ag/AgCl, conventional setup), or a conducting substrate coated with the ion-selective membrane (solid-state electrodes) [21].

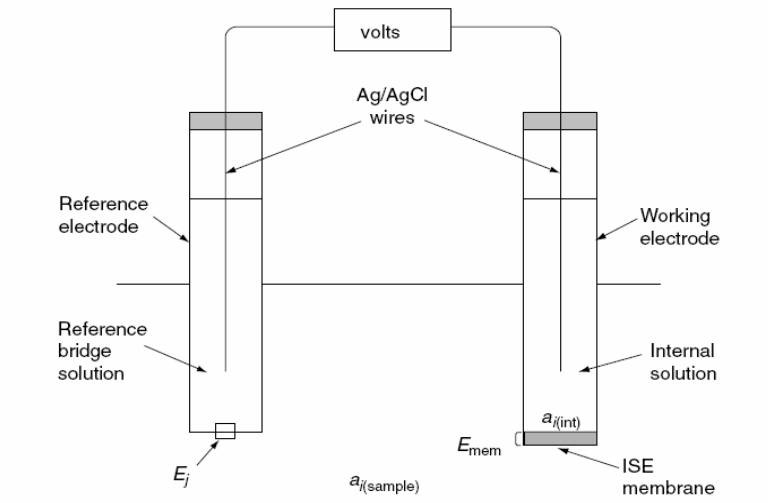


Fig.1.1.3. Schematic diagram of a conventional ion-selective membrane, measuring cell.

The electrochemical cell can be represented as follows:

Ag|AgCl | KCl 3 M | bridge electrolyte | sample | membrane | inner ref. solution | AgCl|Ag

The electromotive force (EMF) or total potential difference across the electrochemical cell, measured under zero current, is the sum of a series of local potentials at various interfaces across the two-electrode cell. The potential difference across the electrodes can be

expressed as follows:

$$EMF = E_{const} + E_M + E_j \qquad (1.1.1)$$

The majorities of the individual local potentials are sample independent, and can therefore be termed constant under standard measuring conditions, E_{const} in Equation 1.1.1 The liquid junction potential, E_j, arises from the different mobilities of ions at the phase boundary between the sample and the bridge electrolyte of the reference electrode, which can either be kept reasonably small and constant under well-defined conditions or be estimated according to the Henderson formalism. It is important to note that it is this liquid junction potential that prohibits the true assessment of single ion activities with ion-selective electrodes; the role of the reference electrode on the overall emf measurement should, therefore, not be overlooked [60]. On the other hand, galvanic cells without liquid junctions (i.e., containing two ion-selective electrodes) respond to ratios or products of ion activities, again prohibiting single ion acitivty measurements. In this work, however, we will only focus on the membrane potential E_M of one electrode which is ideally a function of the sample ion activity.

Phase Boundary Potential. Since the membrane is usually interposed between the sample and an inner reference electrolyte, it is common to divide the membrane potential E_M into three separate potential contributions, namely the phase boundary potentials at both interfaces and the diffusion potential within the ion-selective membrane [82-84]. While the potential at the membrane/inner filling solution interface can usually be assumed to be independent of the sample, the diffusion potential within the membrane may become significant if considerable concentration gradients of ions with different mobilities arise in the membrane. Historically, there have been some debates about the relevance of the membrane diffusion potential [85]. While one reason was that no obvious explanation could be found for the observed permselectivity, another was the excellent correlation between the potentiometric and transport selectivities of such membranes. As a consequence, rather complex models have been used [21] that often make an intuitive understanding difficult.

For ion-selective electrodes, the membrane internal diffusion potential is zero if no ion concentration gradients occur. This is often the case for membranes that show a Nernstian response. For the gain of simplicity, diffusion potentials are treated here as

secondary effects in other cases as well and are neglected in the following discussion. We therefore assume:

$$E_M = E_{const} + E_{PB} \qquad (1.1.2)$$

Where E_{PB} is the phase boundary potential at the membrane-sample interface, which can be derived from basic thermodynamical considerations. First, the electrochemical potential, $\bar{\mu}$, is formulated for the aqueous phase [86]:

$$\bar{\mu}_{(aq)} = \mu_{(aq)} + ZF\,\phi_{(aq)} = \mu^0{}_{(aq)} + RTLna_{1(aq)} + ZF\phi_{(aq)} \qquad 1.1.3$$

and for the contacting organic phase:

$$\bar{\mu}_{org} = \mu_{org} + ZF\,\phi_{org} = \mu^0{}_{(org)} + RTLna_{1(org)} + ZF\phi_{(org)} \qquad 1.1.4$$

