Original Papers

Application of the Mixed-Potential Theory to the Interpretation of the Potential Response of a PVC Membrane Ion-Selective Electrode for Desipramine

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The potential response of an ion-exchanger type PVC ion-selective electrode (ISE) for a drug ion, desipramine$^+$ (DES$^+$), was analyzed by a mixed-potential (MP) theory proposed previously. The transfer of DES$^+$ and its analogous ions, imipramine$^+$ (IMP$^+$) and neostigmine$^+$ (NEO$^+$), at a micro *o*-nitrophenyl octyl ether/water interface was studied by ion-transfer voltammetry; also, the standard ion-transfer potentials ($\Delta_O^W\phi_j^o$) of the ions were then determined. The application of MP theory with the $\Delta_O^W\phi_j^o$ values successfully explained the under-Nernstian response of DES$^+$-ISE due to interference from IMP$^+$ or NEO$^+$. In this study, a universal method based on numerical calculations was developed for evaluating MP associated with plural interfering ions, which was impossible in the previous method based on analytical equations. Using the universal method, we could well predict the detection limit of DES$^+$-ISE theoretically. The MP theory is promising for the sophisticated design of ISEs, which is not due to conventional "trial-and-error" procedures.

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Introduction

Even now, after a variety of analytical methods have been developed for sensing ions, polymer membrane ion-selective electrodes[1,2] (ISEs) hold an important position in practical ion analysis, particularly in clinical analysis[3] (*e.g.*, the determination of $Na^+/K^+/Cl^-$ in blood serum). So far, a large number of polymer membrane ISEs have been developed for many ions;[1–3] however, the design of ISEs is usually by screening or trial-and-error, *i.e.*, by changing the membrane components and their concentrations in a systematic manner. In a preceding paper,[4] we showed that the mixed-potential (MP) theory proposed by Kakiuchi and Senda[5] and Kihara and Yoshida[6] is useful for understanding the potential response not only of unsupported liquid membrane ISEs, but also of polyvinyl chloride (PVC) supported liquid membrane ISEs. The MP theory[5,6] is based on the concept of a zero-current potential of the interface between the unsupported or supported liquid membrane and a sample solution containing interfering ions. Although this concept had previously been described by Cammann[7] and Koryta,[8] the above authors[5,6] presented a rigorous analytical equation for the electromotive force (EMF) of a liquid membrane ISE. Kakiuchi and Senda[5] also showed that the selectivity coefficients of the ISEs could be expressed as a function of the difference between the standard ion-transfer potentials of the primary and interfering ions, the ratios of the mass-transfer coefficients of the ions, and the ratios of their concentrations. In our preceding paper,[4] the potential response of an ion exchanger-type PVC membrane ISE for tetraethylammonium (TEA$^+$) ion was successfully explained by MP theory.

In this study, we have extended our study to another ion exchanger-type PVC membrane ISE for the analysis of a drug, desipramine (DES; for the chemical structure, see Fig. 1). DES is a tricyclic antidepressant, which is also used to treat neuropathic pain, attention deficit hyperactivity disorder, panic disorder, *etc*.[9] Since DES has a pK_a of 10.2,[10] it exists in a neutral or acidic solution in the protonated form (DES$^+$).

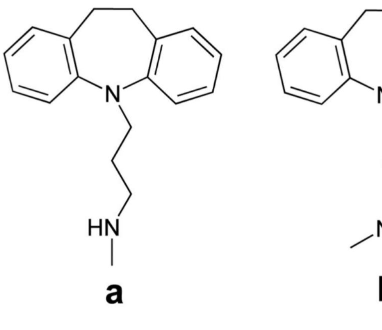

Fig. 1 Chemical structures of the drugs studied: (a) DES, (b) IMP, and (c) NEO$^+$.

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Recently, a PVC membrane DES$^+$-ISE was developed by Gupta *et al.*,[11] who designed it in a conventional screening procedure. In this paper, we have employed a micro PVC membrane/water (W) interface[4] to study the interfacial transfer of protonated forms of DES and its analogues, including imipramine (IMP) and neostigmine (NEO) (also see Fig. 1). The MP theory with the thus-obtained voltammetric data has been successfully used to explain the potential responses of the PVC membrane DES$^+$-ISE in the presence of interfering ions (IMP$^+$ and NEO$^+$). In this paper, we present a "universal" method for obtaining MP values by numerical calculations, which is also available when more than one interfering ion is present in the system.

