NEUTRALIZATION DIALYSIS. PROBLEMS AND OUTLOOK

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Dedicated to Dr Blahoslav Sedlacek on the occasion of his 70th birthday.

Neutralization dialysis (ND) of model systems containing 0.1–0.5 M NaCl and various high-molecular-weight synthetic or natural substances have been investigated. Desalination experiments were carried out in a three-compartment spiral module equipped with heterogeneous Ralex or homogeneous Neosepta membranes. Practically complete desalination proceeds due to the neutralization reaction in the desalination compartment. The time of desalination depends only on the membrane permeability and on the initial salt concentration in solution. An important feature hindering larger application of this method is sharp pH changes occurring in the desalination solution. This phenomenon predicted theoretically is mainly caused by the difference in diffusivities of H^+/Na^+ and OH^-/Cl^- ion pairs. Independently of the type of membrane and desalinated solution, pH value jumps into acidic region at the beginning of the ND. In the course of the process the pH value increases and the ND proceeds mostly at pH < 7. On the basis of theoretical prediction, an experimental method consisting in adjustment of acid concentration is proposed, which makes it possible to maintain constant pH in the desalination compartment. The convenience of this method was demonstrated by the ND of protein solutions.

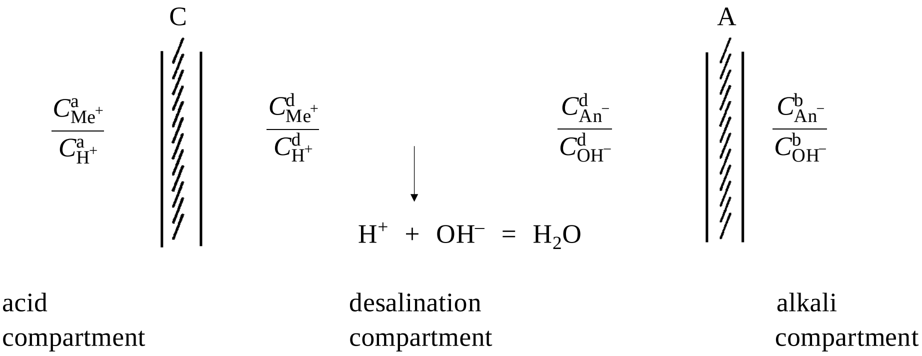
Neutralization dialysis (ND) is a membrane process which uses ion exchange membranes to separate inorganic salts from organic compounds[1]. The process is based on the well-known phenomenon described in all classic reference books on ion exchange[2]: the difference between the rate of diffusion of counterions and that of non-electrolytes and high-molecular-weight compounds across ion exchange membranes. The selectivity of separation of components by this process results from the ability of ion exchange membranes to let counterions pass and prevent the permeation of coions (Donnan exclusion principle) and large organic molecules (sieve effect).

Prerequisite for removing inorganic salts from a solution by the ND method is simultaneous use of cation (C) and anion (A) exchange membranes. The solution to be desalinated circulates in the space between the membranes; cations and anions of a salt are exchanged for hydrogen and hydroxyl ions, respectively permeating through the respective membranes from the acid or alkaline solutions placed on the other side of the membranes. From the point of view of the proceeding reactions, ND can be also regarded as ion exchange across the membranes, driven by a chemical reaction. The principle of ND can be represented by the Scheme 1.

The neutralization reaction, $H^+ + OH^- = H_2O$, which proceeds in the desalination compartment, plays a decisive role in the process. If this reaction did not occur, the ion concentrations at the surfaces of the cation and anion exchange membranes would only reach concentrations governed by the Donnan equilibria and no further desalination of the solution would occur. On the other hand, under ideal conditions, this reaction can provide practically complete desalination of the solution, since the concentrations of H^+ and OH^- ions will approach their minimum values (10^{-7} mol/l).

We started investigation of this process soon after Igawa reported on the application of the ND principle to deionization of aqueous solutions of nonelectrolytes[1]. Basing on the reasoning mentioned above we have set about the task to investigate in more detail the potential of this approach to desalination, using organic compounds of various physico-chemical nature and molecular weight, and ion exchange membranes of various structure.

Our first experiments on desalination of model NaCl solutions by ND were carried out in a three-compartment flat membrane cell equipped with ion exchange membranes of heterogeneous structure. These experiments enabled us to optimize the concentration of acid (HCl) and alkali (NaOH) solutions, i.e., we found that the trans-membrane fluxes of H^+ and OH^- ions increased rapidly with increasing the acid and alkali concentrations in the 0.01 to 0.1 mol/l range. The further increase in these concentrations up



SCHEME 1

to 0.5 mol/l had a negligibly small effect on the exchange fluxes, resulting only in an increased leakage of coions[3].

The next step was to investigate the effect of membrane surface area and of the solution flow rates on the process efficiency, i.e., on its duration and degree of desalination as well as on the loss of the desalinated compound. Having established that the efficiency is directly proportional to the membrane surface area, we designed a spiral membrane module[4,5], which enabled us to attain a higher efficiency of the ND method and to fulfil a number of practically important tasks. For example, we used the module set up from heterogeneous membranes MKK-1 and MAK-2 with an area of 200 cm^2 and 400 cm^2 for the desalination of aqueous solutions of saccharides (glucose, saccharose, lactose, lactulose) containing 0.1 M NaCl and milk whey with 7% content of salts. It was shown[3] that solutions of saccharides can be desalted to 98–99% within 1.5 h with saccharide yields 84–90%. Desalination of milk whey reached 85–88% after 2–2.5 h with a protein yield 88–91%.

General regularities of the ND kinetics were found to be the same for both the heterogeneous and homogeneous ion exchange membranes. In further work, we preferred the latter, since, owing to their smaller thickness and higher selectivity, they exhibited higher permeability to inorganic salts than heterogeneous membranes. As a result, the duration of desalination experiments was decreased twice[6]. All the other experiments were therefore performed in the spiral module equipped with homogeneous Neosepta ion exchange membranes. In the desalination experiments we employed solutions of both low- and high-molecular-weight nonelectrolytes (dextran, m.w. 10 000–500 000, poly(*N*-vinylpyrrolidone), m.w. 40 000). All the experiments exhibited analogous characteristics: with increasing molecular weight of the nonelectrolyte the yield increased to 94–98% and the duration of the process was prolonged by 0.5–1.5 h in comparison with deionization of model NaCl solutions of the same concentration (0.1 to 0.2 mol/l). Moreover, pH of the desalinated solution was found to fluctuate in the course of desalination.

