Charge-Mosaic Membranes: Enhanced Permeability and Negative Osmosis with a Symmetrical Salt

Abstract. *Charge-mosaic membranes are prepared by embedding a single layer of alternating cation and anion exchange beads in silicone resin. Membranes made in an identical manner but containing only one type of exchanger serve as controls. The mosaic membranes are 50 to 100 times more permeable to potassium chloride than the controls; and furthermore they give rise to net volume flow from concentrated to dilute solutions of potassium chloride in the absence of a pressure gradient ("negative osmosis"), whereas the controls exhibit normal osmotic behavior. The negative reflection coefficients of the mosaics suggest potential applications in desalination.*

In 1932 Sollner predicted that a mosaic membrane composed of cation and anion selective elements (that is, a "charge-mosaic") would exhibit unique transport properties arising from electrical interaction between the unlike elements (*1*). He pointed out that if such a membrane were placed between electrolyte solutions of unequal concentration, circulating electric currents should flow between the elements, as shown in Fig. 1. Homogeneous ion exchange membranes are relatively impermeable to salts owing to a more or less complete co-ion exclusion, and accordingly give rise to membrane potentials which may approach ideal Donnan values. However, the juxtaposition of homogeneous elements of opposite fixed charge in a mosaic structure would be expected to short-circuit the potentials partially or completely, permitting an unhindered flow of counterions in each element. This effect should greatly enhance the overall salt permeability. The existence of circulating currents, together with the associated salt flux and electroosmotic water transport, was verified in model systems constructed of two completely separate membranes of opposite fixed charge (*2*). These systems were functionally equivalent to mosaics, but were not characterized by the large numbers of low-resistance current loops which arise when many small elements are packed in a close array. Qualitative observations of enhanced salt diffusion at the borderline between large regions of opposite fixed charge have been made on polyethylene-based ion exchange membranes (*3*).

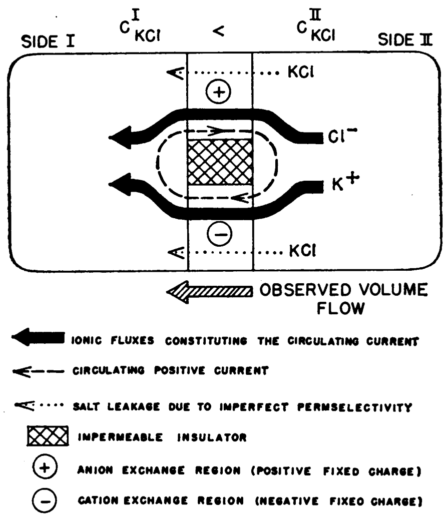

Fig. 1. Mechanism of permeability enhancement and negative osmosis in a charge-mosaic membrane.

Negative osmosis, in a system containing only one solute, may be defined as the occurrence of volume flow across a membrane from a solution of *greater* to one of *lesser* osmotic pressure, in the absence of hydrostatic pressure gradients and net flow of electric current across the membrane (*4*). With highly asymmetric electrolytes, such as K_2SO_4, $MgCl_2$, and strong acids, negative osmosis can take place across membranes having fixed charges of one sign only (*5*). Although the nature of the mechanism is controversial (*5, 6*), it is agreed that with such membranes negative osmosis occurs when the mobility of the co-ion is much greater than that of the counterion. Negative osmosis has not, to our knowledge, been demonstrated in any type of membrane (homogeneous or mosaic) with an electrolyte which is symmetrical in the sense that the mobilities of both ions in aqueous solution are approximately equal. However, the possibility that in charge-mosaic membranes the electroosmotic transport of water due to circulating currents might be large enough to overcome normal osmosis and produce negative osmosis was predicted by Sollner (*1*). This phenomenon should not require an asymmetric electrolyte, as is also shown by the nonequilibrium thermodynamic calculations of Kedem and Katchalsky (*7*).