Experimental

Chemicals

Desipramine tetraphenylborate (DESTPB) was prepared by methathesis of the hydrochloride salt (DES·HCl; >99%; Wako Pure Chemical Industries) with NaTPB (Dojindo Laboratories) in water, followed by washing five times with water and twice recrystallizing from ethanol. Imipramine hydrochloride (IMP·HCl; ≥99%; Wako) and neostigmine bromide (NEOBr; ≥98%; Sigma-Aldrich) were purchased and used as received. Tetrapentylammonium tetraphenylborate (TPnATPB) was prepared in a similar manner as reported previously,[12] and purified finally by twice recrystallizing from acetone. Other electrolytes, including LiCl, tetraethylammonium chloride (TEACl), and tetrapentylammonium chloride (TPnACl), were of the highest grade commercially available, and used as received.

PVC (degree of polymerization = 1100, Wako) was purified as described previously.[4] *o*-Nitrophenyl octyl ether (NPOE; ≥99%) was purchased from Dojindo Laboratories and used as received.

PVC membranes

The PVC membranes (*ca.* 0.2 mm thick) used for voltammetry as well as potentiometry were prepared by dissolving 100 mg of PVC, 250 mg of NPOE, and a given amount of electrolyte in *ca.* 5 mL tetrahydrofuran (THF; stabilizer free), followed by evaporating THF under a hood. For further details, see a previous paper.[4]

Voltammetry

As reported previously,[4] a micro PVC membrane/W interface was formed by pressing the end of a glass pipette (*ca.* 100 μm i.d.) on a PVC membrane, which contained a supporting electrolyte (TPnATPB) at a concentration[13] of 0.05 M. The glass pipette, with an Ag/AgCl electrode inside, was filled in advance with a W-phase solution containing a supporting electrolyte (0.1 M LiCl), a transferring ion, and a 0.040 M NaH_2PO_4–Na_2HPO_4 buffer (pH 5.5).

The two-electrode electrolytic cell used is expressed as

$$\begin{array}{c|c|c||c|c}
\begin{array}{c}\text{Ag/}\\ \text{AgCl}\end{array} &
\begin{array}{c}0.02\text{ M TPnACl}\\ 0.1\text{ M MgSO}_4\\ (\text{W})\end{array} &
\begin{array}{c}0.05\text{ M TPnATPB}\\ \\ (\text{PVC membrane})\end{array} &
\begin{array}{c}1.0\text{ mM X}\\ 0.1\text{ M LiCl, pH 5.5}\\ (\text{W})\end{array} &
\begin{array}{c}\text{AgCl/}\\ \text{Ag}\end{array}
\end{array}, \quad (\text{A})$$

where X stands for the transferring ion, which was added as DES·HCl, IMP·HCl, NEOBr, or TEACl. A Hokuto Denko HA1010mM1A potentiostat[14] was used to control the Galvani potential difference of the test PVC membrane (O)/W interface (indicated by ||), which is denoted by $\Delta_{\rm O}^{\rm W}\phi$ ($\equiv \phi^{\rm W} - \phi^{\rm O}$ with $\phi^{\rm W}$ and $\phi^{\rm O}$ being the inner potential of the W and O phases, respectively). Before a measurement to obtain each voltammogram, the solution resistance (*ca.* 5 MΩ) was determined using a conductivity meter (MY-9, Yanaco), and then compensated for by means of a positive feedback circuit attached to a potentiostat. A Faraday cage was employed for noise reduction; however, a remaining, relatively large current noise was reduced by using a low-pass filter mounted in a HA1010mM1A potentiostat.[14]

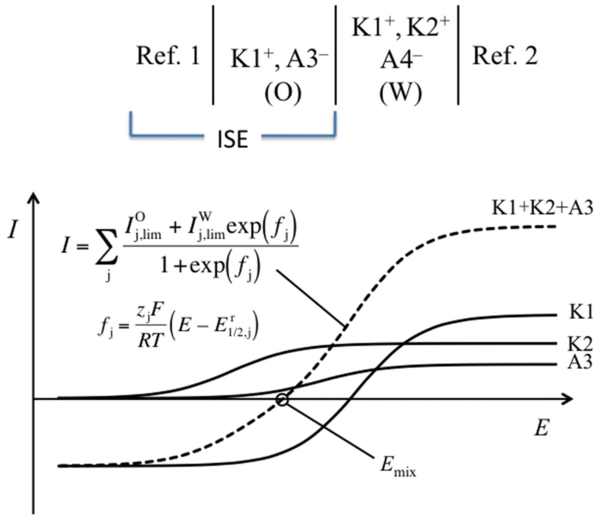

Fig. 2 Interpretation of the MP for a K1$^+$-ISE in the presence of two interfering ions: K2$^+$ in W and A3$^-$ in O. Ref. 1 and Ref. 2 represent appropriate reference electrodes.