Where μ is the chemical potential (μ^0 under standard conditions), z is the valency and a_I the activity of the uncomplexed ion. I, ϕ is the electrical potential, and *R*, *T* and *F* are the universal gas constant, the absolute temperature and the Faraday constant. It is now assumed that the interfacial ion transfer and complexation processes are relatively fast and that, therefore, equilibrium holds at the interface so that the electrochemical potentials for both phases are equal. This leads to a simple expression for the phase boundary potential [86]:

$$E_{PB} = \Delta\phi = -\frac{\dot{\mu}_{(org)} - \dot{\mu}_{aq}}{ZF} + \frac{R}{ZF}\mathrm{Ln}\frac{a_1(aq)}{a_1(org)} \qquad 1.1.5$$

Often, the term comprising of the standard chemical potentials is combined to the symbol k_I; i.e., $k_I = \exp(\{\mu^0(aq) - \mu^0(org)\}/RT)$. Apparently, a simple function of the phase boundary potential on sample ion activities is expected if $a_I(org)$ is not significantly altered by the sample. Complexation reactions with a lipophilic neutral carrier within the organic membrane phase influence $a_I(org)$ and, therefore, also the phase boundary potential.

The fundamental equation 1.1.5 will be used throughout this work to describe the behavior of ion-selective electrode membranes. By combining eqs 1.1.5 and 1.1.2 one obtains

$$E_M = E_{Const} + E_{PB} = E_{Const} - \frac{\dot{\mu}_{(org)} - \dot{\mu}_{(aq)}}{ZF} - \frac{RT}{ZF}Ln\,a_{1_{(org)}} + \frac{RT}{ZF}Ln\,a_{1_{(aq)}} \qquad 1.1.6$$

Under the condition that $a_I(org)$ remains constant, it can, together with all other sample-independent potential contributions, be included in one term (E^0) and eq 1.1.6 reduces to the well-known Nernst equation:

$$E_M = E^\circ + \frac{RT}{ZF} Ln\, a_{1_{(aq)}} \qquad 1.1.7$$

According to eq 1.1.6 it is evident that the composition of the surface layer of the membrane contacting the sample must be kept constant in order to obtain an exact Nernstian response of the electrode [87]. Nevertheless, if eq 1.1.5 is valid, the exact structure of this space charge region is not really relevant to the sensor response. To achieve a constant composition of the membrane bulk, several conditions must be met:

(1) The membrane must have ion-exchanger properties. The simultaneous coextraction equilibrium of sample counterions occurs according to the following reaction: $I^+(aq) + X^-(aq) \leftrightarrow I^+(org) + X^-(org)$. The major factor determining $a_I(org)$ is the presence of a lipophilic ion-exchanger within the membrane, and hence, the concentration of extracted anions $X^-(org)$ is insignificant. This characteristic is, somewhat misleadingly, called permselectivity. If, however, the concentration of the lipophilic ion exchanger is small relative to that of $X^-(org)$, the concentration of primary ions in the organic phase, $a_I(org)$, is roughly proportional to $a_I(aq)$ and the electrode does not respond to ion activity changes in a Nernstian way [29,88,89].

(2) The membrane must have a sufficiently hydrophobic nature to hinder substantial coextraction of sample counterions according to the reaction shown under condition 1. This allows one to measure samples with high electrolyte concentrations. Clearly, hydrophilic polymers such as hydrogels [90] are not suited as membrane bulk materials for ion-selective electrodes.

(3) If ion-exchange reactions with interfering ions with the same charge type occur, the activity $a_I(org)$ of the uncomplexed analyte ion in eq 1.1.6 is decreased and a sub-Nernstian mixed ion response is expected [91]. This can be prevented by incorporating a lipophilic complexing ligand (ionophore or carrier) in the membrane that selectively binds the target analyte ion.

(4) However, the ligand employed should not bind to the analyte ion too tightly, since then coextraction of $I^+(aq)X^-(aq)$ increases $a_I(org)$ and leads to a breakdown of the permselectivity of the membrane. This effect is increasingly likely at high activity and lipophilicity of the sample electrolyte and is known as Donnan failure.

(5) Other (electrically neutral) interfering species that can be extracted into the membrane and alter $a_I(org)$ must not be present in the sample. Examples for this effect include the complexation of analyte ions by neutral surfactants in tetraphenylborate based membranes [92] or in certain pH-selective electrodes [93], where the binding of the

surfactant with the electroactive species changes a_I(org) and, therefore, the cell potential significantly. Similarly, the extraction of higher alcohols into valinomycin-based membranes has been shown to induce considerable emf shifts [94], probably due to changes in the complex formation constant of valinomycin in the now altered matrix. The observed uptake of homogenous water into ion selective membranes [95], although not yet studied extensively, is expected to have similar effects, especially in an asymmetric setup such as with solid contact electrodes, where this influence cannot be counterbalanced at the second membrane/aqueous solution interface.

