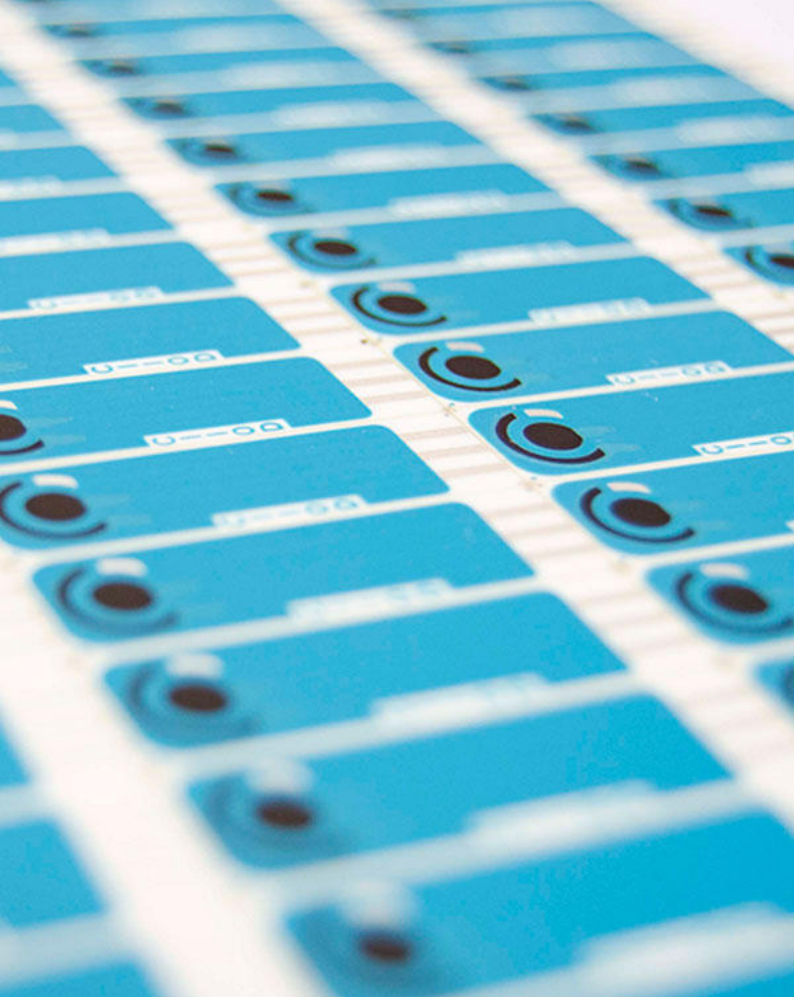




Application Note AN-EC-034

Ion-selective electrodes based on screen-printed technology

Nozioni di base e suggerimenti per l'utilizzo di sensori potenziometrici a contatto solido ionoselettivi basati su elettrodi serigrafici

La potenziometria ha avuto un lungo sviluppo storico, dagli studi di Galvani e Volta della fine del XVIII secolo alla prima titolazione potenziometrica sviluppata nel 1893 da Robert Behrend. Tuttavia fu solo negli anni '60 che nacque la cosiddetta potenziometria moderna. In appena un decennio, furono sviluppati i primi elettrodi a membrana basati su scambiatori di ioni liquidi o polimeri solventi basati rispettivamente sui lavori di Ross [1] e Bloch [2]. Al giorno d'oggi, la

potenziometria è una tecnica analitica standard per la rilevazione di ioni rilevanti comunemente impiegata nei laboratori clinici.

L'uso di membrane polimeriche a solvente favorisce lo sviluppo di sensori in grado di rilevare un'ampia varietà di ioni rispetto alle membrane di vetro. Approfittando di ciò, la tecnologia serigrafata offre miniaturizzazione e portabilità, due caratteristiche essenziali nell'analisi «point-of-care».