Potentiometry

A DES$^+$-ISE was prepared by using a commercial kit for PVC membrane ISEs (7904L, DKK-TOA). A PVC membrane prepared for DES$^+$ was cut to 5-mm ϕ, and glued to the opening of a PVC tip with THF. The PVC membrane was then conditioned in 1.0 mM DES·HCl for 24 h. The electrochemical cell for the potentiometry with the DES$^+$-ISE is shown as

$$\underbrace{\begin{array}{c|c}
\begin{array}{c}\text{Ag/}\\ \text{AgCl}\end{array} &
\begin{array}{c}0.1\text{ M}\\ \text{MgCl}_2\\ (\text{W})\end{array}
\end{array}}_{\text{Reference electrode}}
\ \vdots\
\underbrace{\begin{array}{c}a\text{ M DES·HCl}\\ b\text{ mM Y, pH 5.5}\\ (\text{W})\end{array}}_{\text{Sample solution}}
\Bigg|
\underbrace{\begin{array}{c|c|c}
\begin{array}{c}20\text{ mM DESTPB}\\ \\ (\text{PVC membrane})\end{array} &
\begin{array}{c}1.0\text{ mM}\\ \text{DES·HCl}\\ (\text{W})\end{array} &
\begin{array}{c}\text{AgCl/}\\ \text{Ag}\end{array}
\end{array}}_{\text{DES}^+\text{-ISE}}, \quad (\text{B})$$

where $a = 10^{-6.3}$ - $10^{-2.5}$, $b = 0.1$, 1, 10, and Y = IMP·HCl or NEOBr. The sample solution contained 0.0408 M Na$^+$, added as a 0.040 M NaH_2PO_4–Na_2HPO_4 buffer (pH 5.5). The effect of interfering ions (*i.e.*, IMP$^+$ and NEO$^+$) was evaluated by the fixed interference method (FIM).[15,16] The EMF of the cell was determined by means of an Advantest TR8652 electrometer. Potentiometric as well as voltammetric measurements were performed at room temperature (25 ± 2°C).

Theoretical

In the previous MP theory,[5,6] an analytical equation was presented for the EMF of a liquid membrane ISE in the presence of an interfering ion in the sample solution. However, it was assumed therein that: (1) the primary and interfering ions have the same ionic charge, (2) there is only a single kind of interfering ion, and (3) the interfering ion exists in the sample solution, *i.e.*, not in the membrane. In this paper, we propose a universal method for obtaining MP values under various conditions by means of numerical calculations.

Figure 2 (upper part) shows an electrochemical cell comprising a liquid membrane K1$^+$-ISE in the presence of two interfering ions: K2$^+$ in W and A3$^-$ in O. The MP (denoted by $E_{\rm mix}$) for this case cannot be obtained by the previous analytical equation, but can be obtained from the following numerical calculation. In Fig. 2 (lower part), the reversible current-potential ($I_{\rm j}$-E) curves for the transfer of the respective ions (j = K1$^+$, K2$^+$, and A3$^-$) are shown, which are given by

$$I_{\rm j} = \frac{I^{\rm O}_{\rm j,lim} + I^{\rm W}_{\rm j,lim}\exp(f_{\rm j})}{1+\exp(f_{\rm j})}, \tag{1}$$

with

$$f_{\rm j} = \frac{z_{\rm j}F}{RT}(E - E^{\rm r}_{1/2,\rm j}), \tag{2}$$

where $I^{\rm O}_{\rm j,lim}$ and $I^{\rm W}_{\rm j,lim}$ are the limiting currents for the transfer of the j-ion from the O and W phases, respectively, to the other; $z_{\rm j}$ is the ionic charge of the j-ion including the sign, $E^{\rm r}_{1/2,\rm j}$ is the reversible half-wave potential for the interfacial transfer of the j-ion, and F, R, and T have their usual meanings. The values of $I^{\rm O}_{\rm j,lim}$ and $I^{\rm W}_{\rm j,lim}$ can be obtained by

$$\frac{I^{\rm O}_{\rm j,lim}}{z_{\rm j}FA} = -\frac{D^{\rm O}_{\rm j}}{\delta^{\rm W}_{\rm j}}c^{\rm O}_{\rm j} = -k^{\rm O}_{\rm j}c^{\rm O}_{\rm j}, \tag{3}$$

$$\frac{I^{\rm W}_{\rm j,lim}}{z_{\rm j}FA} = \frac{D^{\rm W}_{\rm j}}{\delta^{\rm W}_{\rm j}}c^{\rm W}_{\rm j} = k^{\rm W}_{\rm j}c^{\rm W}_{\rm j}, \tag{4}$$