While the permselectivity of the membrane is assured by its ion-exchange properties and hydrophobicity, which inhibits considerable coextraction of counterions, it is the selective complexation of the analyte ion by a ligand, the so-called ion carrier or ionophore, in the organic phase that assures that the membrane responds selectively to the target ion within a complex sample matrix. Since the widely used uncharged carriers are neutral when uncomplexed and the complexes have the same charge as the analyte ion, the respective membranes require the additional incorporation of lipophilic ions of opposite charge to ensure permselectivity. In practice, alkali salts of tetraphenylborate derivatives are used for cation-selective membranes and tetralkylammonium salts for anion-selective membranes. Since poly(vinyl chloride) as membrane matrix already contains ionic impurities with cation-exchanger properties, neutral carrier-based cation-selective membranes are usually functional without the incorporation of anionic sites. However, their selectivity and lifetime behavior is not often optimal. There is another important group of ionophores compounds that are electrically charged when uncomplexed and neutral when bounded to the analyte ion. Important representatives of such carriers are metalloporphyrins and cobyrinates that bind selectively to anions by axial binding of the metal center. With charged carriers, permselectivity can be achieved without the incorporation of additional ionic sites, e.g., with pure organic solvents as membranes [96,97]. However, as recently shown, the selectivity is only optimal for membranes containing ionic sites of the same charge type as the analyte ion, so that ionic sites of opposite charges are required for neutral and charged carriers [98-100]. More recently, carriers have been identified that cannot be easily fitted into one of these two general categories. Some of these are apparently insensitive to small amounts of added anionic or cationic sites in the membrane. While the exact carrier mechanism varies from case to case, these ionophores are now often called mixed-mode carriers. Examples for such

carriers include the classical Ca^{2+} ionophore bis[4-(1,1,3,3-tetramethylbutyl)phenyl] phosphate [101] as well as a range of anion carriers [102].

1.1.2.2.1. Selectivity

One of the most important characteristics of ISEs is their preference to primary or measuring ions (I) over secondary or interfering ions (J). The relative selectivity that a membrane shows is one of the fundamental parameters that determine its essential in practical samples. Ideally, the membrane is sensitive to primary ions only and adhere the well-known Nernstian equation (Equation 1.1.8).

$$E = E_I^0 + \frac{RT}{z_I F}\ln(a_I(I)) \qquad 1.1.8$$

Where a_I(I) is the primary ion activity in the sample without interference from other sample ions. The constant potential contributions (see eq 1.1.6) are unique for every ion measured and included in E_I^0. However, in practice, the membrane only obeys this behavior in a limited concentration range and outside this the potential is affected by the presence of other ions. The affinity of one ion over another in the membrane phase can be related to the equilibrium constants of the primary and interfering ion exchange reactions (i.e., K_I and K_J respectively) between the membrane and aqueous phases. According to the Nicolskii-Eisenman formalism, the activity term in the Nernst equation is replaced by a sum of selectivity-weighted activities

$$E = E_I^0 + \frac{RT}{z_I F}\ln(a_I(IJ) + K_{IJ}^{pot} a_J(IJ)^{z_I/z_J} \qquad 1.1.9$$

where a_I(IJ) and a_J(IJ) are the activities of I and J in the mixed sample. The activity a_I(I) can be related to a_I(IJ) of the mixed sample that gives the same potential E by combining eqs 1.1.8 and 1.1.9:

$$a_I(I) = a_I(IJ) + K_{IJ}^{pot} a_J(IJ)^{z_I/z_J} \qquad 1.1.10$$

For extremely selective electrodes, the Nicolskii coefficient K_{IJ}^{pot} is very small and a_I(IJ) approaches a_I(I). If interference is observed, a lower activity a_I(IJ) of the mixed sample will give the same response as the activity a_I(I) of a solution containing no interfering ions.

