

# **CHAPTER ONE**

## **Introduction**

# **1 Introduction**

## **1.1 Ion Selective Electrodes**

### **1.1.1 History**

It was more than 50 years when Pungor have introduced a new field into the literature named ion-selective electrodes. Till that time it was only a sensor, the glass electrode, which was able to measure the ion activities [1].

At the beginning of the 1900s, the phenomenon observed by Haber and Clemensiewith [2] was a great surprise among electrochemical phenomena, namely that the glass electrode produced an electrochemical signal in response to the acidity of solutions (the definition of the pH was given later). It was also a surprise that this potential signal could only be measured by electrometers of high input resistance (impedance), in contrast to the method worked out earlier by the Nernst school.

For electrodes of the first kind, the transfer of electrons was the potential-determining reaction, but this interpretation did not seem to be applicable for glass electrodes. A few years after the discovery of this phenomenon, a new experiment was made by Donnan [3]. He separated a solution of an alkali halide from a solution of a protein by a membrane, and found that there was an equilibrium, if the protein, which did not diffuse through the membrane, and the halide, which diffused through the membrane, established an electrochemical equilibrium, as a consequence of which an electrical potential could be measured across the membrane. Such an explanation of this experiment was plausible and clear. But it was not clear why this explanation could be applied to the phenomena of the glass electrode and why it was assumed that the glass electrode worked on the principle that ions diffused into and through the glass electrode membrane, why the transport mechanism was introduced for the interpretation of the operation of the glass electrode.

When other ion-selective electrodes were also developed besides glass electrodes, this transport mechanism was applied for them, too. A further question of interpretation

was raised by Guggenheim [4], who deduced the electrochemical potential from the chemical potential by applying the new term of the Galvani potential, which changes proportionally to the electrochemical potential. Hereby the only real measurable term in the equation was the chemical potential. He assumed that on both sides of the membrane (inside and on the solution side) the electrochemical potentials have to be defined, and in the case of equilibrium we can obtain a measurable electrical potential [1].

Since several other biologically relevant ions are also monitored with solvent polymeric membrane electrodes, it can be safely stated that yearly well over a billion ISE measurements are performed world-wide in clinical laboratories alone. Moreover, ISEs are also utilized in many other fields, including physiology, process control, and environmental analysis. They thus form one of the most important groups of chemical sensors. The analytes for which carrier based ISEs and their counterparts with optical detection have been developed. The key components of both types of sensors are lipophilic complexing agents capable of reversibly binding ions. They are usually called ionophores or ion carriers. The latter name reflects the fact that these compounds also catalyze ion transport across hydrophobic membranes. As will be shown here, their implementation in ion-selective electrodes or optodes is now straightforward [5].

The group of Bachas published a broad review on ionophore-based potentiometric and optical sensors, aimed at a more general analytical readership, emphasizing mechanistic principles, recognition elements, and most important applications [6]. Umezawa et al. wrote two comprehensive updates of their reference work on selectivity coefficients of ion-selective electrodes (ISEs) that cover papers from 1988 to 1998 [7,8]. Besides actual numerical selectivity coefficients, the reviews also report on the methodology of determination, response slopes, ionophore structures, and chemical compositions. Macca wrote a critical review on the inconsistencies of published selectivity determinations performed in 2000 and 2001 [9]. He suggested that much of the literature data is still of limited significance to other researchers, despite clearer guidance given in the past few years. An Analytical Chemistry A-page article was written on the principles and possibilities of low detection limit potentiometric sensors [10]. Bobacka et al. reviewed the application of conducting polymers to potentiometric sensors [11]. Such polymers are primarily used as inner reference elements, but have been explored as ion-selective membrane materials as well [12].

### 1.1.2 Ion Selective Electrode Theory

Ion selective electrodes (ISEs) are electrochemical sensors that respond selectively to the activity of ionic species. Because no practical electrode is so sensitive to one particular ion that it responds only to its activity, discarding those of the other probably present ionic species, the term selective is preferred to the term specific.

An Ion-selective electrode is an electrochemical device that uses a thin selective membrane or film as the recognition element, and is an electrochemical half-cell equivalent to other half-cells of the zeroth (inert metal in a redox electrolyte). Such a device often contains a 2nd kind electrode as the “inner” or “internal” reference electrode, this device is different from electrode redox-reaction-involving half-cells.