The membrane parameter which determines the magnitude of the negative osmotic effect is the reflection coefficient σ (*8*), defined (for a system containing one solute) by

$$\sigma = \left(\frac{\Delta p}{\Delta \pi}\right)_{J_v = 0,\ I = 0} \qquad (1)$$

where Δp and $\Delta \pi$ are the hydrostatic and osmotic pressure differences, respectively, J_v is the volume flow (*9*), and I is the net flow of electric current across the membrane. For an ideally permselective membrane $\sigma = 1$, whereas for a completely nonselective membrane $\sigma = 0$. Negative osmosis occurs when $\sigma < 0$. The reflection coefficient can also be expressed as (*7*)

$$\sigma = -\frac{1}{L_p}\left(\frac{J_v}{\Delta \pi}\right)_{\Delta p = 0,\ I = 0} \qquad (2)$$

where L_p, the filtration coefficient, is defined by

$$L_p = \left(\frac{J_v}{\Delta p}\right)_{\Delta \pi = 0,\ I = 0} \qquad (3)$$

Since L_p is always positive, σ will be negative if J_v and $\Delta \pi$ have the same sign, that is, if volume flows toward the more dilute solution. The calculation of σ from our experimental results is based on Eq. 2.

Charge-mosaic membranes were prepared by embedding a single layer of alternating cation and anion exchange beads in an impermeable supporting matrix as shown in Fig. 2. The most successful matrix material found was

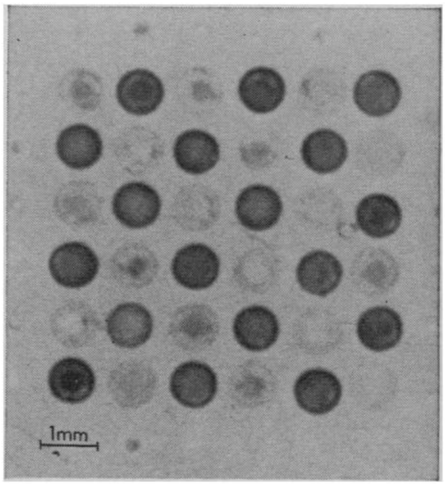

Fig. 2. A charge-mosaic membrane. The lighter and darker beads are, respectively, AG 1-X8 anion exchanger (exchange capacity dry 3.2 meq/g) and AG 50W-X8 cation exchanger (exchange capacity dry 5.1 meq/g) dyed with neutral red (both from Bio-Rad Laboratories, Palo Alto, Calif.).

a flexible silicone resin, Sylgard 184. This provided a tight seal around the beads even when they were subjected to repeated swelling and shrinking in solutions of different concentration. In preparing membranes, beads of the types indicated in the legend to Fig. 2 were first air-dried (in K or Cl form) at ambient temperature and humidity, then examined for flaws and measured to ± 0.02 mm under a dissecting microscope. Beads with diameters of 0.71 ± 0.02 mm were positioned in a shallow Teflon mold previously filled with liquid silicone resin. After preliminary curing overnight at ambient temperature, the upper surface of each bead was exposed with a needle, and the mold was placed in an oven at 38° to 40°C for 5 hours. The membrane was then removed from the mold, the lower surface of each bead was exposed, and the membrane was returned to the oven for several days until completely cured. The cured membrane was transferred to a saturated KCl solution and hydrated slowly over a period of 4 to 5 hours by stepwise dilution of the KCl until the desired concentrations (0.01 to 0.1*M*) were reached.

Values of the reflection coefficient, filtration coefficient, and KCl permeability have been measured on the charge-mosaic membranes and on control membranes prepared in precisely the same way as the mosaics, but with beads of one type only. The coefficients are expressed in terms of active membrane area, estimated by averaging the total exposed areas of bead surface on the two sides as measured under a dissecting microscope. Volume-flow and permeability measurements at a hydrostatic pressure difference of zero were carried out simultaneously in 20-ml glass cells divided into two equal compartments, with Teflon-coated magnetic bars situated close to the membrane surfaces to provide vigorous stirring. The silicone matrix of the membrane furnished a practically leak-free seal against the ground-glass flange of each compartment.