where A is the interfacial area; $D^{\alpha}_{\rm j}$, $\delta^{\alpha}_{\rm j}$, $k^{\alpha}_{\rm j}$, and $c^{\alpha}_{\rm j}$ (α = O or W) are the diffusion coefficient, the diffusion layer thickness, the mass-transfer coefficient, and the bulk concentration, respectively, for the j-ion in phase α. In the case of a semi-infinite linear diffusion, $\delta^{\alpha}_{\rm j}$ has the form of $(\pi D^{\alpha}_{\rm j}t)^{1/2}$, with t being time. Using the above equations, one can calculate the $I_{\rm j}$-E curve for transfer of the respective ion for a given concentration, provided that the values of $E^{\rm r}_{1/2,\rm j}$ and $D^{\alpha}_{\rm j}$ (α = O and/or W) are known. For obtaining the $E_{\rm mix}$ value for the system, it is not necessary to obtain the "absolute" value of the current. Namely, the current may be obtained only in an arbitrary scale, *i.e.*, not as a function of either t or A. Finally, the $E_{\rm mix}$ value is obtained from the zero-current potential for the "total" current-potential curve (*i.e.*, the $\sum_{\rm j} I_{\rm j}$-E curve). This calculation can be numerically performed using a spreadsheet application, such as Microsoft Excel®.

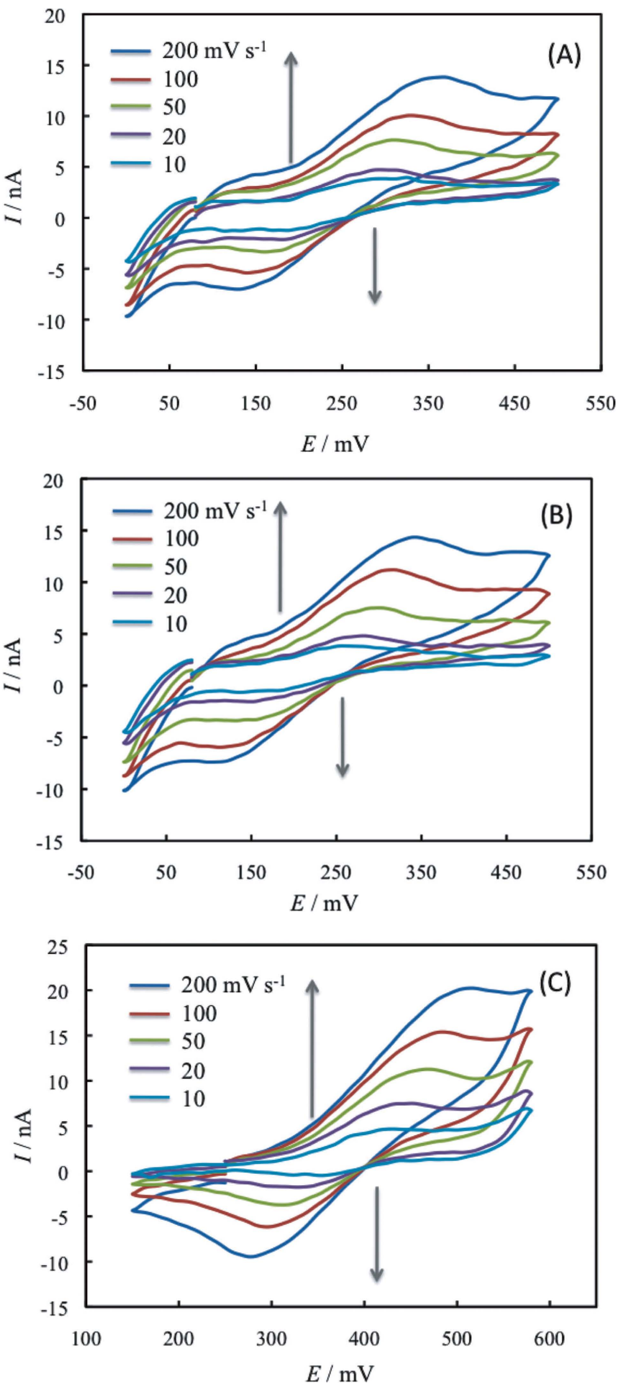

Fig. 3 CVs for the transfer of 1.0 mM (A) DES$^+$, (B) IMP$^+$, and (C) NEO$^+$ at the micro PVC membrane/W interface, which were recorded at five different scan rates.

