THE FALL OR RISE OF ION SELECTIVE ELECTRODES

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Abstract. The development of the ion-selective electrodes as analytical technique has been discussed on the basis of number of publications, which appeared in the eighties. The results in the theory of selectivity coefficient and clinical measurements have been emphasized. In conclusion the theoretical and practical relationships between analytical procedures and their biological aspects have been indicated.

Key words: ion-selective electrodes, selectivity coefficient, clinical applications.

The rapid development of theory and practice of ion selective electrodes as a new potentiometric technique occurred during the last 25 years. This was a consequence of several decades of research on fundamental problems of chemistry. The first practical ion selective electrode invented in 1909 by Haber and Klemensiewicz was preceded and followed by extensive investigations in at least two main fields - electrochemistry and biological membrane processes. These two aspects are until now closely interrelated in the field of ion selective electrodes both in theory and in practical applications.

As an analytical tool the ion selective electrodes were born in the sixties. The decade of the seventies was characterized by a rapid and constant growth of the technique. The most important expectations for the new technique were the unique possibility of measuring activity of free (hydrated) ions, specific sensing of ionic species and application in trace analysis.

Those expectations met general tendencies in analytical chemistry significantly emphasized in that period. Speciation analysis demanded direct determination of free ions *versus* complexed or total concentrations. The need of monitoring of various species in a continuous manner met the possibility of using ion selective electrodes as convenient sensors. To the contemporary chemist there is no need to explain the role of trace determinations and therefore the detection limit of the technique became the point of interest. In this respect however no much success was achieved especially comparing with the possibilities of other modern techniques as e.g., atomic spectroscopy.

The next decade - the eighties - was devoted to an extensive proof of the utility of ion selective electrodes to solution of practical analytical aims. This can be considered as the mature period, and it is the matter of our days and our efforts whether this mature period will be continued. Except of the very beginning the total number of publications was, within an experimental error, nearly constant at the level from 400 to 600 per year [1] (Fig.1).

The number of publications devoted to development of solid state and liquid state electrodes based on liquid ion exchangers is constant. It seems that for the solid state electrodes most possibilities have been exploited. For ion exchangers the list of potentially available substances is practically unlimited but they do not offer new concept, except the case when they offer a selectivity sequence different from the Hofmeister series. Examples of such interesting systems now vitamin B₁₂ derivatives, metal porphyrin complexes and organotin compounds. On the contrary the interest for neutral

Fig.1. Histogram showing the number and topics of publication 1980-1989 [1].

carriers increases. Those ionophores are more lipophilic which among other properties extends the electrode life time [2]. In the group of the most studied compounds are macrocyclic compounds (crown ethers, cryptands, podands etc.) with different number and size of rings and various combinations of donor atoms and side substituents. Also open chain molecules are of interest as this is a case of ionophores for calcium and magnesium. These compounds often occupy the place of formerly used ion exchangers. In many commercially available analyzers for blood and serum for all electrolytes except chloride, the neutral carriers are used. Among other sensors the ISFETs still deserve restricted attention, many patents are announced but the interest is to a large extent fundamental and in practical applications there is not much progress.

The number of papers devoted to theory and methodological problems remain on a constant level. In this group many papers are devoted to the application of computer technique, which offer new possibilities in experiment optimization, non-linear regression procedures, selectivity evaluation, curve fitting, response simulation or multicomponent analysis. They are important for practical applications especially in automated and flow systems, but rarely they throw new light on understanding of the electrode properties and mechanisms. In this respect are important papers which are devoted to study of the response time and transient phenomena, to composition and morphology changes of the membranes and to selectivity of electrodes and factors affecting it.

In the mechanistic approach an understanding has been reached that beside thermodynamic parameters also kinetic ones influence the potential and in consequence the selectivity coefficients. The traditional total equilibrium

theory is based on the following assumptions:

- concentrations and electrical potential differences are the only driving forces,
- concentration and potential gradients are perpendicular to the macrosurface of the membrane,
- ion-binding, exchange and transfer processes are fast and reversible,
- bulk and surface concentrations are equal,
- adsorption, redox, contamination and dissolution processes are negligible,
- activity coefficients of all species in the membrane are equal one,
- mobilities and standard chemical potentials in the membrane are invariant,
- the site concentrations is constant,
- the membrane is permeable to one type of ions only,
- discrete charge and polarization effects at the membrane surface are neglected.

In practical measurements many of these assumptions are not fulfilled and this results in the fact that the selectivity coefficients are strongly condition dependant [3]. Some older and newer examples of our research may illustrate this.

The selectivity coefficients of solid state electrodes depend in a limiting case of total equilibrium on the solubility products of the participating solid phases. In the non-equilibrium conditions, when the ion concentrations are low and the convectional transport insufficient they depend to a large extent on the transport parameters of the ions to and from the electrode. In a limiting case the selectivity coefficients depend on the diffusion coefficients. This reflects the situation that the bulk and surface concentrations are different [4]. The general equation which describes this behaviour is

$$E = E^0 + \frac{RT}{F} \ln \frac{K_{xy} \{ [X] + (D_y/D_x) [Y] \}}{(1-s)K_{xy} + s(D_y/D_x)}$$

where K_{xy} stands for the exchange reaction constant, D_y and D_x - for diffusion coefficients of respective ions and s is a time dependent apparent coverage factor.