As may be concluded from what said above, in order to form a complete electrochemical cell, an ISE must be used in conjunction with a reference electrode (i.e., “outer” or “external” reference electrode). In the case of an ion selective electrode, the measured potential differences of the resulting electrochemical cell (ISE versus outer reference electrode potentials) have a linear dependence with the logarithm of the activity of a given ion in the solution. Using a high-input-impedance millivolt-meter, which makes the current passing through the electrode during the potentiometric measurements very small (about  $10^{-12}$  A), the measured potential is essentially the equilibrium potential of the electrode. The essential of a potentiometric measurement is the observation of the potential, arising between two electrodes under zero current conditions, which is a very simple and useful electroanalytical method, and makes the application of the devices very easy and useful.

The key component of any potentiometric ion-selective sensor is undoubtedly its ion-selective membrane, or the recognition element, because it is the element, which leads to the selectivity with which the sensor responds to the analyte in the presence of other ions in the sample. If an ion can pass through the boundary between the two phases, which is herein the sensing element (or ion-selective membrane), an electrochemical equilibrium in which different potentials in the two phases are formed, will be reached.

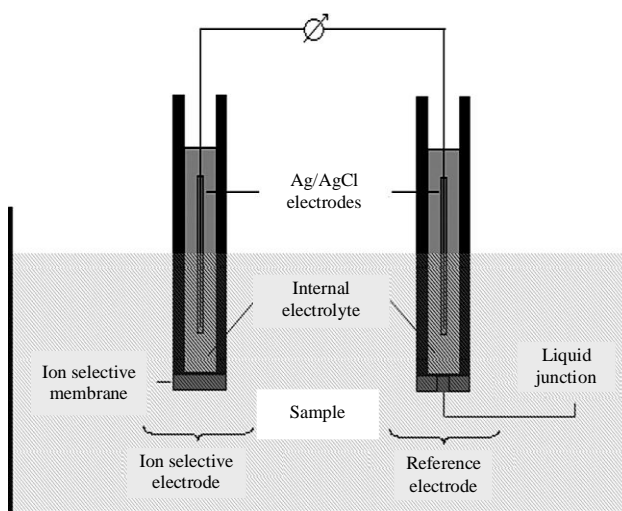
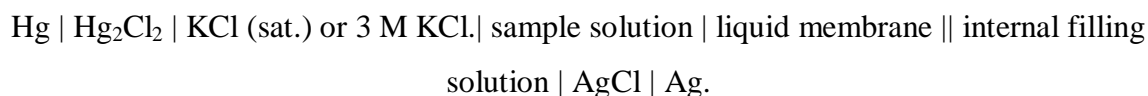
That is why the sensing element is the source of the selectivity of the sensor, because if it can exchange only one type of ion between the two phases, the resulting potential difference formed between the phases, will then be governed only by the activities of this specific ion in these phases (namely the two solution phases, and also the membrane

phase) [13,14]. Fig. 1.1 show the schematic diagram of an ion-selective electrode measuring circuit and cell assembly.

The theory of ISE response is well-established, especially owing to the pioneering work of Eisenman's group and others. Formally, the membrane potential can be described as the sum of the two phase boundary potentials and the diffusion potential within the membrane, the latter being negligible in electrodes of practical relevance. The selectivity dependence on ion exchange and complex formation properties is also well-understood, but only recently a proper description of the ISE response to solutions containing ions of different valences was given [15-20]. The extended semiempirical Nicolskii-Eisenman equation, which had been generally used, is not appropriate in such cases.

### 1.1.3 Response Mechanism of Ion Selective Electrodes

Ion-selective electrode membranes are typically investigated under zero-current conditions in a galvanic cell such as the following (see Fig. 1.1):



**Fig.1.1.** The schematic diagram of an ion-selective electrode measuring circuit and cell assembly [13].

The electromotive force (emf) across this cell is the sum of all individual potential contributions. Many of these are sample-independent, and the measured emf can usually be described as:

$$emf = E_{const} + E_J + E_M \quad (1.1)$$

where  $E_M$  is the membrane potential, and  $E_J$  is the liquid junction potential at the sample/bridge electrolyte interface, which can either be kept reasonably small and constant under well-defined conditions [5]. 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 [21]. On the other hand, galvanic cells without liquid junctions (containing two ion-selective electrodes) respond to ratios or products of ion activities, again prohibiting single ion activity 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.