This specific feature of the ND should be analyzed in more detail. Some changes in pH during the ND of aqueous methanol solutions were also observed by Igawa[1], but the reason for this phenomenon was not elucidated. After completing the experimental studies[3,6,7] and theoretical analysis of the ND kinetics[8–11], we have realized that the phenomenon is not simple. Detailed consideration of the theoretical aspects of ND kinetics is made elsewhere[11]; here we will only briefly present main results.

The theory predicts that, as long as the concentration of the desalinated solution is sufficiently high (0.05 mol/l or more), the process will proceed at a pH value far from the neutral region. That means, the pH will be in either acid or alkaline region for the most time of the experiment, and the change in pH, if any, will be jumply. Further, as the concentration of the desalinated solution is lowered down to some “threshold” value, its pH will spontaneously shift to the alkaline region and then, with a further decrease in the concentration, will tend to the neutral value. The jumps of pH at a high concentration of the desalinated solution are controlled by a small parameter (see below) and indicate the existence of temporal thin “layers”. Mathematically, these “layers” are similar to the “spatial” thin layers arising in the interior of a membrane positioned between acid and alkaline solutions[10,12,13]. The possibility of the temporal pH jumps can thus be regarded as the characteristic feature of the ND kinetics.

Accordingly, any investigator attempting at practical realization of the ND method will have to face the problem of searching for the experimental conditions which make it possible to control pH in the desalination compartment, and in which a sufficiently high desalination rate can be attained. Our theoretical consideration showed[11] that the position of the pH jumps on the time axis depends, to a considerable extent, on the volume and concentration of the acid and alkaline solutions. It can thus be expected that the control of these concentrations will allow maintaining pH within the desirable range. Another yet unstudied possibility of controlling the pH is to control the process temperature. Actually, it is known[14] that variation of temperature may significantly influence the ion exchange membrane transport.

In the present paper we will show, using a very simple theoretical model, that the stabilization of the concentrations of the acid and alkaline solutions will decrease the total number of the pH jumps occurring in the course of the ND run. Then, a new experimental method will be proposed which allows to control pH in the desalination compartment by an appropriate choice of the concentration in the acid compartment and by stabilization of the process temperature. Finally, we will indicate the examples which are expected to be the most promising for desalination by the ND method.

THEORETICAL

In our previous paper[11], a theoretical model of the kinetics of ND experiments carried out in a three-compartment membrane cell was proposed. The model was based on a number of assumptions, among which we mention here finite volumes of all the compartments and the existence of unstirred layers of solution near the membrane surfaces. As explained in ref.[11], the latter assumption is important only if the solution concentration is sufficiently low, so that the following inequality is valid[2]:

$$C << \overline{D}X\delta/DL \quad .$$

In our system, $X = 1$ mol/l, L and δ are of the same order of magnitude (ca 200–500 μm, and $\overline{D}$ is approximately one order of magnitude lower than D. Hence, the unstirred layers are important if $C < 0.01$ mol/l.

In this section, we consider the case of high concentration and thus neglect the presence of the unstirred layers. Moreover, in contrast to ref.[11], we assume that the volumes of both the acid and alkali solutions are infinite, i.e., their concentrations and contents are constant (this assumption corresponds to the experimental conditions in ref.[3] where the acid and alkali solutions were continuously renewed in the course of desalination). The rest of the model assumptions is identical to those of ref.[11], namely:

– ion membrane transport is quasistationary and unidimensional;

– both the membranes are ideally selective;

– the activity coefficients of all species are equal to unity;

– there exists a chemical equilibrium between H^+, OH^- and H_2O in the desalination compartment;

– the membrane–solution boundary equilibria obey the Nikolskii equations

$$C_{\mathrm{H}}\,\overline{C}_{\mathrm{Na}}/\overline{C}_{\mathrm{H}}\,C_{\mathrm{Na}} = K_{\mathrm{H}}^{\mathrm{Na}}\ , \qquad C_{\mathrm{OH}}\,\overline{C}_{\mathrm{Cl}}/\overline{C}_{\mathrm{OH}}\,C_{\mathrm{Cl}} = K_{\mathrm{OH}}^{\mathrm{Cl}}\ .$$

Using these assumptions, the equations of species balance and electroneutrality in the desalination compartment are

$$V^{\mathrm{d}}\,\mathrm{d}(C_{\mathrm{H}}^{\mathrm{d}} - C_{\mathrm{OH}}^{\mathrm{d}})/\mathrm{d}t = S^{\mathrm{C}}J^{\mathrm{C}} - S^{\mathrm{A}}J^{\mathrm{A}} \tag{1}$$

$$V^{\mathrm{d}}\,\mathrm{d}C_{\mathrm{Cl}}^{\mathrm{d}}/\mathrm{d}t = S^{\mathrm{A}}J^{\mathrm{A}}\ , \qquad V^{\mathrm{d}}\,\mathrm{d}C_{\mathrm{Na}}^{\mathrm{d}}/\mathrm{d}t = S^{\mathrm{C}}J^{\mathrm{C}} \tag{2}$$

$$C_{\mathrm{H}}^{\mathrm{d}}C_{\mathrm{OH}}^{\mathrm{d}} = K_{\mathrm{w}}\ , \qquad C_{\mathrm{H}}^{\mathrm{d}} - C_{\mathrm{OH}}^{\mathrm{d}} + C_{\mathrm{Na}}^{\mathrm{d}} - C_{\mathrm{Cl}}^{\mathrm{d}} = 0\ . \tag{3}$$