Results and Discussion

Voltammetry

Figure 3A shows cyclic voltammograms (CVs) for the transfer of DES$^+$ at the micro PVC membrane/W interface, which were recorded at five different scan rates (10, 20, 50, 100, and 200 mV s^{-1}). In a similar manner as reported for the transfer of TEA$^+$,[4] a relatively simple CV was obtained. The anodic (positive-current) peak corresponds to the transfer of DES$^+$ from W to the PVC membrane, while the cathodic (negative-current) peak corresponds to its transfer back to W. Because the transferring ion is added into a glass pipette, a semi-infinite "planar" diffusion of the ion appears to occur on the forward voltage scan. Therefore, we did not observe any significant effects characteristic of conventional microelectrodes, though the cathodic peak became somewhat smaller at lower scan rates, possibly due to a hemispherical diffusion of DES$^+$ in the PVC membrane. It should be noted here that the cathodic wave as well as the anodic one exhibits a so-called "diffusion tail", suggesting no significant adsorption of DES$^+$ on the PVC membrane/W interface, *i.e.*, the existence of a certain diffusion process in the PVC membrane. Thus, it has been found that the transfer of DES$^+$ at the PVC membrane/W interface is analogous to that at the liquid/liquid interface. As is shown in Fig. 3A, however, the peak separation is considerably increased with the scan rate, most probably due to uncompensated solution

Table 1 Reversible half-wave potentials and standard ion-transfer potentials for the transfer of drug ions and some relevant ions at the PVC membrane/W interface and their diffusion coefficients in W

Ion	$E^{\rm r}_{1/2,\rm j}$ [a]/mV	$\Delta^{\rm W}_{\rm O}\phi^{\rm o}_{\rm j}$ [b]/mV	$D^{\rm W}_{\rm j}$[c]/10^{-6} cm^2 s^{-1}
DES$^+$	224	–126	3.4
IMP$^+$	207	–143	2.9[e]
NEO$^+$	379	29	5.6
TEA$^+$	376	26[d]	8.68[f]
TPB$^-$		316[d]	5.59[f]
Na$^+$		376[d]	13.34[f]

a. Approximated from the midpoint potential of a CV.
b. Determined from $E^{\rm r}_{1/2,\rm j}$ using Eq. (5).
c. Measured by NPV.
d. Determined at the NPOE/W interface and reported in Ref. 17 or 19 (for Na$^+$).
e. Possibly underestimated to some extent; see Fig. S2 (Supporting Information).
f. From Ref. 22.

resistance. Nevertheless, the midpoint potential between the anodic and cathodic peaks is practically independent of the scan rate. We thus assume that the midpoint potential can be approximated by the reversible half-wave potential ($E^{\rm r}_{1/2,\rm j}$) of the ion-transfer reaction,

$$E^{\rm r}_{1/2,\rm j} = \Delta^{\rm W}_{\rm O}\phi^{\rm o}_{\rm j} + \frac{RT}{z_{\rm j}F}\ln\frac{\gamma^{\rm O}_{\rm j}}{\gamma^{\rm W}_{\rm j}} + \frac{RT}{z_{\rm j}F}\ln\sqrt{\frac{D^{\rm W}_{\rm j}}{D^{\rm O}_{\rm j}}} + \Delta E_{\rm ref}, \qquad (5)$$

where $\Delta^{\rm W}_{\rm O}\phi^{\rm o}_{\rm j}$ is the standard ion-transfer potential of the j-ion at the O/W interface, $\gamma^{\alpha}_{\rm j}$ its activity coefficient in phase α (here, we assume $\gamma^{\rm O}_{\rm j}/\gamma^{\rm W}_{\rm j} = 1$), and $\Delta E_{\rm ref}$ a constant determined by the reference electrode system employed. Using the reported value[17] of $\Delta^{\rm W}_{\rm O}\phi^{\rm o}_{\rm j}$ (= 26 mV) for TEA$^+$ at the NPOE/W interface and the previously estimated value[4] of $D^{\rm W}_{\rm j}/D^{\rm O}_{\rm j} = 150$, we obtain $\Delta E_{\rm ref} = 286$ mV from the value of $E^{\rm r}_{1/2,\rm j}$ (= 376 mV) for TEA$^+$ as the reference ion (data not shown). Using this $\Delta E_{\rm ref}$ value, we determined the $\Delta^{\rm W}_{\rm O}\phi^{\rm o}_{\rm j}$ of DES$^+$ to be –126 mV from its $E^{\rm r}_{1/2,\rm j}$ (= 224 mV).

