Potentiometric Sensors with Ion-Exchange Donnan Exclusion Membranes

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Abstract

Potentiometric sensors that exhibit a non-Hofmeister selectivity sequence are normally designed by selective chemical recognition elements in the membrane. In other situations, when used as detectors in separation science, for example, membranes that respond equally to most ions are preferred. With so-called liquid membranes, a low selectivity is difficult to accomplish since these membranes are intrinsically responsive to lipophilic species. Instead, the high solubility of sample lipids in an ionophore-free sensing matrix results in a deterioration of the response. We explore here potentiometric sensors on the basis of ion-exchange membranes commonly used in fuel cell applications and electrodialysis, which have so far not found their way into the field of ion-selective electrodes. These membranes act as Donnan exclusion membranes as the ions are not stripped of their hydration shell as they interact with the membrane. Because of this, lipophilic ions are no longer preferred over hydrophilic ones, making them promising candidates for the detection of abundant ions in the presence of lipophilic ones or as detectors in [...]
Potentiometric Sensors with Ion-Exchange Donnan Exclusion Membranes

Ewa Grygolowicz-Pawlak, Gastón A. Crespo, Majid Ghahraman Afshar, Günter Mistlberger, and Eric Bakker*

Department of Inorganic and Analytical Chemistry, University of Geneva, Quai E.-Ansermet 30, CH-1211 Geneva, Switzerland

Supporting Information

ABSTRACT: Potentiometric sensors that exhibit a non-Hofmeister selectivity sequence are normally designed by selective chemical recognition elements in the membrane. In other situations, when used as detectors in separation science, for example, membranes that respond equally to most ions are preferred. With so-called liquid membranes, a low selectivity is difficult to accomplish since these membranes are intrinsically responsive to lipophilic species. Instead, the high solubility of sample lipids in an ionophore-free sensing matrix results in a deterioration of the response. We explore here potentiometric sensors on the basis of ion-exchange membranes commonly used in fuel cell applications and electrodialysis, which have so far not found their way into the field of ion-selective electrodes. These membranes act as Donnan exclusion membranes as the ions are not stripped of their hydration shell as they interact with the membrane. Because of this, lipophilic ions are no longer preferred over hydrophilic ones, making them promising candidates for the detection of abundant ions in the presence of lipophilic ones or as detectors in separation science. Two types of cation-exchanger membranes and one anion-exchange membrane were characterized, and potentiometric measuring ranges were found to be Nernstian over a wide range down to about 10 μM concentrations. Depending on the specific membrane, lipophilic ions gave equal response to hydrophilic ones or were even somewhat discriminated. The medium and long-term stability and reproducibility of the electrode signals were found to be promising when evaluated in synthetic and whole blood samples.

Researchers have been aiming to improve ion-selective electrode selectivity for numerous decades. The simplest liquid or polymeric membranes are composed of lipophilic ion-exchanging salts dissolved in a water-immiscible organic solvent. Their selectivity is based on the energy of transfer of ions from the aqueous sample to the membrane phase and therefore on ion lipophilicity. This order of preference is well established as the Hofmeister selectivity sequence. When used as detectors in separation science, potentiometric sensors should ideally respond to all eluted ions equally. This is difficult to accomplish with the principle outlined above since more lipophilic ions will typically give a larger signal, with the exception of dilute interferences (Hulanicki effect) and short readout time (kinetic discrimination). When these effects apply, the potentiometric sensors respond equally to all ions in the sample.1 On the other hand, the detection of abundant ions in physiological samples may also be hampered by the presence of dilute but lipophilic species, for example, thiocyanate or salicylate for the detection of chloride in blood.2 Moreover, the hydrophobic nature of the membrane has been found to result in a substantial extraction of lipids from the sample, drastically altering the membrane matrix and resulting in unacceptable sensor drifts.3 These undesired effects can be mitigated to some extent by the use of ionophores (ion carriers) in the membrane phase. Many such ionophores have been introduced in the past few decades, and their aim is to achieve a selectivity pattern that deviates from the Hofmeister selectivity sequence.4 While this has been an important success story in the field, numerous applications exist where a better tolerance to lipid compounds, organic solvents, and higher temperature are desired.

This has recently initiated the search for alternate membrane materials that are not lipid-like, chiefly by the use of fluorous membrane materials as put forward by the group of Buhlmann.5,6 Such membrane materials reject hydrophilic and hydrophobic species and represent an important new direction in ion sensor development.

More recently, Gyurcsanyi reported on a new class of potentiometric sensors based on chemically functionalized nanopore membranes.7 These pores are understood as high charge density nanochannels where the passage of charge is dictated by Donnan exclusion effects. Such materials are very promising because they are solvent free and can potentially make use of water-soluble biochemical receptors as well.