PRINCIPIO DI MISURAZIONE

La potenziometria è un metodo elettrochimico che misura il potenziale elettrico, o tensione, di una cella elettrochimica composta da due elettrodi: un elettrodo di lavoro e uno di riferimento. Il potenziale dell'elettrodo di riferimento rimane costante mentre il potenziale dell'elettrodo di lavoro varia in proporzione alla concentrazione dell'analita nel campione. Il potenziale relativo tra i due elettrodi viene misurato in condizioni di corrente zero, quindi la tecnica elettroanalitica impiegata con questi sensori è nota come potenziometria a circuito aperto (OCP).

Gli elettrodi ionoselettivi (ISE) classici sviluppati all'inizio del XX secolo erano costituiti da una membrana (come fase di rilevamento) in contatto con una soluzione interna per formare un'interfaccia di contatto con il liquido. Fu solo nel 1971 che il primo ISE senza soluzione interna fu proposto da Hirata e Dato [3], seguiti l'anno successivo da Catrall and Freiser [4]. Questi nuovi sensori si basano su uno strato di contatto solido tra la membrana e il substrato conduttore (Figura 1), che Cadogan et al. [5] nel 1992 denominato «strato trasduttore da ione a elettrone».

Il meccanismo di risposta completo è stato descritto altrove in modo approfondito [6], ma il segnale analitico è lo stesso in entrambi i tipi di ISE (cioè contatto liquido o solido): la somma dei potenziali interfacciali di fase. In termini pratici, a seconda del

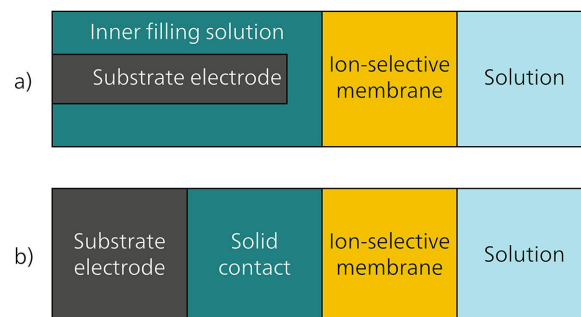


Figure 1. Grafica illustrata di un ISE con a) un'interfaccia a contatto con il liquido e b) un'interfaccia a contatto con il solido. Entrambe le versioni mostrano la configurazione più comune utilizzata durante lo sviluppo di elettrodi ionoselettivi.

tipo di ione misurato, il segnale analitico segue l'equazione di Nernst, che se semplificata a 25 °C e applicando un logaritmo comune risulta nella seguente equazione:

$$E_{meas} = K + \frac{0.05916}{z_A} \log(a_A)$$

Equation 1.

dove K è una costante, z_A è la carica dello ione A dell'analita e può essere positiva (catione) o negativa (anione) e a_A è l'attività dello ione nella soluzione. Questo potenziale misurato (E_{meas}) è il segnale

La **Figura 2** mostra un tipico segnale OCP in cui E_{meas} è il plateau raggiunto dopo diversi secondi quando l'ISE raggiunge l'equilibrio. Questo potenziale rimane costante e il suo valore è linearmente proporzionale al logaritmo comune della concentrazione dello ione analita nell'**Equazione 1** (i.e., $\log [a_A]$).

Sebbene l'equazione di Nernst non abbia limiti e sia ben correlata con la parte lineare del grafico di calibrazione (**Figura 2b**), i sensori reali hanno due limiti pratici. Gli elettrodi raggiungono il limite inferiore a una bassa concentrazione di analita e smettono di rispondere poiché non si osservano potenziali cambiamenti. Il limite superiore può essere raggiunto quando gli elettrodi diventano insensibili alle attività ioniche elevate, determinando un plateau.

Per calcolare entrambi i limiti, IUPAC raccomanda che il limite inferiore (definito come limite di rilevamento) e il limite superiore siano i punti di intersezione rispettivamente del segmento lineare medio estrapolato e della risposta di attività inferiore o superiore limitante [7]. Considerando che il segno della pendenza può cambiare a seconda del tipo di ione misurato, la **Figura 3** mostra entrambi i tipi di curve di calibrazione sperimentale tipicamente osservate con elettrodi cationici o anionici selettivi e i loro limiti corrispondenti.

analitico che può essere osservato durante la misurazione con ISE in OCP in cui il potenziale viene monitorato nel tempo.