These equations will be defined completely if the ion membrane fluxes J^{C} and J^{A} are expressed in terms of the bulk ion concentrations in the desalination compartment. These expressions can be arrived at by solving the Nernst–Planck equations describing the ion transport through a membrane[2]; they have the following form[2,10]

$$J^{\mathrm{C}} = \overline{D}_{\mathrm{H}}\overline{D}_{\mathrm{Na}}X^{\mathrm{C}}/L^{\mathrm{C}}(\overline{D}_{\mathrm{H}} - \overline{D}_{\mathrm{Na}})\ \ln\,[(K_{\mathrm{H}}^{\mathrm{Na}}C_{\mathrm{H}}^{\mathrm{d}} + C_{\mathrm{Na}}^{\mathrm{d}})/\,(K_{\mathrm{H}}^{\mathrm{Na}}C_{\mathrm{H}}^{\mathrm{d}} + C_{\mathrm{Na}}^{\mathrm{d}}\overline{D}_{\mathrm{Na}}/\overline{D}_{\mathrm{H}})] \tag{4a}$$

and

$$J^{\mathrm{A}} = \overline{D}_{\mathrm{OH}}\overline{D}_{\mathrm{Cl}}X^{\mathrm{A}}/L^{\mathrm{A}}(\overline{D}_{\mathrm{OH}} - \overline{D}_{\mathrm{Cl}})\ \ln\,[(K_{\mathrm{OH}}^{\mathrm{Cl}}C_{\mathrm{OH}}^{\mathrm{d}} + C_{\mathrm{Cl}}^{\mathrm{d}})/\,(K_{\mathrm{OH}}^{\mathrm{Cl}}C_{\mathrm{OH}}^{\mathrm{d}} + C_{\mathrm{Cl}}^{\mathrm{d}}\overline{D}_{\mathrm{Cl}}/\overline{D}_{\mathrm{OH}})]\ , \tag{4b}$$

where, according to Eq. (*3*)

$$C^{d}_{H,OH} = \pm(C^{d}_{Na} - C^{d}_{Cl})/2 + [(C^{d}_{Na} - C^{d}_{Cl})^{2}/4 + K_{w}]^{1/2} = f_{H,OH}(C^{d}_{Na},C^{d}_{Cl}) \ . \qquad (5)$$

Combining Eqs (*2*), (*4a*), (*4b*) and (*5*) we obtain the final set of two differential equations describing the desalination kinetics:

$$\mathrm{d}C^{d}_{Na,Cl}/\mathrm{d}t = -(S^{C,A}/V^{d})J^{C,A} f_{H,OH}(C^{d}_{Na},C^{d}_{Cl})\ C^{d}_{Na,Cl} \ . \qquad (6)$$

Note that the membrane diffusion coefficients $\overline{D}_i$ (i = H^+ , OH^-, Na^+, and Cl^-) involved in these equations can be evaluated from experimental data by making use of the relationships derived in ref.[15].

In general, the solutions of these equations can be obtained only by numerical methods. It is worth noting, however, that main peculiarities of the pH dynamics described by this model can be well accounted for by another, extremely idealized model[8] for which the respective equations have an analytical solution.

Actually, let us assume that the ion exchange Nikolskii constants K^{Na}_{H} and K^{Cl}_{OH} are equal to unity, the concentrations of the solutions in the compartments are comparable and the difference in the diffusivities of counterions transported across a membrane is neglected. Then

$$C^{d} = C^{d}_{H} + C^{d}_{Na} = C^{d}_{OH} + C^{d}_{Cl} = C_{HCl} = C_{NaOH} \qquad (7)$$

$$\overline{D}_{H} = \overline{D}_{Na} = \overline{D}^{C} \quad \text{and} \quad \overline{D}_{OH} = \overline{D}_{Cl} = \overline{D}^{A} \ . \qquad (8)$$

Equation (*2*) then reduces to

$$V^{d}\ \mathrm{d}C^{d}_{Na}/\mathrm{d}t = S^{C}\ P^{C}(C_{HCl} - C^{d}_{H})/L^{C} \qquad (9)$$

$$V^{d}\ \mathrm{d}C^{d}_{Cl}/\mathrm{d}t = S^{A}\ P^{A}(C_{NaOH} - C^{d}_{OH})/L^{A} \ . \qquad (10)$$

Here, $P^{C} = \overline{D}^{C}X^{C}/S^{C}$ and $P^{A} = \overline{D}^{A}X^{A}/S^{A}$, and C^{d}_{H} and C^{d}_{OH} are defined by Eq. (*5*).

The approximate analytical solution of these equations is obtained[8] in terms of the function $G(t) = C^{d}_{H}(t) - C^{d}_{OH}(t)$ which, for the system at hand, can be of only two types, shown in Fig. 1*a*, provided that $G(0) > 0$.

$$G(t) = (G(0) - Q/\alpha^{C}) \exp(-\alpha^{C} t) + Q/\alpha^{C} \qquad \text{for } G(t) > 0 \;,$$

$$G(t) = -\,(Q/\alpha^{A}) \exp(-\alpha^{A}(t - t_1)) + Q/\alpha^{A} \qquad \text{for } G(t) < 0 \;, \tag{11}$$

where $Q = \alpha^{C} C_{HCl} - \alpha^{A} C_{NaOH}$ and $\alpha^{C,A} = S^{C,A} P^{C,A} / V^{d} L^{C,A}$.

It is easily seen that function $G(t)$ cannot have more than one zero value

$$t_1 = (\alpha^{C})^{-1} \ln(1 + \alpha^{C} |\, G(0)/Q \,|) \tag{12}$$

and this zero value corresponds to a temporal thin layer with pH jump (Fig. 1) similar to those described in ref.[11]. However, in contrast to ref.[11] where two thin “layers” are