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Similarly structured nanochannels are thought to also be present in ion exchange Donnan exclusion membranes (IEDEM), whose exact structure and mechanism is still being debated (for more details, see refs 8–10). Nonetheless, a vast amount of applications in fuel cells, electrochemistry, and electrodialysis has been reported employing this class of membranes.11–17

Nafion is perhaps the most prominent example of IEDEM that is composed by a tetrafluoroethylene-based polymer substituted with sulfonate groups.18–21 Recent work by Schmidt-Rohr’s group suggests that the charge transport occurs along nanopores of high charge density, thereby forming hydrated channels with diameters on the order of 2.5 nm.22,23 The high sulfonate density gives the polymer its ion-exchanging properties by Donnan exclusion while the structure of the backbone gives excellent mechanical, chemical, and thermal stability while not serving as a solvent. Because of the lack of a traditional solvent extraction process, this polymer does not exhibit a selectivity pattern based on the lipophilicity of ions as with the ion-exchanger-based solvent polymeric membranes discussed above.

Early work reporting on the potentiometric response characteristics of unmodified or “bare” Nafion membranes exhibited a very limited measuring range,24 and this result has perhaps discouraged progress in this area. Despite the documented benefits of such materials, only a limited number of reports on using IEDEM as potentiometric sensor materials have appeared in the literature.25,26 In contrast, we find here that commercially available ion-exchange membranes are well suited for this purpose, with a wide response range and an attractive selectivity for selected applications.

**EXPERIMENTAL SECTION**

**Reagents, Materials, and Equipment.** Aqueous solutions were prepared by dissolving the appropriate salts in deionized water (>18 MΩ cm). FKL (cation-exchanging) and FAB (anion-exchanging) membranes, both of thicknesses of 100 μm, were purchased from Fumatech (FuMA-Tech GmbH, Am Grubenstollen 11, 66386 St. Ingbert, Germany) while Nafion membrane NR-211 of a thickness of 25 μm was obtained from Ion Power (Inc. 720 Governor Lea Rd, New Castle, DE 19720). Membranes of 7 mm diameter were punched from the parent membrane and mounted in OSTEC bodies (Oesch Sensoren Technologie AG, Ragazerstrasse 35, 320 Sargans, Switzerland). A solution of 10 mM NaCl was used as the inner electrolyte. FAB membranes were stored in 4 g L−1 NaCl + 0.1 g L−1 NaN3 solution before electrode preparation, while cation-selective membranes were used as obtained. Potentiometric measurements were taken against a double-junction Ag/AgCl sat. KC1/1 M LiOAc reference electrode (Metrohm AG, Ionenstrasse, CH-9100 Herisau, Switzerland), using a 16-channel EMF interface (Lawson Laboratories, Inc., Malvern, PA). All experiments were carried out at laboratory ambient temperature of 22 °C.

**Procedures.** Selectivity measurements were performed by adding appropriate aliquots of salts and evaluated using the modified separate solutions method.27 The obtained separate calibration curves were extrapolated to 1 M, and the selectivity coefficient was calculated from this potential difference by dividing by the theoretical slope of 59.2 mV.28 The activities of the ions were calculated with a two-parameter Debye–Hückel approximation.29

Sodium and chloride ions analysis in undiluted whole blood was performed at 22 °C. Before analysis, the sample was heated up in a water bath to ambient temperature. For the standard addition procedure, electrodes were left in continuous contact with undiluted heparinized human blood (5 U/mL heparin, University Hospital of Geneva, HUG) for 1 h to evaluate possible potential drifts in this sample matrix. NaCl additions increased its concentration in blood by 0.029, 0.057, 0.09, 0.152, and 0.231 M, while for KSCN the concentration was being changed by concentration steps of 1 order of magnitude in the 10−6−10−2 M range. External calibration before and after contact with blood (5 min contact time) was performed with 0.03, 0.1, and 0.3 M NaCl solutions. The entire procedure was repeated twice for each electrode.