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 [16]. 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. 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.

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 sake of simplicity, diffusion potentials are treated here as secondary effects in other cases as well and are neglected in the following discussion. We therefore postulate:

$$E_M = E_{const} + E_{PB} \quad (1.2)$$

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 [22]:

$$\bar{\mu}(aq) = \mu(aq) + zF\Phi(aq) = \mu^o(aq) + RT \ln a_I(aq) + zF\Phi(aq) \quad (1.3)$$

and for the contacting organic phase:

$$\bar{\mu}(org) = \mu(org) + zF\Phi(org) = \mu^o(org) + RT \ln a_I(org) + zF\Phi(org) \quad (1.4)$$

where  $\mu$  is the chemical potential ( $\mu^o$  under standard conditions),  $z$  is the valency and  $a_I$  the activity of the uncomplexed ion I,  $\Phi$  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 [22]:

$$E_{PB} = \Delta\Phi = - \frac{\mu^o(org) - \mu^o(aq)}{zF} + \frac{RT}{zF} \ln \frac{a_I(aq)}{a_I(org)} \quad (1.5)$$

The fundamental equation 1.5 will be used throughout this work to describe the behavior of ion-selective electrode membranes. By combining eqs 1.5 and 1.2 one obtains:

$$E_M = E_{const} + E_{PB} = \Delta\Phi = E_{const} - \frac{\mu^o(org) - \mu^o(aq)}{zF} - \frac{RT}{zF} \ln a_I(org) + \frac{RT}{zF} \ln a_I(aq) \quad (1.6)$$

Under the condition that  $a_I(org)$  remains unaltered, it can, together with all other sample-independent potential contributions, be included in one term ( $E^0$ ) and eq 1.6 reduces to the well-known Nernst equation:

$$E_M = E^o + \frac{RT}{zF} \ln a_I(aq) \quad (1.7)$$

According to eq 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. Only within the extremely thin charge separation layer at the interface, where electroneutrality does not hold, are sample-dependent changes in the concentrations of complex and ionophore and ionic sites allowed to occur [23]. Nevertheless, if eq 1.5 is valid, the exact structure of this space charge region is not really relevant to the sensor response.

### **1.1.4 The Composition of Ion Selective Membranes**

Any polymeric membrane ion-selective sensor comprises of some components, the nature and amount of which has great effects on the nature and characteristics of the sensor. These components are:

1. The ionophore
2. The polymeric matrix
3. The membrane solvent
4. Ionic additives

#### **1.1.4.1 The Ionophore**

The ionophore, also called the “ion carrier,” is the most important component of any polymeric membrane sensor with respect to selectivity and selectivity, because the molecular-level phenomenon that is sensed by the ISE is the binding between the ionophore and target ion. The different selectivities of an ISE toward other ions, hence, may be considered to originate from the difference in binding strengths between any chosen ionophore, to be used in the sensor, and various ions.

For ISEs to operate, a phase transfer of aqueous ions into an organic medium of the ISE, which is typically plasticized PVC as will be discussed later, should take place. During this process, the transferred ions interact with the components of the membrane. If the incorporated ionophore is a simple ion-exchanging species like, an lipophilic ionic additive, the process of the transfer of ion(s) from the aqueous phase into the polymeric membrane of the sensor will be controlled by the lipophilicity of the ions being exchanged



[5]. When the selectivity behavior of an ion-exchanger based ISE, in which the ionophore does not have any chemical recognition abilities, is evaluated, the resulting pattern will undoubtedly always reflect the relative lipophilicities of the ions studied. It means that more lipophilicity of an ion, will lead to a greater response of the sensor to the ion [5,24,25].

The incorporation of a selectively binding ionophore into the ion-sensing membrane decreases the total free energy for the transfer of the ionophore-bound ions to organic phase in comparison to that of the simply aqueous-ion [5]. As a result, the more strongly the ionophore binds to an ion, the greater is its effect on the ion's phase transfer equilibrium. The complex formation constant ( $K_f$ ) of an ionophore and one or more of the ions being sufficiently strong, one can expect a difference in the observed/calculated selectivity for the ionophorebased sensor compared to the lipophilicity series shown above. In the same way, in the case of stronger ionophore-ion complexes, a larger difference is expected in the magnitude of the selectivity coefficients versus the lipophilicity series [26,27].