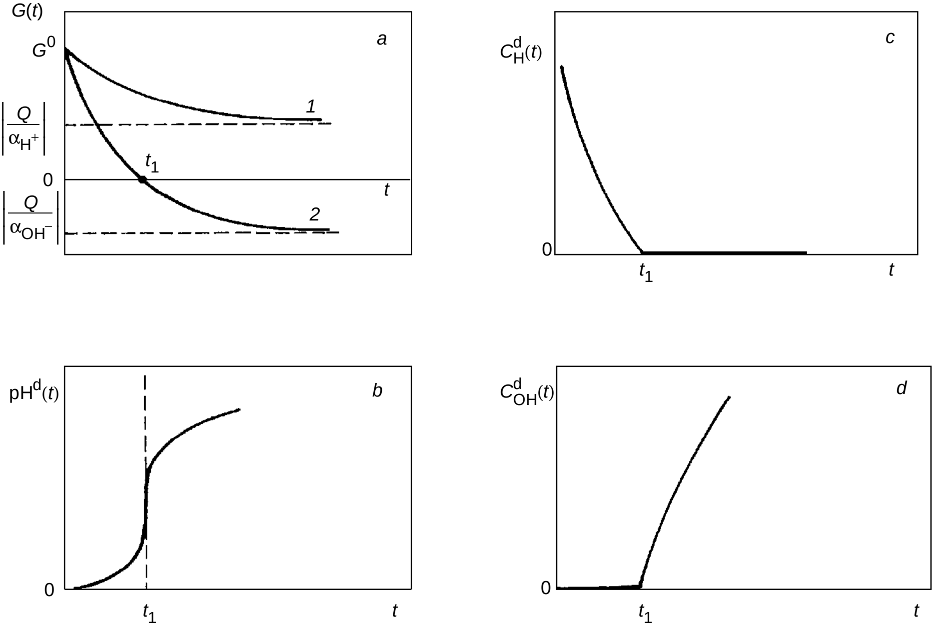


FIG. 1
Types of behaviour of function $G(t)$ for $G(0) > 0$ according to the model: *1* $Q > 0$, *2* $Q < 0$, and schematic plots of: *a* $G(t)$, *b* $pH^{d}(t)$, *c* $C^{d}_{H}(t)$ and *d* $C^{d}_{OH}(t)$ in the vicinity of $t = t_1$

observed, the model considered here predicts the existence of only one thin “layer”. The “layer” is estimated as a time-interval $\Delta t = K_w^{1/2}/|Q|$.

EXPERIMENTAL

Spiral modules of improved design[5], with active membrane areas 160 cm^2 and the distance between membranes 1 mm were used. The modules were set up from both homogeneous membranes Neosepta CM-2, AM-2 and AMH (Tokuyama Soda, Japan) and heterogeneous membranes MKK-1 and MAK-2 (Plastmassy, Russia) or RALEX KS-1 and VA-2 (Mega, Czech Republic). Circulation of solutions in the compartments was maintained by a peristaltic pump (PP1-05, Zalimp, Poland) at the flow rate 1.18 ml/s. The initial concentration of alkali solution was 0.08 M NaOH, the initial concentration of acid solution varied from 0.001 to 0.08 M HCl, the initial concentration of salt solution in the model experiments varied from 0.1 to 0.5 M NaCl. The solution to be desalinated was supplied into the desalination chamber from a thermostatted vessel (25 ± 0.1 °C) equipped with pH and conductometric electrodes. Electric conductivity and pH of the solution were continuously checked (CDM 83 conductivity meter, Radiometer and microprocessor pH/ion meter MX-200, WTW). Concentrations of acid and alkali solutions in the outer compartments and concentration of Cl^- ions in all the three compartments were determined by titration.

Aqueous solutions of dextran 70 (Pharmacia, Uppsala, Sweden) with m.w. 74 300 and poly(*N*-vinylpyrrolidone) K30 (Fluka) with m.w. 40 000 containing 0.1 M NaCl and solutions of serum albumin (Serva), cellulase, catalase (Reanal), lysozyme, ovalbumin, ribonuclease (Reachim) and gelatin (Fluka), containing 0.2 M NaCl were used. The initial concentrations of non-electrolytes were 20 and 40 g/l and the protein concentrations varied from 10 to 70 g/l. Desalination of proteins was carried out at pH values ensuring stability of proteins and enzymes. Ash content was determined in lyophilized samples.

Experiments, aimed at establishing the effect of concentration of acid and alkali solutions on trans-membrane fluxes of components in the system HCl solution–C-membrane–NaCl solution–A-membrane–NaOH solution and the dependence of the magnitude of these fluxes on the rate of circulation of solutions in the compartments, were carried out in a flat three-compartment cell, with active membrane surface 5.72 cm^2 and a 3-mm distance between the membranes.

The effect of membrane structure on trans-membrane fluxes of components was studied in the two systems: HCl solution–C-membrane–NaCl solution and NaOH solution–A-membrane–NaCl solution in a flat two-compartment cell. The same cell was used for measurements of coionic fluxes in the system: NaOH solution–C-membrane–NaCl solution and HCl solution–A-membrane–NaCl solution. Model experiments in the flat cell were stopped after 3 h while experiments in spiral modules were finished when 95–98% of desalination was reached.

The average trans-membrane fluxes of components in model experiments were calculated using the following relations:

$$J^{a}_{HCl} = J^{C}_{H} + j^{C}_{Cl} = (C^{0}_{a} - C_{a})V^{a}/S^{C}t \qquad (14)$$

$$j^{C}_{Cl} = (C^{0}_{a} - C^{Cl}_{a})V^{a}/S^{C}t \qquad (15)$$

$$J^{C}_{H} = J^{C}_{Na} = (C^{Cl}_{a} - C_{a})V^{a}/S^{C}t \qquad (16)$$

$$J^{\mathrm{b}}_{\mathrm{NaOH}} = J^{\mathrm{A}}_{\mathrm{OH}} + j^{\mathrm{A}}_{\mathrm{Na}} - j^{\mathrm{A}}_{\mathrm{H}} = (C^{0}_{\mathrm{b}} - C_{\mathrm{b}})V^{\mathrm{b}}/S^{\mathrm{A}}t \qquad (17)$$

$$J^{\mathrm{b}}_{\mathrm{Cl}} = J^{\mathrm{A}}_{\mathrm{Cl}} + j^{\mathrm{A}}_{\mathrm{Na}} + j^{\mathrm{A}}_{\mathrm{H}} = C^{\mathrm{Cl}}_{\mathrm{b}}V^{\mathrm{b}}/S^{\mathrm{A}}t \qquad (18)$$

$$J^{\mathrm{d}}_{\mathrm{NaCl}} = J^{\mathrm{A}}_{\mathrm{Cl}} - j^{\mathrm{C}}_{\mathrm{Cl}} + j^{\mathrm{A}}_{\mathrm{Na}} = (C^{0}_{\mathrm{d}} - C_{\mathrm{d}})V^{\mathrm{d}}/S^{\mathrm{A}}t \ , \qquad (19)$$

here C^0 and C are the initial and final concentrations, V is the volume of solution, J is the trans-membrane flux, S is the membrane area, t is time. The superscripts and subscripts a, d, and b refer to the acid, desalination and alkali compartments, respectively, A and C refer to anion and cation membranes, respectively, $j^{\mathrm{C}}_{\mathrm{Cl}}$, $j^{\mathrm{A}}_{\mathrm{Na}}$, and $j^{\mathrm{A}}_{\mathrm{H}}$ are coion fluxes of Cl^- , Na^+ and H^+ ions through the respective membranes.