Horizontal capillaries graduated in microliters were used to monitor volume flow J_v. The presence of a capillary in each compartment provided an internal check against leakage and thermal volume change. All experiments were conducted in an air thermostat at 25.0 ± 0.2°C. Salt flow, J_s, was determined by measuring the concentration of KCl in each compartment at the beginning and end of a run with a Fiske freezing-point osmometer (the decrease in $\Delta\pi$ being generally about 40 percent). The compartments were initially filled with 0.1 and 0.2*M* KCl solutions (freshly boiled before use), and the position of the meniscus in each capillary was recorded at intervals over a period of several days. In a typical experiment on a mosaic membrane (Fig. 3) the volume flow takes place towards the more dilute solution, and the overall volume loss from the system is small by comparison. The reflection coefficient σ is calculated from the initial rate of volume flow by means of Eq. 2, using the mean value for L_p measured directly on membranes of the same type.

For both mosaic and control membranes, L_p was determined by measuring J_v at hydrostatic pressure differences of approximately 0.5 to 1.0 atm in the glass cells described previously. The membrane was supported by a fine-mesh metal grid. In these studies leakage from the cell was extremely slight, usually less than 0.01 μl/hour. Both compartments were filled with freshly boiled 0.05*M* KCl (except as noted in Table 1) at the beginning of an experimental run, and the position of the meniscus in each capillary was recorded at intervals over a period of 2 to 3 days. The results for L_p and σ are given in Tables 1 and 2, respectively.

For the purpose of calculating σ, it has been assumed (i) that properties of the membranes do not vary significantly over the range of pressures used, and (ii) that the filtration coefficients measured in 0.05*M* KCl are not significantly different from those applicable in 0.145*M* KCl (that is, the logarithmic mean of the concentrations used in the measurements of negative osmosis). The unexpectedly high values of L_p (and the corresponding low values of σ) obtained for the anion exchange controls have not yet been explained.

The KCl permeability ω (*7*), defined by

$$\omega = \left(\frac{J_s}{\Delta\pi}\right)_{J_v = 0,\ I = 0} \qquad (4)$$

was calculated from the measured values of J_s (*10*). As shown by the results in Table 2, the KCl permeabilities of the mosaics were 50 to 100 times those of the controls, indicating that salt "leakage" through the more or less permselective ion-exchange material ac-