It seems to be clear that any molecule, having the ability to strongly bind to specific ion(s) can not be used as ionophores in sensors. It should also be mentioned that complexation process of the ionophores to be incorporated in the ISE sensing membranes must be kinetically fast. This requirement is necessary so that the thermodynamic equilibrium that governs the response can be established quickly, avoiding deviations of the expected response slope and long response times [28]. To gain this quality, that lowers the overall free energy barrier for the free to complexed states much enough for the complexation to occur quickly, an ionophore is required to be preorganized and flexible to some degree [29,30]. However, although the  $K_f$  between the ion and the ionophore is required to be high enough to produce a noticeable selectivity, this constant must not be so large that ions are tightly bound, making the complexation process kinetically irreversible. The useful range of ionophore complex formation constants in an ISE, although dependent on the stoichiometry of the complex, usually covers several orders of magnitude [31].

Lipophilicity may be considered to be the largest limiting factor to the applicability of an ionophore in a sensing device, because this necessity generally assures that the used compound will be compatible with the polymer membrane. This will substantially decrease the leaching of the ionophore, from the sensing membrane, into the aqueous phase occurs over time, a phenomenon that limits the lifetime and reproducibility of the sensor. An

ionophore is normally given the property of high lipophilicity by simply adding long alkyl chains or other bulky organic groups to its binding framework.

In practice, the selectivity behavior of an ionophore is mostly studied after its incorporation into the sensor. However, some methods are available, and used to study selectivities as a supplement to sensor results, or even to predict the potentials of a compound to for becoming an ionophore. To evaluate the binding constants of an ionophore, membranebased techniques, in which the response of ISEs having a membrane that contains two ionophores is studied, have been used. In other methods ionophore-based membranes have been sandwiched with an ionophore-free membrane and the responses at the different interfaces are compared [26,27,32]. The strengths of the ion–ionophore interactions are also studied in solution via NMR, using the differences in chemical shift patterns between free and complexed ionophore to estimate or explain observed selectivities [33].

#### **1.1.4.2 The Polymeric 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 [13]. The application of polymers as homogeneous membrane matrices was first suggested for use with charged carriers [34]. 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, or PVC [35,36], without the addition of lipophilic ionic sites. However, it is now understood that the Nernstian response of these ISEs had been just because of the probable presence of ionic impurities in the used PVC [37], and also in the other components of the membrane [38]. That is due to the experimental facts, like 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 [38].

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 [36], 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 [5,39]. With polymers of high  $T_g$ s (e.g., high molecular weight PVC:  $T_g \approx 80^\circ$ ), application of plasticizers will be necessary. However, regarding what mentioned above, polymers of low  $T_g$ s (e.g., soft polyurethanes with a low content of crystalline units [40], siliconerubber [35], poly(vinylidene chloride) [41], and polysiloxanes [42] can be used without plasticizers, thus avoiding the handicap of plasticizer leaching. The absence of the plasticizers, however, leads to another handicap of losing the possibility to modify ion selectivities by varying the plasticizer. A number of other polymers have also been investigated [43]. Although, the type of polymer has only a slight effect on the performance of ISEs, detailed investigations show that it is not just an inert matrix because it may influence various membrane properties.

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 [37,44,45].

Polyurethanes were shown to reduce the inflammatory response [40], and are attractive also because of their excellent adhesive properties [46]. Moreover, by covalently bonding hydrophilic poly (ethylene oxide) to the surface of polyurethane membranes, their biocompatibility is improved [47]. Blood compatibility can be also improved by covalently attaching heparin to the membrane surface [48]. For preparing miniaturized electrodes by standard photolithography, as applied in microelectronics technology, photocurable polymer matrices are of interest. Among them, acrylates and methacrylates [49], methacrylated siloxane resins [50], epoxyacrylates [51], polystyrene [52], and acrylates of urethane oligomers [53,54] have been studied in ISE membranes.