RESULTS AND DISCUSSION

The equations governing the kinetics of ND enable us to establish how the pH value in the desalination compartment depends on the boundary conditions of the system. For a given pair of ion exchange membranes with fixed surface area, ion exchange capacity and known constant permeability and for constant volumes of solutions in the system, the pH value will be given by the ratio of H^+ and OH^- concentrations in the desalination compartment, which in turn depends on the ratio of diffusion coefficients of ions, on the thickness of the unstirred layers adjacent to the membrane surfaces and on the initial concentrations of the acid, alkali and salt solutions. Out of the above parameters the initial concentrations are the easiest to control. It follows from our previous investigations that the initial concentrations of the acid and alkali solutions should not exceed 0.1 mol/l in order to maintain the condition of steady-state transport. The volumes of solutions should be such that their electrolyte capacity exceeds by more than one order of magnitude the membrane ion exchange capacity and, at the same time, is four to five times higher than the electrolyte capacity of the desalinated solution. In deriving the kinetic equations we made the assumption that the HCl and NaOH solutions were continuously renewed to keep their concentrations constant. This assumption was not satisfied in actual experiments, since no attempt was made to keep the initial HCl and NaOH concentrations. Nevertheless, the main predictions of the kinetic theory of ND concerning the behaviour of pH in the desalination compartment have been fully confirmed. Figure 2 shows several typical examples of neutralization dialysis of model NaCl solutions. It is apparent that the curves of pH fluctuations which take place in the desalination compartment exhibit the typical shape predicted by the theory. At the beginning of the ND experiment pH jumps into the acid region, whereas at the end of ND pH jumps into the alkaline region and the ND proceeds mostly at pH < 7. When the concentration of the desalinated solution is increased from 0.1 to 0.5 mol/l, pH values are shifted into a more acid region (from 2.4 to 1.4) and the position on the time axis of the pH jumps to the alkaline region changes. At the very end of the process, as the NaCl concentration in the desalinated compartment drops, pH shifts to the neutral region as a result of the controlling effect of the unstirred layers adjacent to the membrane surfaces. Graphs describing the desalination process have an exponential shape, thus confirming the decrease in permeability of the ion exchange membranes at the low electrolyte concentrations. The observed sharp drop of pH in the desalination compartment is primarily given by the difference in the diffusion coefficients of ion pairs H^+/Na^+ through the cation membrane, and OH^-/Cl^- through the anion membrane (in cm^2/s , $9.34 . 10^{-5}/ 1.35 . 10^{-5}$ and $5.23 . 10^{-5}/2.03 . 10^{-5}$, respectively). At the same time, a higher volume concentration of fixed charges in the cation exchange membrane also ensures a steeper electrochemical gradient of ions in membrane CM-2 in comparison with anion exchange membranes AM-2 and AMH, leading to a predominant flux of H^+ ions into the desalination compartment (Table I). A comparison of the characteristics of membranes AMH and AM-2 leads to the conclusion that increasing the thickness of membrane AMH, decreasing its volume capacity and increasing the coion permeability results in a decrease of the desalination efficiency.

All these assumptions have been confirmed by ND experiments carried out with the ND-2 module. Also here, the already described specific features of ND were observed but, owing to the lower selectivity of the AMH membrane, the duration of desalination was prolonged by 30–40% compared to the experiments carried out with the ND-1 module and pH in the desalination compartment shifted into a more acid region. It

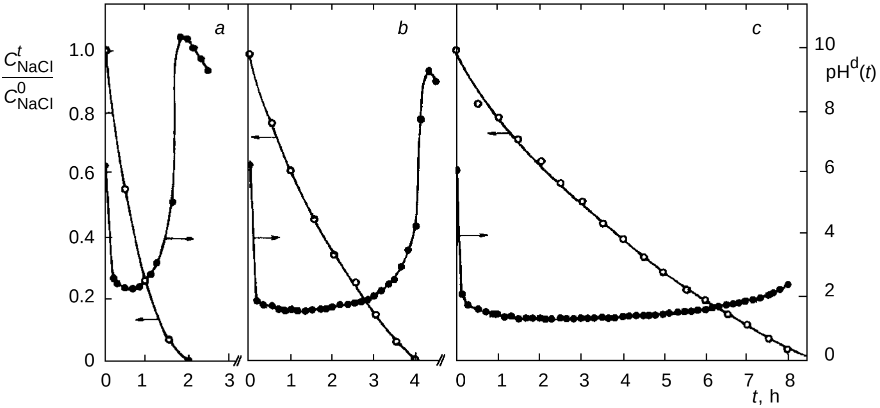


FIG. 2

Time dependence of the desalination rate and pH in the desalination compartment in ND of NaCl solutions of various concentrations (mol/l): *a* 0.1, *b* 0.25, *c* 0.5. Conditions: module ND-1, temperature 25 ± 1 °C, initial acid and alkali concentrations 0.08 mol/l, flow rate 1.18 ml/s follows from a comparison of membrane permeability to counterion and coions that the most significant contribution to the trans-membrane ion fluxes stems from the coion flux of H^+ ions across the anion exchange membrane, while the coion flux of OH^- ions through the cation exchange membrane may be neglected. From the results of model experiments we were able to calculate the mean trans-membrane fluxes of counterions and coions (see Table II). These data demonstrate the effect of equilibrium and kinetic parameters of the anion exchange membrane on the trans-membrane fluxes in the system. Since all ion fluxes must obey the condition of electroneutrality, the less permeable membrane, in our case the AMH anion exchange membrane, plays the rate-limiting role, and governs the rate of counterions H^+ flux across the cation exchange membrane. Some of the discrepancies observed in the trans-membrane fluxes of HCl, NaCl and NaOH and in the Donnan ratios of ion concentrations in both the acid and alkaline compartments can be attributed to the difference of physico-chemical characteristics of membranes causing a difference of the equilibrium concentrations at the cation and anion exchange membranes which is smoothed out due to the neutralization reaction.