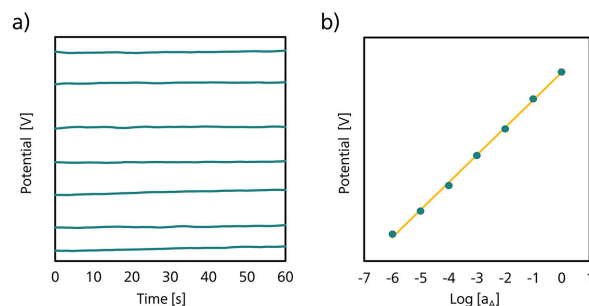


Figure 2. a) Dati sperimentali osservati in OCP eb) un grafico di calibrazione ottenuto rappresentando il potenziale misurato rispetto al logaritmo dell'attività ionica dell'analita.

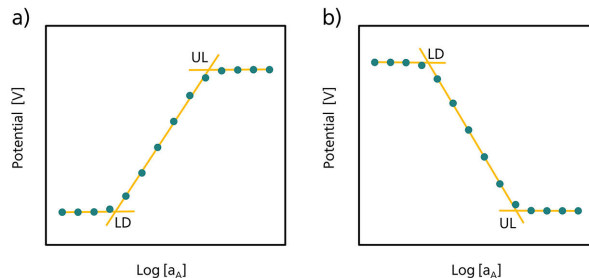


Figure 3. Interi grafici di calibrazione ottenuti con a) cationi e b) anioni insieme al rispettivo limite inferiore (indicato come limite di rilevamento, LD) e limite superiore (UL) contrassegnati su ciascun grafico.

PRINCIPLE OF SELECTIVITY

The analytical performance of ion-selective electrodes is determined by their membrane properties. As their name suggests, the main advantage of these electrodes is that they have a high degree of selectivity. Therefore, the membrane composition ideally must only respond to one specific ion—either cation or anion.

Although the glass pH electrode was invented in 1906 by Cremer [8], it took another 60 years before Frant and Ross [9] invented the most successful solid-contact ISE—the fluoride ISE—made of a single crystal of LaF₃. In the same year, Stefanac and Simon [10] developed the potassium ISE using valinomycin as a neutral ionophore incorporated in a plasticized membrane. Both approaches rapidly became the

standard of solid-contact ISE development, expanding the possibilities to other new successful developments based on these setups.

In general, the prepared plasticized membrane must have reversible ion/electron transfer and be highly stable in aqueous media to avoid leaching the components of the membrane [11]. In solid-contact ISEs, the membrane is commonly a PVC-based polymer, usually prepared by evaporating a cocktail of several components mixed in well-known proportions. A typical recipe is comprised of the polymer matrix (with or without a plasticizer), an ionophore, and a lipophilic ionic additive to lower electrical resistance.

Table 1. Components commonly found in classical recipes of potentiometric solid-contact electrodes. Acronyms: BPA: bis(1-butylpentyl) adipate, CHA: cyclohexanone, DBS: dibutyl sebacate, DOS: dioctyl sebacate, KTCBP: potassium tetrakis(4-chlorophenyl)borate, NaTPB: sodium tetraphenylborate, NaTFPB: sodium tetrakis(4-fluorophenyl)borate dihydrate, O-NPOE: 2-nitrophenyl octyl ether, PVC: polyvinyl chloride, THF: tetrahydrofuran

Component	Examples
Solvent	CHA, THF
Polymer matrix	PVC
Plasticizer	BPA, DOS, O-NPOE
Lipophilic ionic additive	KTCBP, NaTPB, NaTFPB
Ionophore	See refs. [12–14]

Apart from the physical and chemical properties related to structural considerations of the polymer matrix itself, the most important component of the «cocktail» (Table 1) is the ionophore that lends selectivity to the finished electrode. The nature of the ionophore depends on the type of cation or anion that is to be quantified. Initially, ion-exchangers were usually employed to develop these sensors, but they

suffer from a lack of ion-recognition function as their selectivity follows the Hofmeister series. A classical successful example of this is the calcium ion electrode developed by Ross in 1967 [1]. Based on an ion-exchange process, the cation-exchanger is an aliphatic diester of phosphoric acid where the phosphate group has a strong affinity for calcium ions.