#### **1.1.4.3 The Membrane Solvent (Plasticizer)**

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 have optimum physical properties and ensure relatively high mobilities of their constituents. In order to give a homogeneous organic phase, the membrane solvent must be physically compatible with the polymer, 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 [13]. 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*-NPOE or nitrobenzene (NB) to the apolar dibutyl phthalate (DBP) reduced the  $M^{2+}$ -selectivity of the ISE with the ionophore 2,3,8,9-tetraazacyclododeca-1,3,7,9-tetraene [55]. 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) [56]. With more polar solvents, divalent ions are preferred over monovalent ones, the effect being especially pronounced with thin ligand layers. The nature of the plasticizer strongly influences the measuring range (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 or coordination compounds 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 [57] and/or occur in the membrane, a slope characteristic for monovalent ions can be obtained [39,57]. Furthermore, ion association may influence the selectivity factors as well. The formation of ion-pairs in the membrane decreases the concentration of the uncomplexed 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, deteriorates 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 relationship between the hard/soft character of the plasticizing molecules and the resulting selectivity was studied, investigating the effect of more than 15 plasticizers on the selectivity of ISEs constructed from the same ionophore [13]. Comparable results have been observed in the case of the detection limits and degrees of ion-pairing, and the results

showed that parameters are dependent on the nature of the plasticizer employed [202]. However, the selection of the plasticizer is based on its being compatible with the ionophore (solubility reasons) and the also ultimate application of the ISE [5]. In Table 1.1 the names and abbreviations of most common plasticizers that used in the construction of ISEs are summarized.

#### 1.1.4.4 Ionic Additives

The prerequisite for obtaining a theoretical response with ISE membranes is their permselectivity, 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) confined 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 motive 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 [13]. At the same time, the electrical resistance of the membrane is lowered, which is especially important with microelectrodes [58].

**Table 1.1.** The names and abbreviations of most common plasticizers that used in the construction of ISEs [13].

<b>Plasticizer</b>
Benzyl acetate (BA)
Bis-(2-hydroxyl ethyl) phthalate (BEHP)
Bis(1-butylpentyl) adipate (BBPA)
Bis(2-ethylhexyl) adipate (DOA)
Bis(2-ethylhexyl) phthalate {'dioctyl phthalate'} (DOP)
Bis(2-ethylhexyl) sebacate (BEHS)
Bis(n-octyl) sebacate (DOS)
Bibenzyl ether (DBE)
Dibutyl phthalates (DBP)
Dibutyl sebacate (DBS)
Didecyl phthalate (DDP)
Didecyl sebacate (DDS)
(R,R)-2,3-Dimethoxysuccinic acid bis(1-butylpentyl) ester (DMSNE)
Ethylididecyloctadecylammonium nitrate (EDOA)
2-Fluorophenyl 2-nitrophenyl ether (FNDPE)
2-Nitrophenyl phenyl ether (oNPPE)
Ortho nitro phenyl octyl ether (O-NPOE)
Tri-n-butyl phosphate (TBP)

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 [59,60]. 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 in that their amount in the membrane determines that of 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 1.2 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 [61]. The stability could be increased by introducing electron withdrawing substituents [5,62]. 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.

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 [63]. Such a polymer may however show modified selectivity behaviors, because of direct interaction of the sulfonate group with cations [63]. The names of the most important salts used as lipophilic cationic additives are given in Table 1.2.

If the incorporated ionophore is a neutral carrier, the used lipophilic additive is opposite in sign to the ion of interest. According to this rule a sufficient amount of analyte ions can be extracted into the membrane, while all counter ions are being excluded. The presence of ionic sites in the membrane stabilizes charged complexes formed between the ion and the ionophore [64]. Ionic sites also reduce the electrical resistance of the membranes, and allow greater ion mobilities within the organic layer [60].

## 1.1.5 Types of Potentiometric Membrane Sensors for the Monitoring of Ions

An ion-selective electrode (ISE) can selectively recognize an ion in a mixture of ions in a solution. There are various types of ion-selective electrodes, the most commonly used ones are:

1. Glass membrane: a framework of silicate glass with interstitial sites for  $H^+$  and  $Na^+$ .
2. Crystal membrane: a crystal lattice containing defined gaps for the ion to be measured.
3. Polymer membrane: a polymer membrane containing a molecule (an ionophore or ion exchanger) that only binds the ion to be measured [65].