Similar CVs have also been obtained for the transfer of IMP$^+$ and NEO$^+$ at the PVC membrane/W interface (see Figs. 3B and 3C). The values of $E^{\rm r}_{1/2,\rm j}$ and $\Delta^{\rm W}_{\rm O}\phi^{\rm o}_{\rm j}$ obtained for these ions and DES$^+$ are given in Table 1. As described previously,[4] the $\Delta^{\rm W}_{\rm O}\phi^{\rm o}_{\rm j}$ values can be considered as those for the corresponding liquid/liquid (NPOE/W) interface. It should be noted that the PVC matrix has a small effect on the thermodynamics of ion transfer at the PVC membrane/W interface, as described by Langmaier *et al.*[18] In Table 1, the literature values[17,19] of $\Delta^{\rm W}_{\rm O}\phi^{\rm o}_{\rm j}$ for some relevant ions (TEA$^+$, TPB$^-$, and Na$^+$) at the NPOE/W interface are also shown.

For the application of MP theory, it is necessary to know the values of $D^{\rm W}_{\rm j}$ for the primary and interfering ions. However, it is difficult to obtain the $D^{\rm W}_{\rm j}$ values of the drug ions accurately from the anodic peak currents of the CVs in Fig. 3. This is because the CVs are rather distorted by the ohmic effect, and also because the area of the micro O/W interface cannot be measured with high accuracy. We thus performed normal pulse voltammetry (NPV) for the transfer of drug ions at a 1,2-dichloroethane (DCE)/W interface (with $A = 0.49$ cm^2). The four-electrode electrolytic cell used is as shown previously,[20] and the electrochemical cell system is the same as the previous one,[21] shown in Scheme S1 (Supporting Information). The current-potential curves observed for DES$^+$, IMP$^+$, and NEO$^+$ are presented in Figs. S1, S2, and S3 (Supporting Information), respectively. From the limiting current ($I_{\rm lim,j}$), the $D^{\rm W}_{\rm j}$ values for the drug ions were determined using the Cottrell equation: $I_{\rm lim,j} = z_{\rm j}FAc^{\rm W}_{\rm j}\{D^{\rm W}_{\rm j}/(\pi t)\}^{1/2}$. The $D^{\rm W}_{\rm j}$ values determined for the drug ions are given in Table 1, together with those reported for TEA$^+$, TPB$^-$, and Na$^+$.[22]

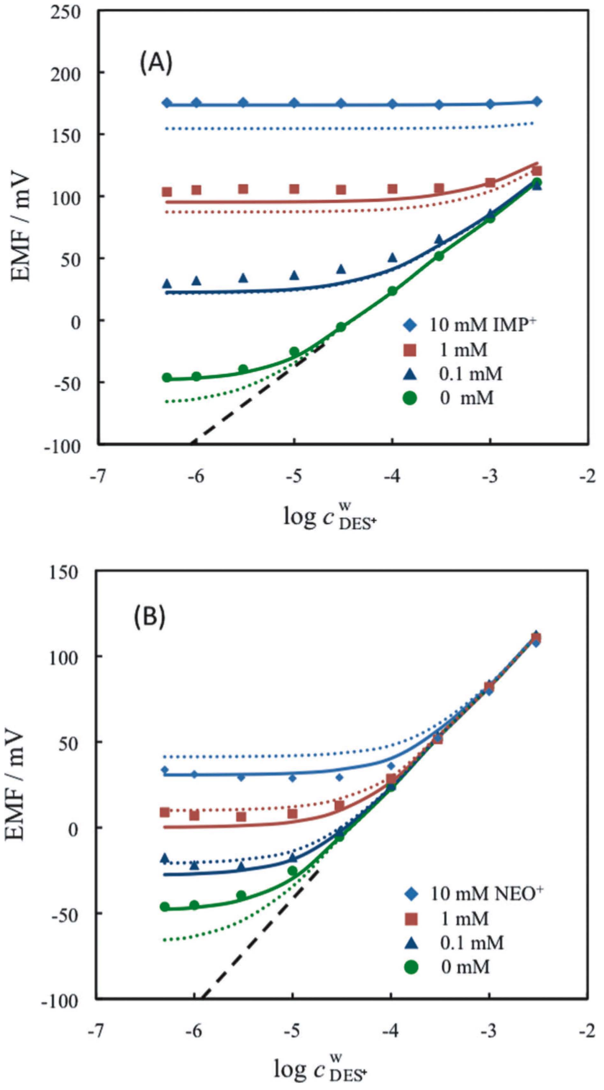

Fig. 4 Potential responses of the PVC membrane DES$^+$-ISE in both the absence and presence of 0.1, 1, and 10 mM (A) IMP$^+$ and (B) NEO$^+$ as the interfering ion. The dotted lines show theoretical curves, which were predicted by MP theory with the standard ion-transfer potentials of the drug ions determined by ion-transfer voltammetry. The solid lines show regression curves based on MP theory. The dashed line in each panel shows the Nernstian response.