The term «ionophore» was born later in the 1960s and defines chemical compounds that reversibly bind and transport ions. Ionophores can be natural or synthetic, and usually contain a hydrophilic center that interacts with the ions and a hydrophobic portion that interacts with the membrane. An example of a successful natural ionophore is valinomycin, a neutral carrier molecule that selectively binds potassium ions due to its cavity with very similar dimensions to K^+ . Many synthetic ionophores are developed to mimic

behavior similar to valinomycin. After years of development, a plethora of different structures have been produced varying from macrocyclic species (e.g., crown ethers, cryptands and calixarenes) to chelating agents based on organometallic molecules, or even simple organic compounds that also exhibit ionophoric properties (e.g., phenols). Selectivity and stability are the main considerations when selecting one ionophore over another.

EVALUATING SELECTIVITY

Despite being known for their good selectivity, ion-selective electrodes are not ideal – there can be interferences introduced by the sensor responding to the presence of other ions. The Nernst equation (Equation 1) assumed that E_{meas} is only related to the electrode's response to one specific ion. If we consider the existence of other ions that can also be

present in the same sample, it is necessary to use a new equation.

Considering the interfering ion as B , its corresponding activity as a_B , and its charge as z_B , we can incorporate a selectivity coefficient ($K_{A,B}$), extending the Nernst equation to the empirical Nicolsky-Eisenman equation (Equation 2):

$$E_{meas} = K + \frac{0.05916}{z_A} \log \{a_A + K_{A,B}^{pot} (a_B)^{z_A/z_B}\}$$

where $K_{A,B}^{pot} = \frac{a_A}{(a_B)^{z_A/z_B}}$

Equation 2.

The selectivity coefficient of a particular ISE can be defined as a numerical value that reflects how well the sensing membrane can discriminate against a certain interfering ion in comparison to the analyte ion. It is denoted as $K_{A,B}^{pot}$, where A is the analyte ion and B is the interferent ion. If a sensor exhibits a similar response to both ions, then $K_{A,B}^{pot} = 1$, meaning no selectivity is achieved. If the selectivity

constant is <1 , then the membrane is more selective to the analyte ion. However, if this value is >1 , the ISE is more selective to the interfering ion. The smaller the $K_{A,B}^{pot}$ value is, the less impact the interfering ion has on the measured potential, E_{meas} . For example, if $K_{A,B}^{pot} = 10^{-3}$, then the ISE is 1000 times more responsive to ion A (analyte) than ion B (interferent).

Experimental data when an interfering ion is present is shown in **Figure 4**, with three different situations provided depending on the strength of the interferent. The stronger the interferent is considered against the membrane, then the higher the detection limit (LD) is, so the analytical range that can be measured shortens.

There are several protocols to calculate selectivity coefficients according to IUPAC recommendations that also work with sensors where no Nernstian but linear response is obtained [15]. Discussion about the selectivity and limit of detection is covered in depth elsewhere [16] and their values must be considered carefully when analyzing real samples as interfering ions are usually present, so linear range can be compromised depending on the sample matrix.

MINIATURIZATION AND PORTABILITY

All-solid-state ISEs are internal solution-free and employ a conducting polymer or nanostructures (e.g., nanowires, nanoparticles, or nanotubes) as a solid contact beneath the ion-selective or reference membrane. This enables the miniaturization of ISEs, facilitating portability and making the development of handheld setups possible (**Figure 5**). Working with portable potentiostats allows on-site measurements, while working with ion-selective screen-printed electrodes makes ion quantification possible in complicated scenarios or in circumstances where conventional probes cannot be adequately cleaned so they must be discharged.

Sensors developed with screen-printing technology offer new possibilities for in-situ measurements where only a very small sample volume is required, as samples can be expensive or scarce. Several examples of such requirements can be found in the environmental, biotechnology, quality control, or industrial fields, and especially in biomedical research. Moreover, these sensors do not require maintenance or complex pretreatments such as those needed when using non-portable optical devices.