## 1.1.6 Characteristics of Potentiometric Sensors

The properties of an ion-selective electrode are characterized by parameters like:

1. Selectivity
2. Detection limit
3. Measuring range
4. Response time
5. Lifetime
6. Reproducibility

**Table 1.2.** The names of the most important salts used as lipophilic cationic and anionic additives [63].

### **Cationic additives**

Potassium tetrakis [3,5-bis(trifluoro methyl) phenyl] borate (KTFPB)

Potassium tetrakis (4-chloro-phenyl-borate) (KTK)

Potassium tetrakis (p-chlorophenyl) borate (KTPCIPB)

Sodium tetra kis-[3,5-bis(1,1,1,3,3,3-hexafluoro-2-methoxy-2-propyl)-phenyl] borate (NaHFPB)

Sodium Tetra phenyl borate (NaTPB)

### **Anionic additives**

Cobalticboranes

Hexadecyl pyridinium bromide (HDPB)

Hexadecyl trimethyl ammonium bromide (HTAB)

Hexadecyl trioctadecyl ammonium bromide (HDTODAB)

Tetradodecyl ammonium Bromide (TDDAB)

Tetraoctylammonium bromide (TOABr)

Tridodecyl methyl ammonium chloride (TDDMACl)

Trioctyldodecylammonium bromide (TODAB)

Trioctylmethylammonium chloride (TOMACl)

---

### 1.1.6.1 Selectivity

As their names indicate selectivity, which describes an ISE's specificity toward the target ion in the presence of other ions that are also called the "interfering ions," is the most important characteristics of these devices. For polymer membrane sensors, interferences by other sample ions are mainly dictated by their competitive extraction into the membrane phase. Consequently, the response of these ISEs can be fully predicted from thermodynamic constants, ionophore and ionic sites concentrations, and, in the case of ionophorebased membranes, from the complex formation constants of each ion-ionophore complex in the membrane.

Selectivity is most often expressed as the logarithm of ( $K_{xy}$ ). Negative values indicate a preference for the target ion relative to the chosen interfering ion. Positive values of  $\log K_{xy}$  indicate the better preference of an electrode for the interfering ion. The experimental Potentiometric selectivity coefficients depend on the activity and a method of their determination.

The potential of such an "approximately non-permeable" membrane is, mainly governed by the activity of the target (primary) ion and also, to some extent, by the activity of other secondary (hereinafter called the "interfering") ions.  $a_y$  being the activity of an imaginary interfering ion  $y$ ,  $z_y$  being its charge, and  $K_{xy}$  being the empirically determined selectivity coefficient, also called Nicolskii coefficients the effect of interfering species, present in a sample solution, on the desired-to-measure potential difference is taken into account by the so-called Nikolski- Eisenman equation:

$$E = Const + \frac{59.16}{z} \log(a_x) + \frac{z_x}{z_y} \log(k_x \cdot a_y) \quad (1.8)$$

There are a number of different methods for the determination of potentiometric selectivity coefficients ( $K_{XY}$ ), among which three methods have been, however, much more widely accepted [5], which are namely:

1. The Separate Solution Method (SSM)
2. The Mixed Solution Method (MSM)
  - (a) Fixed Interference Method (FIM)
  - (b) Fixed Primary Method (FPI)