Potentiometry

Figure 4 shows the potential responses of the PVC membrane DES$^+$-ISE in both the absence and presence of (A) IMP$^+$ and (B) NEO$^+$ as the interfering ion. In the absence of either interfering ion, a Nernstian response of the primary ion (DES$^+$) is obtained in the higher concentration range of $>10^{-4.5}$ M. In the lower concentration range, an under-Nernstian response, *i.e.*, a deviation from the Nernstian response (shown by the dashed line in each panel) is observed. It has been suggested by the theoretical analysis shown below that the under-Nernstian response is due to interference from TPB$^-$ (and possibly also impurity anions) in the PVC membrane. Besides, in the presence of 0.1, 1, and 10 mM IMP$^+$ or NEO$^+$, a typical interference is observed, depending on the interfering-ion concentration. Such potential responses of the PVC membrane ISE can be elucidated based on MP theory. The dotted lines in Fig. 4A or 4B represent the theoretical curves,[23] which have been obtained based on the numerical calculation of MP values described above. In this theoretical calculation, not only IMP$^+$ or NEO$^+$ in the sample solution, but also TPB$^-$ in the PVC membrane has been included as possible interfering ions against the primary ion, DES$^+$; the values of $\Delta_{\rm O}^{\rm W}\phi_{\rm j}^{\rm o}$ (j = DES$^+$, IMP$^+$, NEO$^+$, and TPB$^-$) used herein are those determined by ion-transfer voltammetry, or obtained from the literature[17] (for TPB$^-$). These $\Delta_{\rm O}^{\rm W}\phi_{\rm j}^{\rm o}$ values are also given in Table 1, together with the values of $D_{\rm j}^{\rm W}$ determined by NPV, or obtained from the literature.[22] The $D_{\rm j}^{\rm O}$ values used in the calculation have been obtained from the $D_{\rm j}^{\rm W}$ values by using the ratio $D_{\rm j}^{\rm W}/D_{\rm j}^{\rm O}$ (= 150), which was estimated in a previous paper.[4] The concentration of DES$^+$ and TPB$^-$ in the PVC membrane were corrected for the dilution effect[4] by the PVC matrix: $c_{\rm DES^+}^{\rm O} = c_{\rm TPB^-}^{\rm O} = 20 \times 0.72 =$ 14 mM. As can be seen in Fig. 4A or 4B, there is a satisfactory agreement between the theoretical and experimental values of EMF, though there are some deviations. This result clearly demonstrates that MP theory is useful for predicting the potential response of an ion exchanger-type PVC-membrane ISE.

It should also be noted that if TPB$^-$ is excluded from the above calculation, the deviation from the Nernstian response (dashed line in Fig. 4A or 4B) cannot be reproduced; a perfect Nernstian response should be obtained even in the lower concentration range. Thus, it has been found that the anions in the membrane (TPB$^-$) also interfere with the potential response for the primary ion (DES$^+$) in the lower concentration range. Also, it has been shown from a theoretical calculation that 0.0408 M Na$^+$ being added to the sample solution as a buffering agent has no detectable effect on the potential response of ISE. The detection limit[24] of ISE has been estimated to be $10^{-5.17}$ M from an experimental plot, which is slightly higher than, but in reasonable agreement with, the value of $10^{-5.53}$ M obtained from the theoretical curve. We would like to add that the theoretical EMF values in the presence of the interfering ion (IMP$^+$ or NEO$^+$) are hardly affected by including TPB$^-$ in the calculation. In these cases, pragmatically, only IMP$^+$ or NEO$^+$ interfere with the Nernstian response of DES$^+$-ISE.

Thus, it has been found that the potential response of the PVC membrane DES$^+$-ISE can be predicted rather well using the values of $\Delta_{\rm O}^{\rm W}\phi_{\rm j}^{\rm o}$ and $D_{\rm j}^{\rm W}$, which are obtained from either voltammetric measurements or the literature. However, as can be seen in Fig. 4A or 4B, there are still some differences between the theoretical and experimental values. We have thus tried manual curve-fitting analysis by using the $\Delta_{\rm O}^{\rm W}\phi_{\rm j}^{\rm o}$ values for IMP$^+$, NEO$^+$, and TPB$^-$ as adjusting parameters (note that the other parameters including $\Delta_{\rm O}^{\rm W}\phi_{\rm DES^+}^{\rm o}$ (= –126 mV) and the diffusion coefficients of ions are the same as those used in the above theoretical calculation). As shown by the solid lines in Fig. 4A or 4B, the regression curves agree well with the experimental plots. The obtained adjusting parameters are: $\Delta_{\rm O}^{\rm W}\phi_{\rm IMP^+}^{\rm o} = -163$ mV, $\Delta_{\rm O}^{\rm W}\phi_{\rm NEO^+}^{\rm o} = 39$ mV, and $\Delta_{\rm O}^{\rm W}\phi_{\rm TPB^-}^{\rm o} = 278$ mV. The former two values are negatively and positively different by 20 and 10 mV, respectively, from those determined by ion-transfer voltammetry (see Table 1). Considering the experimental errors in the voltammetric and potentiometric measurements, the difference of less than 20 mV in $\Delta_{\rm O}^{\rm W}\phi_{\rm j}^{\rm o}$ seems not to be significant. Nevertheless, the adjusting parameter of $\Delta_{\rm O}^{\rm W}\phi_{\rm TPB^-}^{\rm o}$ is as much as 38 mV more negative than the literature value[17] (*i.e.*, 316 mV). This difference seems not to be negligible, and suggests possible interference from impurity anions contained in the PVC membrane.[25]