Screen-printed ion-selective sensors do not require cleaning and can be discarded when the assay is complete, facilitating their use for myriad purposes. They are especially practical for analyzing hazardous samples.

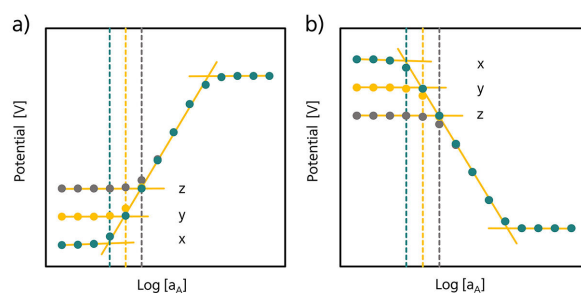


Figure 4. Experimental data for a) cations and b) anions where interferences are absent (x), weak (y), or strong (z).



Figure 5. Example of a novel handheld setup where a miniaturized ion-selective screen-printed electrode is utilized with a portable potentiostat to make on-site measurements.

GENERAL TIPS FOR WORKING WITH ION-SELECTIVE SCREEN-PRINTED ELECTRODES

To work with ion-selective SPEs from Metrohm DropSens, below are several tips that users can follow to achieve good results. Some advice may seem obvious, but it is still important to consider for good laboratory practices. Typical ions detected by these sensors are employed as examples in each section.

Use solutions with a known amount of analyte to obtain the calibration plot. This can be achieved by weighing the correct amount of analyte and dissolving it in a known volume of ultrapure water or by purchasing the correct standard for the desired sensor. In the case of, e.g., Na^+ and K^+ ion-selective SPEs, use standard solutions of NaCl or KCl, respectively. Good calibration data can be easily obtained by using standards prepared based on these reagents. Other sensors in the Metrohm DropSens catalog also use chloride as the counter ion in the salt to study their analytical performance.

Prepare standard solutions with a concentration of the analyte inside the linear range of the sensors. For each application developed, consider the linear range of the sensor employed. This information is given in the brochure included with each sensor made by Metrohm DropSens. In the case of K^+ ion-selective SPEs, the linear range spans from 10^{-6} to 1 mol/L, and the linear range spans from 10^{-4} to 1 mol/L for Na^+ sensors. Linearity with potentiometric sensors can

only be achieved by representing the potential obtained as an analytical response versus the logarithm of the analyte concentration assayed. A typical representation plots the potential against the exponent of the concentration tested, as previously shown.

It is recommended to measure each solution in triplicate to obtain enough data to evaluate the precision of the electrodes. This is a general recommendation when employing any purchased sensor, not only for ion-selective SPEs. Metrohm DropSens electrodes assure a precision of 10% with Na^+ and K^+ ion-selective SPEs.

As a general matter, accuracy and precision always depend on the solutions tested. If the target solution presents matrix effects, the accuracy and precision of the electrodes could change due to the nature of the solution itself. Sensor response must always be tested with the target solution because sometimes a correction factor or a sample pretreatment must be done. This is a common behavior not only for potentiometric but also for voltamperometric sensing devices.

The calibration curve belongs to each batch of electrodes, so it is not necessary to recalibrate the electrode. However, if the target solution evolves or changes, it is recommended to test the sensor again

CONCLUSION

In contrast to larger traditional liquid-contact probes, the development of solid-contact potentiometric sensors based on screen-printing technology makes miniaturization possible, which is a crucial advantage in many industrial or research fields. Due to their low energy consumption, low cost, and user-friendly operability, ion-selective screen-printed electrodes are not only capable of detecting both positively and negatively charged ions but are also very suitable for practical applications in point-of-care testing.

Considering the importance that potentiometric sensors have nowadays (reflected by common examples of potassium, calcium, or fluoride ISEs), it is interesting to understand how these kinds of electrodes work, how their analytical performances rate, and what can they offer to users. In this way, a broader understanding of these sensors is presented with several practical tips that make these electrodes more accessible to analysts, helping them to develop their own applications.

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