There are several methods for the determination of selectivity coefficients ($K_{I,J}^{pot}$), among them the three below methods are much usual:

1- The Separate Solution Method (SSM)

2. The Mixed Solution Method (MSM)

(a) Fixed Interference Method (FIM)

(b) Fixed Primary Method (FPM)

3- The Matched Potential Method (MPM)

1.1.2.2.1.1. Mixed Solution Method (MSM)

In the mixed solution method [103], the selectivity coefficient, K_{MSM}, was evaluated graphically from potential measurements on solutions containing a fixed concentration of primary ion (i) (≈ 1×10^{-4} M) and varying amounts of interfering ions (M^{n+}) according to the Eq. 1.1.4.2:

$$K_{i,x}^{Pot} \times a_x^{\frac{2}{n}} = a_i \left\{ \exp\left[(E_2 - E_1)(\frac{F}{RT}) \right] \right\} - a_i \qquad (1.1.11)$$

Where E_1 and E_2 are the potentials of the primary ions alone and primary ions with interfering ions(a_x), a_i and a_x are the activities of primary and interfering ions, respectively, and n is the charge of the interfering ion. The potentiometric selectivity coefficients can be evaluated from the slope of the graph of $a_i \left\{ \exp\left[(E_2 - E_1)(\frac{F}{RT}) \right] \right\} - a_i$ versus $a_x^{\frac{2}{n}}$.

1.1.2.2.1.2. Match potential methods (MPM)

According to the MPM, the selectivity coefficient is defined as the activity ratio of the primary ion (A) and the interfering ion (B) that gives the same potential change in a reference solution [104]. The selectivity coefficient, K_{MPM}, is determined as:

$K_{MPM} = \Delta A / a_B$, $\Delta A = a_A' - a_A$

Where a_A is the initial primary ion activity and ?$_A$ the activity of A in the presence of interfering ion, a_B.

Generally, the matched potential method can be used without regard to the electrode slopes being Nernstian or even linear. For these reasons, it has gained popularity in the last few years and has even been advised by IUPAC in a recent technical report.

1.1.2.2.1.3. Separate solution method (SSM) [60]

The SSM involves the measurement of two separate solutions, each containing a salt of the determined ion only. The Nicolskii coefficient is then calculated from the two observed emf values (cf. Fig. 1.1.4).

$$E_I = E_I^{\circ} + \frac{2/303RT}{Z_I F} Log\ a_I \qquad (1.1.12)$$

$$E_J = E_J^{\circ} + \frac{2/303RT}{Z_J F} LogK_{IJ}^{POT}\ a_J^{ZI/ZJ} \qquad (1.1.13)$$

$$Log\ K_{IJ}^{POT} = \frac{Z_I F(E_J - E_I)}{2/303RT} + Log\left(\frac{a_I}{a_J^{Z_I/Z_J}}\right) \qquad (1.1.14)$$

Where E_i and E_x are the measured emf for the solutions of primary and interfering ions, respectively; Z_i and Z_x are the charges of primary and interfering ion. S is the calibration slope of the sensor and a_i and a_x are the activity of primary and interfering ion, respectively.

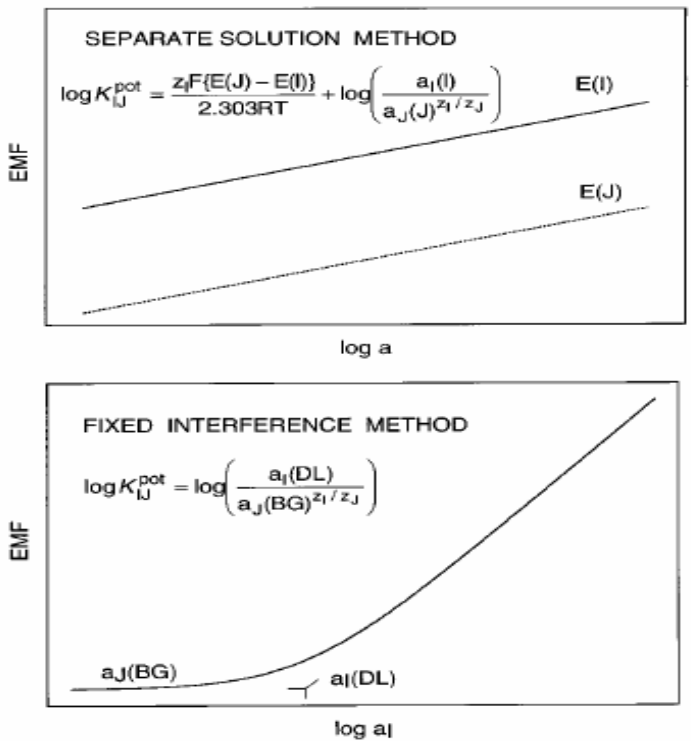


Fig. 1.1.4. Determination of the Nicolskii coefficients according to the separate solution method (SSM, top) and the fixed interference method (FIM, bottom) as proposed by the IUPAC commission [60]