Indeed, assuming that

$$C^{a}_{\mathrm{H}}/C^{a}_{\mathrm{Na}} = C^{d}_{\mathrm{H}}/C^{d}_{\mathrm{Na}} \quad \text{and} \quad C^{b}_{\mathrm{OH}}/C^{b}_{\mathrm{Cl}} = C^{d}_{\mathrm{OH}}/C^{d}_{\mathrm{Cl}}$$

and, with concentrations of ions at the end of the process defined by

$$C^{d}_{\mathrm{H}} = C^{d}_{\mathrm{Na}} \approx 10^{-6}\ \mathrm{mol/l} \quad \text{and} \quad C^{d}_{\mathrm{OH}} = C^{d}_{\mathrm{Cl}} \approx 10^{-6}\ \mathrm{mol/l}\ ,$$

we obtain the following relation:

TABLE I
Permeability coefficients (cm^2/s) of membranes

Membrane	Membrane thickness cm	IEC	$P_{\mathrm{H}} \cdot 10^6$	$P_{\mathrm{OH}} \cdot 10^6$	$P_{\mathrm{HCl}} \cdot 10^7$	$P_{\mathrm{NaOH}} \cdot 10^{10}$	$P_{\mathrm{NaCl}} \cdot 10^8$
CM-2	0.013	2.05	9.8	–	–	3.9	0.4
AM-2	0.013	1.08	–	9.1	1.2	–	0.9
AMH	0.025	0.46	–	7.3	1.8	–	1.8

IEC ion exchange capacity of membrane, meq/g dry membrane.

$$C^{a}_{H}/C^{a}_{Na} = C^{b}_{OH}/C^{b}_{Cl} \ ,$$

where

$$C^{a}_{H}/C^{a}_{Na} = x \ , \quad C^{b}_{OH}/C^{b}_{Cl} = y \ .$$

Calculated equilibrium compositions of model NaCl solutions subject to neutralization dialysis have shown that an equilibrium exists between the amount of counterions exchanged across the cation and anion exchange membranes. However, the total amounts of Na^+ and H^+, and OH^- and Cl^- ions in the acid and alkaline compartments are equal only if the ion distribution in the membrane phase is taken into account. An analysis of experimental data obtained for model NaCl solutions has shown that for controlling pH in the desalination compartment one must continuously control the concentrations of external acid and alkaline solutions, at least to such an extent that the difference between the fluxes of H^+ and OH^- counterions into the desalination compartment is minimized and, consequently, pH is maintained in the neutral region. As expected, the desalination is in this case substantially prolonged, but strong fluctuations of pH in the desalination compartment can be avoided (Fig. 3).

An additional approach to pH control becomes possible when the temperature dependence of the diffusion coefficients of individual ions is taken into account. By increasing the temperature of the desalinated solution, not only a substantial shortening

TABLE II
Trans-membrane fluxes J (meq/cm^2 s) in the neutralization dialysis of model NaCl solutions

C^{0}_{NaCl}	$J^{a}_{HCl} \cdot 10^5$	$J^{b}_{NaOH} \cdot 10^5$	$J^{d}_{NaCl} \cdot 10^5$	$j^{C}_{Cl} \cdot 10^5$	$J^{C}_{H} \cdot 10^5$	$J^{A}_{Cl} \cdot 10^5$	x	y
				Module ND-1				
0.1	1.10	0.98	0.98	0.04	1.05	0.96	1.7	1.8
0.25	1.32	1.33	1.26	0.01	1.31	1.29	1.7	1.9
0.5	1.40	1.43	1.32	0.04	1.43	1.39	1.9	2.0
				Module ND-2				
0.1	0.78	0.83	0.75	0.05	0.73	0.83	2.0	1.8
0.25	0.91	0.84	0.75	0.01	0.90	0.85	1.7	2.0

J^{a}_{HCl} total (ion and coion) flux of H^+ across the cation exchange membrane, J^{b}_{NaOH} total flux of OH^- across the anion exchange membrane, J^{d}_{NaCl} total flux of Na^+ and Cl^- across the cation and anion exchange membranes, j^{C}_{Cl} Cl^- coion flux across the cation exchange membrane, J^{C}_{H} H^+ counterion flux across the cation exchange membrane, J^{A}_{Cl} Cl^- counterion flux across the anion exchange membrane, $x = C^{a}_{H}/C^{a}_{Na}$; $y = C^{b}_{OH}/C^{b}_{Cl}$.

of the desalination process is achieved, but also the range of pH variation during desalination is narrowed from 4.2–6 (at 25 °C) to 5.3–6 (at 40 °C). These model experiments enabled us to optimize desalination of high-molecular-weight nonelectrolytes and polyelectrolytes. It is apparent from the results presented in Fig. 4 that analogous features as before were observed when dextran T 70 or poly(*N*-vinylpyrrolidone) K 40 were desalinated in module ND-1 without controlling the acid and alkali concentrations during a ND run. The only difference was that the jump of pH into the alkaline region was not always observed. Its absence during the ND of poly(*N*-vinylpyrrolidone) K 40 may be attributed to possible adsorption of oligomeric molecules on the surfaces of the membrane, leading to a change in their permeability. With these systems, we also verified the validity of the effect of the solution flow rate on the position on the time axis of the pH jumps. It can be assumed that a decrease in the extent of turbulence may depress the variation of pH in the desalination compartment owing to the increased regulatory effect of unstirred layers caused by their higher thickness. It is, however, apparent from the data presented in Figs 4*c* and 4*d* that a decrease in the flow rate of solutions from 1.18 to 0.33 ml/s results in an increased time of desalination rather than in depressed pH variation.