Another deviation from the ideal model exists when the ionic solutions are mutually contaminated or when the dissolution of the membrane is significant. This gives additional sources of sensed ions not taken into account in the elementary description. In such case the expected, usually very small values of selectivity coefficients cannot be reached and the experimental values are blocked at a much higher level. Such case was investigated for solid state electrodes [5]. The selectivity coefficient, k_{xy}^{pot} , is then given as

$$(k_{xy}^{pot})^{1/X} = (K_{xy})^{1/X} + \frac{C_x^c + C_x^v}{(C_y^a)^{Y/X}} + \frac{sol}{(C_y^a)^{Y/X}}$$

where concentration of ions, C_x and C_y with superscripts a , c , v represent analytical, contamination and other sources of ions, respectively, sol corresponds to total dissolution contribution while the exponents X and Y refer to respective stoichiometric coefficients.

The redox processes may also affect the formal approach to selectivity in several ways. This makes often the evaluation of a selectivity coefficient impossible. Species with strong redox properties towards the membrane components induce reactions not considered in a classical electrode description [7,8]. In the presence of strong redox systems excessive electronic conductivity of the membrane may influence the potential response of the electrode. It is also expected that the adsorption processes cannot be neglected in discussion of the electrode behaviour [9].

For the liquid state electrodes the contamination and dissolution processes play a similar role as in the case of solid state electrodes [6]. It is however more difficult to separate individual processes as there are insufficient equilibrium data for two immiscible phases of complex composition. On the contrary to the solid state electrodes the assumption on the constancy of site concentration may be not valid especially when the lipophilicity of the membrane components is insufficient [10]. In such a case during prolonged use of the electrode the membrane components are leached from the membrane phase influencing the selectivity coefficient in particular at low ionic concentrations. This confirms the suggestion presented initially by Jyo and Ishibashi [11] on the diffusional effects at

the electrode surface.

The graph showing the number of published papers indicates two trends in a group of papers devoted to direct applications. First, there is a distinct decrease in number of papers dealing with environmental problems. It was expected that such applications can be especially promising in particular in respect to water and waste water analysis [12]. Except a few well established procedures, as for example, determination of nitrates or fluorides, for other instances the technique appeared to have insufficient detectability and selectivity.

The second tendency is connected with the application to analysis of biological objects: mineralized hard and soft tissues, body fluids, study of subtle effects in cells and cells organelles. Often the determinations are made for *in vivo*, automatic and flow systems are used for discrete samples or for continuous monitoring. A large part of such studies is devoted to determination of blood serum electrolytes [13]. The usually determined species are: Na, K, Cl, Ca, HCO_3 , Li and recently Mg. In this field there are still several problems which need more research and which are actually investigated in particular because especially high precision and accuracy are required. Among these problems are: activity vs. concentration, total sample volume vs. plasma water volume, liquid junction construction, protein and suspension effects and total concentration vs. ionized ion level.

The measurement of ionized and total ion concentration is of vital importance for calcium and certainly also for magnesium. These two cations are in nearly 50% bound in complexes with proteins and simple ligands. The measurement of ionized ion level is for calcium a common procedure in spite of the fact that there are still discussions about the reference activity standards. An important step has been made by the proposal that the readout of ionized calcium vs. pH should be normalized by special correction function [14].

The determination of total calcium may be carried out either by spectroscopic techniques or potentiometrically. In the latter case the calcium complexes in the serum sample should be dissociated. This may be achieved by dilution or acidification. Another possibility is to transform all natural complexes into one, strictly defined, more stable complex [15].

A more complicated situation exist for magnesium. In contrary to calcium where the electrode of excellent selectivity is available the magnesium electrodes in spite of intensive studies show poor selectivity towards calcium [16]. This is the worse because the amount of calcium in the human blood serum is larger than that of magnesium. The best ionophores are the ETH 5220 and ETH 7025 but the selectivity coefficient for calcium is still 0.625 [17]. In such case the measurement is possible only when numerical computer corrections are introduced which eliminate the interference of accompanying ions. A detailed knowledge of kinetics of signal formation for both ions is also necessary. The finally achieved precision is not worse than 3%.

The referred examples illustrate in greater detail the parallel development of theory and practical applications. Due to progress in theory a number of applications of ion selective electrodes gained an established and well accepted position in selected fields of analytical chemistry. In those instances they are competitive to other methods, became routine procedures and in some cases cannot be replaced by other. This stabilizes their importance in analytical chemistry.

In fundamental studies they also are invaluable tool. The number of publications is not large but they pay a tribute to measurements of complexation and precipitation equilibria, activity coefficients, kinetic investigations. The models firmly based on empirical practice created by analytical chemists, as it is in potentiometry, enable their implementation for data base computer controlled experiments. Ionized magnesium determination is a case where its fundamental medical role stimulates the development of analytical procedure and its wide routine application. This is another most recent example of strong coupling biomedicine and analytical chemistry.

The development of ion selective electrodes has also influenced other areas

of analytical chemistry. Their contribution to the progress in sensors is evident. Many systems studied initially for potentiometric electrodes were later explored by other techniques, e.g., in optodes, in amperometric detectors. Ion selective electrodes made possible progress in sensitized systems as enzymatic electrodes or gas sensors. The recently developing conducting polymers electrodes also profit from the ion selective technology. The questions solved in this fruitful area generate new problems ensuring further progress. Therefore it can be stated that beside of its present firm position in the array of numerous analytical techniques the theory still stimulates new concepts being on the other hand continuously activated by discoveries in other, often quite distant areas of science.

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