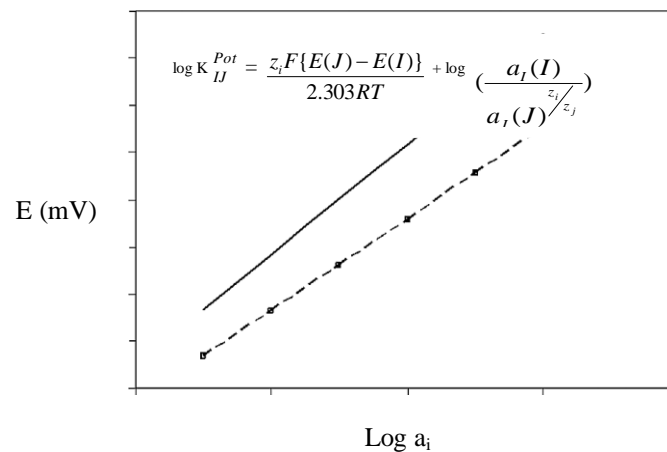


3. The matched potential method (MPM)

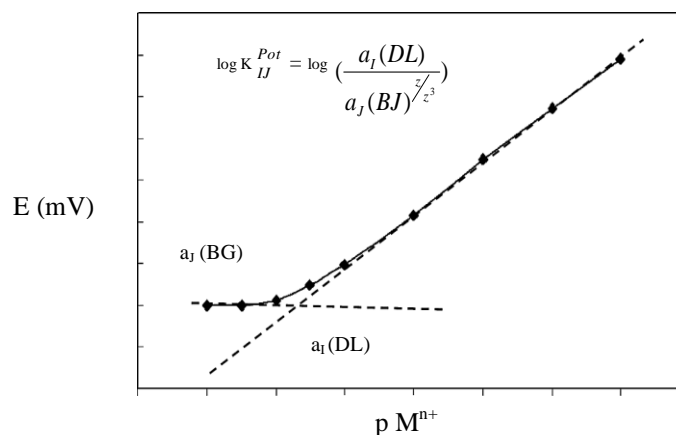
4. The Unbiased Selectivity Coefficients

The IUPAC commission of 1976 recommended the use of two different procedures, namely the so-called separate solution method (SSM) and the fixed interference method (FIM), to determine the Nicolskii coefficients of ISEs. 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 (Fig. 1.2).

In the FIM, an entire calibration curve is measured for the primary ion in a constant interfering ion background ( $a_J$  (BG) in Fig. 1.3). The linear (i.e., Nernstian) response curve of the electrode as a function of the primary ion activity is extrapolated until, at the lower detection limit  $a_I$  (DL), it intersects with the observed potential for the background alone. The Nicolskii coefficient is then calculated from these two extrapolated linear segments of the calibration curve, each relating the analytical response of the ISE to one respective ion only [13].



**Fig. 1.2.** Determination of the Nicolskii coefficients according to the separate solution method (SSM).



**Fig. 1.3.** Determination of the Nicolskii coefficients according to the fixed interference method (FIM).

Other methods have also been used by various researchers [66]. Only previously, the actual mixed ion response has been fitted to the Nicolskii-Eisenman equation [67,68]. As it stands, it seems unfortunate that in many cases the chosen theoretical model is not appropriate to describe the analytically relevant mixed response range. Nonetheless, with the use of more accurate models such a procedure will ultimately be very convincing from a practical standpoint. With other, traditional methods to determine selectivity coefficients, the part of the calibration curve that is not correctly described by the Nicolskii-Eisenman equation [Eq. (1.8)] is not considered for calculating selectivity coefficients. Therefore, any of these latter experimental procedures should ideally give identical selectivity values. However, they are all based on the assumption that the interfering ion completely displaces the primary ion from the interfacial layer of the membrane, no mixed ion response is observed [69,70]. Indeed, it has repeatedly been stated that the reporting of Nicolskii coefficients is only meaningful if Nernstian slopes are observed for every ion involved [71,72]. However, in many practical situations, this is observed for primary ions only and heavily discriminated ions often show non-Nernstian behavior. Umezawa and co-workers have pointed out that it is actually desirable to discriminate other ions to an extent that no response to them is observed and the requirement of Nernstian slopes toward all ions in the Nicolskii equation is in fact a paradox [72,73]. Indeed, a recent study on the issue found that only very few electrodes showed Nernstian slopes toward all ions of interest. The causes of non-Nernstian slopes can vary. If the interfering ion is highly discriminated, the response is partially dictated by the detection limit of the sensor, which is a still-under-investigation characteristic.

It is most likely that low levels of target ions constantly released from the membrane often dictate this detection limit. In such a case, non-zero levels of primary ions are continuously present at the sample-membrane interface and successfully compete with the measured discriminated ion in the exchange process. This only leads to partial ion exchanges at the interface, and therefore to non-Nernstian slopes for the discriminated ion. As a consequence, Nicolskii coefficients calculated from such experiments are too large compared to values that reflect the true ion-exchange selectivity.

An additional effect is sometimes observed in the case of the target ions that can be protonated, complexed, or form ion pairs in solution. In these cases, the activity of the potential determining species (usually the free ion) is often not proportional to the total sample concentration and an apparent non-Nernstian electrode slope can be observed. Examples of such analytes are mercury, uranyl, or salicylate ions. Such effects can,

however, be corrected by calculating the equilibrium concentration of the extracted species, or by employing a pH or ionic strength buffer. In principle, analogous equilibria within the membrane phase can also lead to non-Nernstian behavior. Another disturbing effect is the electrolyte coextraction into the membrane and the subsequent loss of membrane perm selectivity (Donnan failure) [73,74]. Therefore, Nicolskii coefficients should only be calculated from the Nernstian portion of the calibration curves. In contrast, a non-classical response is sometimes even preferred, as this is for example required for successful analytical use of poly ion sensors [75].