Nevertheless, when a high level of desalination was reached (98 to 99.5%), pH in the desalination compartment increased attaining almost neutral values. This feature then makes it possible to use ND as an effective desalination method for high-molecular-weight substances that are insensitive to variations in pH. When ND is to be used to desalinate proteins, the pH fluctuation should be kept at minimum in order to preserve their native structure. As shown by our results, the conditions of ND are to a consider-

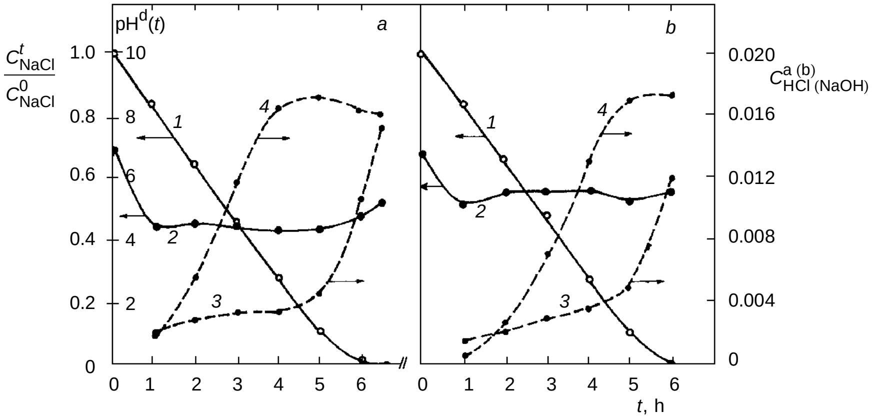


FIG. 3

Time dependence of the desalination rate (*1*) and pH in the desalination compartment (*2*) in ND of 0.1 M NaCl solution at the stepwise change of acid (*3*) and alkali (*4*) concentrations (mol/l). Conditions: module ND-1, temperature (°C): *a* 25 ± 1, *b* 40 ± 1 able extent simplified here, since proteins, being of polyampholytic character, act to a certain extent as buffers. Especially due to this property of proteins, it was sufficient in a number of cases (serum albumin, gelatin) to lower the starting concentration of the acid to 0.02–0.03 mol/l, keeping always the alkali concentration at 0.08 mol/l. In this case (Fig. 5), the entire process proceeded in a pH range that ensured stability of the protein without the necessity of controlling the concentrations of the acid and alkali solutions. By controlling the acid concentration continuously one may carry out the entire process in a pH range close to neutral. It is important to note that the time required here for serum albumin desalination is several times shorter in comparison with the time necessary for desalination of a model NaCl solution of the same concentration, even with the serum albumin concentration in solution as high as 70 g/l. This unexpected effect was caused by a sharp decrease in the non-selective flux of HCl into the desalination compartment, resulting from the control of the acid concentration. Desalination of gelatin proved to be similarly effective. In this case, ND was carried out at 40 °C to avoid gel formation (Fig. 5*c*). In an attempt to increase the efficiency of ND by a continuous control of the acid solution concentration we calculated the range of minimum concentrations that must be maintained in the acid compartment in order to keep the desalination rate at a reasonable level and, at the same time, to maintain pH within the limits corresponding to protein stability. The calculations have shown that the concentration of the acid should be maintained between 0.005 and 0.01 mol/l. The rate of addition of 10 M HCl into the outer, acid compartment was calculated from the concen-

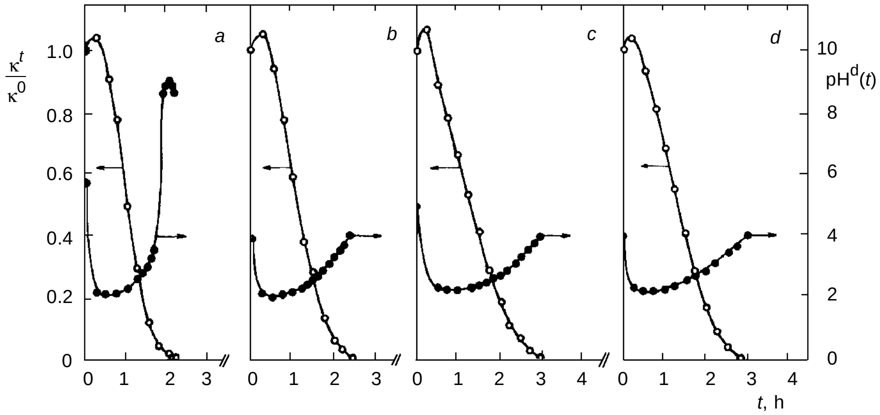


FIG. 4
Kinetics of desalination by ND of aqueous dextran T70 (*a*, *c*) and PVP K40 (*b*, *d*) solutions, containing 0.1 M NaCl. Conditions: module ND-1, initial acid and alkali concentrations 0.08 mol/l, flow rate (ml/s): *a*, *b* 1.13, *c*, *d* 0.33; κ^0, κ^t electric conductivity (mS/cm) of desalination solution in time $t = 0$ and t, respectively

tration dependence of trans-membrane fluxes. As shown in Fig. 6, desalination of lysozyme, ribonuclease, and ovalbumin under conditions of continuous control of acid concentration proceeds in the pH range that ensures stability of these proteins. In spite