**RESULTS AND DISCUSSION**

Unlike classical organic solvent-based membranes used for decades in potentiometry, ion-exchange membranes used for electrodialysis applications exhibit highly reduced selectivity toward different ions. Polar groups (sulfonic or quaternary ammonium) present in high concentration within the polymer structure form aggregates allowing a water content of up to 50 vol % in the membrane phase. Ion-exchange may only take place at the water–polymer interface without ion extraction into the polymer phase. As a result, the selectivity is expected to be less dependent on ion lipophilicity (see below Table 1) and more on Coulombic interactions. Moreover, possible diffusion potential contributions may arise in the case of mixed ion solutions.30

**Table 1. Potentiometric Selectivity Characteristics of Ion-Exchange Membranes**

<table>
<thead>
<tr>
<th>Membrane</th>
<th>Ion (J)</th>
<th>Slope (mV)</th>
<th>$E^\text{°}$ (mV)</th>
<th>$\log(K_i)$ (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAB</td>
<td>Cl−</td>
<td>−57.8 ± 0.3</td>
<td>13.5 ± 0.7</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>ClO4−</td>
<td>−60.5 ± 0.6</td>
<td>−78.9 ± 3.4</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>SCN−</td>
<td>−58.4 ± 0.9</td>
<td>−75.4 ± 4.2</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>NO3−</td>
<td>−57.7 ± 1.0</td>
<td>−19.4 ± 3.1</td>
<td>0.5 ± 0.1</td>
</tr>
<tr>
<td>Nafion</td>
<td>Na+</td>
<td>59.5 ± 0.3</td>
<td>242.2 ± 2.7</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Li+</td>
<td>61.5 ± 0.1</td>
<td>243.5 ± 0.3</td>
<td>0.02 ± 0.01</td>
</tr>
<tr>
<td></td>
<td>K+</td>
<td>56.7 ± 0.2</td>
<td>245.8 ± 1.2</td>
<td>0.06 ± 0.02</td>
</tr>
<tr>
<td></td>
<td>Ca2+</td>
<td>57.8 ± 0.6</td>
<td>250.7 ± 2.5</td>
<td>0.15 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>Mg2+</td>
<td>60.3 ± 0.9</td>
<td>256.8 ± 2.5</td>
<td>0.5 ± 0.1</td>
</tr>
<tr>
<td>FKL</td>
<td>Na+</td>
<td>51.5 ± 0.4</td>
<td>255.1 ± 2.5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Li+</td>
<td>51.9 ± 0.8</td>
<td>230.2 ± 3.6</td>
<td>−0.4 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>K+</td>
<td>64.8 ± 0.6</td>
<td>289.3 ± 0.7</td>
<td>0.6 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>Ca2+</td>
<td>59.4 ± 2.5</td>
<td>287.1 ± 6.1</td>
<td>1.1 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>Mg2+</td>
<td>58.4 ± 3.4</td>
<td>284.1 ± 5.1</td>
<td>1.0 ± 0.3</td>
</tr>
</tbody>
</table>

Nafion, FKL, and FAB electrodialysis membranes were studied here in potentiometry. Three electrodes of each type were prepared, and their working characteristics were evaluated with Na+, K+, Li+, Ca2+, and Mg2+ for cation-exchange membranes and Cl−, ClO4−, SCN−, NO3−, and OAc− for anion-exchange ones. Figure 1 shows the corresponding calibration curves upon adding aliquots of NaCl to the sample solution with pure water as background. The key characteristics are summarized in Table 1. The estimated error in Table 1 is a result of three calibrations performed during the same day ($n = 3$). Calibrations were also repeated three times on consecutive days but only for the primary anion (giving a RSD ≤ 0.5%) All membranes responded rapidly ($t_{50} ≤ 5$ s) to concentration changes in the contacting solution, giving a stable signal. Short-
term stabilities (3 min) were extracted from Figure 1. The drift (EMF/time) after each addition gives us information about the stability at short times, giving 0.1 mV min$^{-1}$ for cation exchange membranes and 0.02 mV min$^{-1}$ for anion exchange membranes on average. Long-term stability was evaluated over 15 h in the presence of 0.1 mM CaCl$_2$ and 100 mM NaCl using a concentrated NaCl solution as inner solution (see Figure 1S, Supporting Information). For FAB (0.05 mV h$^{-1}$) and FKL (0.4 mV h$^{-1}$), the obtained values are promising for practical applications. Nafton membranes showed a considerably higher drift (2 mV h$^{-1}$). All electrodes responded with a theoretical slope within a 10 μM to 300 mM NaCl concentration range.

In contrast to established liquid membrane cation-selective electrodes, cation-exchange membranes responded to divalent cations with a monovalent slope; see Figure 2S in the Supporting Information. For Nafton membranes, this behavior was observed until the divalent ion concentration in the solution approached that of NaCl in the inner electrolyte, after which point only the expected divalent ion slope was observed. On the other hand, when the membranes were conditioned in divalent cations such as Ca$^{2+}$ for one day, a Nernstian response slope of 29.8 mV was found for both divalent and monovalent ions (Na$^+$) (see Figure 3S in the Supporting Information). This peculiar effect cannot be readily explained, but it is clearly related to kinetic, rather than thermodynamic, characteristics of the membrane.