Here, the selectivity can be either described for experimental conditions that closely resemble those of intended samples [76,77] determined in an equilibrium mode where the thermodynamic preference of different poly ions can be evaluated [78]. The reporting of Nicolskii coefficients of real-world liquid membrane electrodes that show non-Nernstian slopes is in most cases not meaningful. In fact, this dilemma is one of the important reasons for why the published Nicolskii coefficients for similar membrane compositions vary so much in different reports. Non-Nernstian slopes are often not very reproducible, and the Nicolskii coefficients obtained depend heavily on the experimental conditions, such as sample concentrations, characteristics of previously measured solutions (memory effect), and sample stirring rate, to mention a few.

Two main solutions to this dilemma have been proposed, one being the introduction of a different selectivity formalism that describes the empirical situation as closely as possible [71,79], while the other is to change the experimental conditions in order to observe Nernstian slopes as required by the formalisms discussed above [80]. Choosing each approach depends on the question that is addressed with the experiment.

In the second MSM sub-method, namely the fixed primary method, fixed amount of the target ion (say  $1.0 \times 10^{-4}$  M) is investigated, while the amounts of the interfering ions are varied. The FPM selectivity coefficient can then be calculated by Eq. (1.9):

$$k_A^{Pot} a_M^{2/n} = a_A \left\{ \exp \left[ \frac{(E_2 - E_1)F}{RT} \right] - a_A \right\} \quad (1.9)$$

where  $E_1$  and  $E_2$  are the respective potentials of the solution before and after the addition of the interfering ion.

MPM method was first introduced in the mid 1980s by Gadzekpo and Christian. The aim of the introduction of this method was to offer a selectivity formalism that would give empirically more meaningful results [79,80]. For practical application of this method, a

specified amount of the target ion solution is added to a reference solution and the membrane potential is measured. In another experiment, known amounts of different interfering ion solutions are successively added to an identical reference solution until the membrane potential matches the one obtained before with the primary ion. The MPM selectivity coefficient is then defined by calculation of the ratio of the primary ion and interfering ion activity differences in the two experiments [Eq. (1.10)]:

$$k_{ij}^{MPM} = \frac{\Delta a_i}{\Delta a_j} \quad (1.10)$$

The symbol  $k_{ij}^{MPM}$  is used to represent the MPM selectivity coefficient so that it is clearly distinguishable from the Nicolskii coefficient [81]. A lowercase  $k$  is chosen since this selectivity coefficient is generally not constant for a particular electrode (as opposed to the Nicolskii coefficient) and depends on the exact experimental conditions [82]. The meaning of the selectivity coefficients, determined with this method, is convincing because they clearly reflect what is observed with real-world sensors in relevant samples.

This method can generally be used without regarding the fact whether electrode slopes are Nernstian or even linear. For this reasons, the MPM has gained a great popularity in recent years, and has even been advocated by IUPAC in a recent technical report [71]. Nonetheless, it is important to realize that the such-obtained selectivity values, will widely vary by changing experimental conditions and large discrepancies among different authors have to be expected. Because the MPM does not rely on theoretical assumptions, it has no predicting power for varying analytical situations, and the electrode has to be characterized in solutions that carefully match the target sample. Similarly, a correlation of the selectivity to the extraction behavior of the membrane is not directly possible and it is very difficult to obtain information about optimum membrane compositions or binding characteristics of ion carriers from these data. Neither do these coefficients allow one to judge whether the interference is due to thermodynamic reasons or, actually, kinetic effects, or even if experimental artifacts are masking the signal.

Various experimental conditions have been described that allow the determination of Nicolskii coefficients which are not biased by the difference of sample ion activities at the membrane surface and in the bulk. Hulanicki and coworkers suggested measurement of the response of calcium ion-selective electrodes in ion buffered solutions to obtain the thermodynamic or so-called true selectivity coefficient [79]. The fact that the detection