Table 2 Selectivity coefficients of the PVC membrane DES$^+$-ISE determined experimentally and theoretically

Interfering ion	$c_{\rm K2}^{\rm W}$/M	$\log k_{\rm K1,K2}^{\rm pot}$	
		Exp.[a]	Theor.[b]
IMP$^+$	0.1	0.12	–0.05
	1	0.37	0.07
	10	0.58	0.20
NEO$^+$	0.1	–0.76	–0.76
	1	–1.25	–1.24
	10	–1.88	–1.71

a. From the experimental potential–response curves shown by dots in Figs. 4A and 4B.

b. From the theoretical potential–response curves shown by dotted lines in Figs. 4A and 4B.

According to the IUPAC recommendation,[16] the selectivity coefficient, $k_{\rm K1,K2}^{\rm pot}$ (here, K1 = DES$^+$; K2 = IMP$^+$ or NEO$^+$), defined in FIM is given by

$$k_{\rm K1,K2}^{\rm pot} = \frac{c_{\rm K1}^{\rm W}}{\left(c_{\rm K2}^{\rm W}\right)^{z_{\rm K1}/z_{\rm K2}}}, \qquad (6)$$

where $c_{\rm K1}^{\rm W}$ is evaluated graphically from the intersection of the extrapolated linear portions of a potential–response curve. Because EMF has been plotted as a function of $\log c_{\rm K1}^{\rm W}$ (K1$^+$ = DES$^+$) in Figs. 4A and 4B, we here formulate $k_{\rm K1,K2}^{\rm pot}$ by using the concentrations of K1$^+$ and K2$^+$ instead of their activities. The $k_{\rm K1,K2}^{\rm pot}$ values were estimated from both the experimental potential–response curves (shown by the dots in Figs. 4A and 4B) and from the theoretically predicted curves (shown by the dotted lines). The logarithmic values of $k_{\rm K1,K2}^{\rm pot}$ estimated by these two methods are given in Table 2. For the use of NEO$^+$ as the interfering ion, there is a fairly good agreement between the values determined both experimentally and theoretically. For the use of IMP$^+$, the agreement is worse than for NEO$^+$, but satisfactory considering the relatively large interference to DES$^+$-ISE. It has thus been found that the $k_{\rm K1,K2}^{\rm pot}$ of a PVC membrane ISE can be, though roughly in some cases, predicted by the MP theory, provided that the values of $\Delta_{\rm O}^{\rm W}\phi_{\rm j}^{\rm o}$ and $D_{\rm j}^{\rm W}$ for the primary and interfering ions are available.

Conclusions

In conclusion, the MP theory is useful for predicting the potential response of an ion-exchanger type PVC membrane ISE. The transfer of a drug ion, DES$^+$, and its analogue ions can be observed by cyclic voltammetry at a micro PVC membrane/W interface, and the $\Delta_{\rm O}^{\rm W}\phi_{\rm j}^{\rm o}$ values determined for the ions are useful for elucidating the under-Nernstian response due to an interfering ion(s). In this paper, we have presented a universal method for the application of MP theory by numerical calculations, which has been successfully used to investigate interference from plural ions, including the anion in the PVC membrane. The present approach using MP theory would also be applied to the more popular, neutral ionophore-based ISEs for such hydrophilic ions as alkali metal ions. Such a study is currently in progress. The MP theory would be available for the sophisticated design of ISEs, which is not due to conventional "trial-and-error" procedures.

Supporting Information

The electrochemical cell used in NPV (Scheme S1), current-potential curves obtained by NPV for the transfer of DES^+, IMP^+, and NEO^+ at the DCE/W interface (Figs. S1 – S3). This material is available free of charge on the Web at http://www.jsac.or.jp/analsci/.

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