The strength of the Coulombic interaction should increase with increasing ion charge, but the data presented in Table 1 suggest that any such interaction translates in a rather weak potentiometric preference.

With anion exchange membranes, ion-exchange theory predicts that ions with smaller hydrodynamic (stokes) radii should interact more weakly with the ion-exchanger. Indeed, perchlorate and thiocyanate, by virtue of their weaker hydration, are preferred over better hydrated ions such as chloride (see Table 1). As with the cation-selective membranes, and also in some analogy to liquid membrane ion-selective electrodes, the calibration curves were found to be most linear if the membrane was conditioned with the ion to be measured (in this case both Na$^+$ and Cl$^-$). While hydrodynamic radii do impose a selectivity pattern on the membrane response, the magnitude of this effect is dramatically smaller than with established anion-selective electrodes. With polymeric liquid membranes, for example, perchlorate is typically preferred by about 4.5 orders of magnitude over chloride, giving rise to a ca. −270 mV potential change at the same concentration (compared to the −89 mV shown in Table 1).

This type of behavior is very much desired if the electrode is applied as a detector together with a separation technique. One additional potential advantage of nonselective membranes is, however, when the analyte of interest is in excess to a dilute but much more lipophilic interfering ion. This situation is for example observed with sodium and chloride ions in the presence of potassium, thiocyanate, or salicylate in blood samples. The sodium concentration in blood plasma is about 140 mM, while potassium levels are about 30 times lower. For chloride and thiocyanate ions, the difference is even larger, with 95−110 mM chloride compared to at least a thousand times less thiocyanate. Modern ionophore-based potentiometric sensors for sodium exhibit the required selectivity for analysis of sodium in blood. For the detection of chloride, on the other hand, thiocyanate and salicylate may be a serious interference owing to its greater lipophilicity.

Electrodes with each of the three studied ion-exchanging membranes were explored in the analysis of sodium and chloride in blood samples. Figure 2 presents results of NaCl additions to blood for electrodes with FKL and FAB.
membranes. Electrode potentials changed by at most 2.7 and −2.8 mV for FKL and FAB membranes, respectively, during continuous contact with undiluted heparinized human blood for half an hour. All of them also responded quickly ($t_{50} \lesssim 5$ s) to a 0.03 M NaCl addition, which corresponds to a ca. 20% concentration increase for sodium and about 30% for chloride. The standard addition calibration gave a linear response for both ions, suggesting an absence of interferences from other ions present in the sample. In the case of NaF membranes, trans-membrane fluxes resulted in significant potential drifts and made the analysis unreliable (see Figure 4S in the Supporting Information). To confirm the lack of interferences from potassium and thiocyanate, standard additions of KSCN were performed in blood. A significant electrode response was only found at a concentration of $10^{-2}$ M KSCN, which is significantly outside the physiologically possible concentration range and therefore of no concern in practice. Moreover, therapeutic concentrations of salicylate (720 μM) were confirmed not to interfere with the chloride response at 0.1 M NaCl, see Figure 5S in the Supporting Information, giving a mere 75 μV potential response.

While a careful clinical evaluation is outside the scope of this work, preliminary data on blood assays using repeated external calibrations are presented here to encourage further work in this direction. Figure 3 demonstrates external calibrations for the FAB and FKL membranes in electrolyte solutions followed by exposure to blood for 30 min. The data suggest attractive analytical stability, especially for the anion-exchanging membrane where reproducibilities of the electrode potential in the external calibration readings were just 1.3 mV while the deviations in potential readings during contact with blood were below 0.8 mV.

**CONCLUSIONS**

Ion-exchange membranes such as FKL or FAB are a promising class of alternate materials in the design of potentiometric sensors. Their fast and stable response makes them attractive candidates for situations where their added ruggedness (compared to liquid or plasticized polymeric membranes) and their selectivity characteristics are of polaronic concern. In contrast to liquid ion-exchanger-based ion-selective membranes, FKL and FAB membranes show no preference to lipophilic ions, although the selectivity is a function of the hydrodynamic radius of the ion. They may be of particular interest to the analysis of abundant hydrophilic ions where lipids and lipophilic ions ordinarily give rise to serious interference. It was shown here that these membranes allow one to detect sodium and chloride ions in undiluted whole blood sample, even in the presence of an excess of potassium and thiocyanate/salicylate ions over physiologically possible levels. An application not yet explored here and for which the membranes are expected to be attractive as well as their use as detectors in separation science.

**REFERENCES**

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