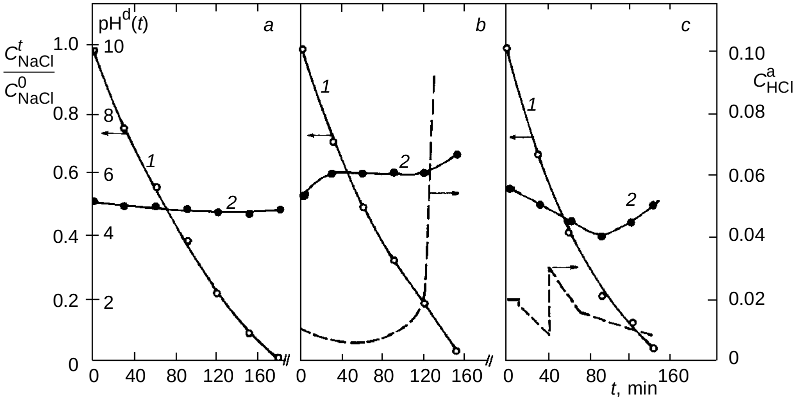


FIG. 5

Time dependence of the desalination rate (*1*) and pH in the desalination compartment (*2*) of serum albumin (*a*, *b*) and gelatin (*c*) solutions in ND at various initial NaCl concentrations (mol/l): *a* 0.23, *b* 0.2, *c* 0.21. Conditions: module ND-1, temperature (°C): *a*, *b* 25 ± 1, *c* 40 ± 1, initial concentration of serum albumin 70 g/l, gelatin 35 g/l, initial alkali concentration 0.08 mol/l, initial acid concentration (mol/l): *a* 0.02, *b* 0.01, *c* 0.03. Stepwise change of acid concentration

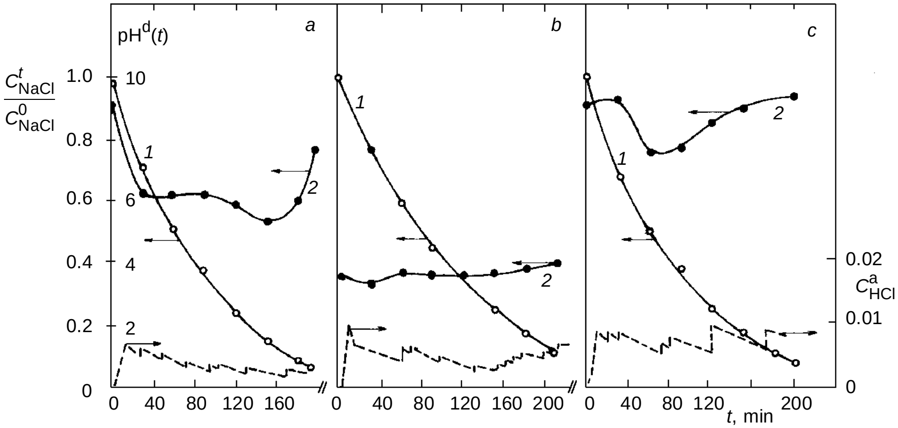


FIG. 6

Time dependence of the desalination rate (*1*) and pH in the desalination compartment (*2*) in ND of lysozyme (*a*), ribonuclease (*b*) and ovalbumine (*c*) solutions at 0.23 mol/l NaCl concentration. Conditions: module ND-1, temperature 25 ± 1 °C, initial protein concentration (g/l): *a* 30, *b* 15, *c* 10. Stepwise change of acid concentration of the relatively high protein concentrations in the desalinated solution (10–30 g/l), the process can be finished within 3 to 4 h. In the ND of cellulase and catalase the situation was similar. In all instances the native structure of the protein was preserved and the yield of the process was high.

CONCLUSIONS

Kinetics of neutralization dialysis was described theoretically and the results were checked experimentally on the example of desalination of aqueous solutions of high-molecular-weight nonelectrolytes and polyelectrolytes. In all instances investigated, the theoretical conclusions concerning the variation of pH in the desalination compartment were confirmed by the experimental results. It has been shown that the kinetic parameters of ion exchange membranes are not decisive for the pH variation. Changes in membrane permeability affect only the position of the pH jumps on the time axis and the rate of desalination. It has been found that the most appropriate way of stabilizing pH in the desalination compartment is to control continuously the concentration in the acid-containing external compartment and/or to raise the temperature of the desalination solution. By optimizing the concentration and temperature conditions we were able to carry out desalination of proteins and enzymes within the pH r ange of their stability, with a high yield and in a reasonably short time.

Summarizing the results of our investigations, we may state that ND as a method of desalination of low- and high-molecular-weight nonelectrolytes and polyelectrolytes has considerable advantages, in particular in those instances when a high level of desalination is desirable. The spiral design of the membrane module enabled us to propose ND as a universal desalination method since a single spiral module is required for desalination of various nonelectrolytes and polyelectrolytes on both laboratory and preparative scale.

LIST OF SYMBOLS

C_{HCl}	the concentration of acid solution, mol/l
C_{NaOH}	the concentration of alkali solution, mol/l
C^{d}	the concentration of desalination solution, mol/l
$C, \overline{C}$	ion concentration in solution and membrane, respectively, mol/l
$D, \overline{D}$	ion diffusion coefficient in solution and membrane, respectively, cm^2/s
$G = C^{\mathrm{d}}_{\mathrm{H}}(t) - C^{\mathrm{d}}_{\mathrm{OH}}(t)$	function of pH changes in desalination compartment during ND, mol/l
J, j	ion and coion flux, respectively, meq/cm^2 s
$K^{\mathrm{Na}}_{\mathrm{H}}, K^{\mathrm{Cl}}_{\mathrm{OH}}$	Nikolskii constants for cation and anion exchange membranes, respectively
K_{w}	water product, mol^2/l^2
L	membrane thickness, cm
P	permeability coefficient, cm/s
$Q = \alpha^{\mathrm{C}} C_{\mathrm{HCl}} - \alpha^{\mathrm{A}} C_{\mathrm{NaOH}}$	mol/l s
S	membrane area, cm^2
t	time, s
V^{d}	the volume of the desalination compartment, cm^3

X	exchange capacity of unit membrane volume of wet membrane, meq/cm^3
x, y	ratios of counterion concentrations in acid and alkali compartments, respectively
$\alpha = SP/V^{\mathrm{d}}L$,	s^{-1}
δ	thickness of the unstirred layer, cm
κ	electric conductivity of the desalination solution, mS/cm
Subscripts	
i	ionic species, i = H$^+$, Na$^+$, OH$^-$, Cl$^-$, Me$^+$ (cation), An$^-$ (anion)
Superscripts	
C	cation exchange membrane
A	anion exchange membrane
a	acid compartment
b	alkali compartment
d	desalination compartment
0, t	value of any parameter in time t = 0 and t

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