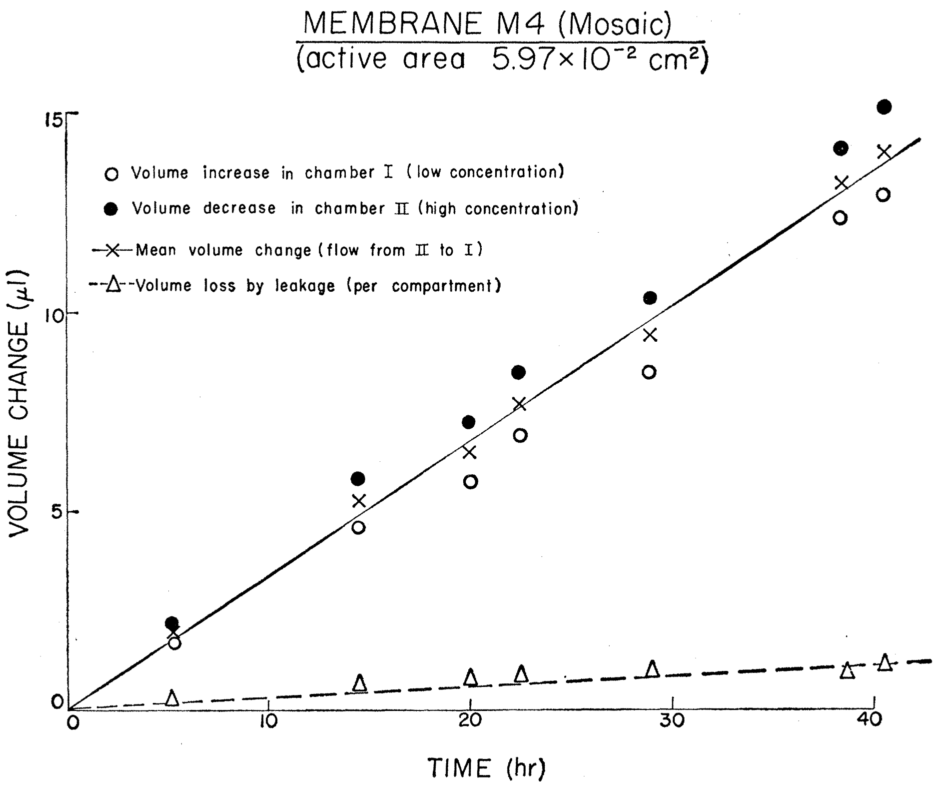

Fig. 3. Negative osmosis with KCl. A typical volume-flow experiment at zero hydrostatic pressure difference on a charge-mosaic membrane composed of equal areas of anion and cation exchange material. Volume is seen to flow from the more concentrated to the more dilute solution.

Table 1. Experimentally determined values of the filtration coefficient, L_p, for the mosaic and the control membranes. The fraction of active membrane surface area occupied by cation exchanger, γ_c, is indicated. Values in parentheses are means of values listed above them.

Membrane	γ_c	$\Delta p \times 10^{-6}$ (dyne/cm²)	$L_p \times 10^{13}$ (cm³/dyne • sec)
	Anion exchange controls		
A3	0	0.80	4.7
A4	0	.62	4.9
		.64	4.8
			(4.8)
	Cation exchange controls		
C3	1	1.00	3.5
		0.50	3.5
		1.00	3.3
		0.72	3.3
C4	1	1.00	3.0
			(3.3)
	Mosaic membranes		
M6	0.51	1.00	3.3
		1.00	3.6*
		0.54	3.0
M7	0.48	1.00	3.0
		0.80	2.5
			(3.1)

* One experimental run with 0.14M KCl.

counted for only 1 to 2 percent of the overall flux.

The results given in Table 2 indicate that the reflection coefficients of the mosaic membranes are all negative. The proximity of some of the reflection coefficients to − 1 is fortuitous since this value, unlike + 1, has no special significance.

It can be shown, on the basis of Onsager's reciprocal relations, that membranes capable of negative osmosis may in principle be used for "piezodialysis," that is, extrusion through the membrane of a salt solution which is more concentrated than that on the high-pressure side. This process could possibly have important applications in the field of desalination, but its practicability has yet to be demonstrated. Charge-mosaic membranes may be of use in applications requiring high electrolyte permeability in an otherwise relatively impermeable structure.

Table 2. Experimentally determined values of the KC1 permeability, ω, and reflection coefficient, σ, for the mosaic and control membranes. The fraction of active membrane surface area occupied by cation exchanger, γ_c, is indicated.

Membrane	γ_c	$\omega \times 10^{15}$ (mole/dyne • sec)	σ
	Anion exchange controls		
A1	0	0.07	+ 0.43
A2	0	.05	+ .46
		.10	+ .42
	Cation exchange controls		
C1	1	.10	+ .96
C2	1	.09	+ .86
		.10	+ .88
		.13	+ .84
	Mosaic membranes		
M1	0.52	5.6	− 1.15
M2	.51	4.6	− 0.96
M3	.51	5.2	− 1.24
M4	.51	5.4	− 1.13
		4.8	− 1.04
M5	.52	5.2	− 1.07

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9. Volume flow, J_v, and salt flow, J_s, are considered positive if they take place from side I to side II of the membrane, when $\Delta p = p^{I} - p^{II}$ and $\Delta\pi = \pi^{I} - \pi^{II}$.
10. The KCl permeability obtained directly from the experiments is ω^*, defined by

$$\omega^* = \left(\frac{J_s}{\Delta\pi}\right)_{\Delta p = 0,\ I = 0}$$

Since the mean salt concentration changes only slightly during an experimental run, ω^* is assumed constant and its value calculated (with a correction for volume flow) from the relation

$$\omega^* = \frac{V}{4\,ART\ t}\ \ln\left(\frac{\Delta\pi_{\text{initial}}}{\Delta\pi_{\text{final}}}\right)$$

where A represents the active membrane area, t the time of the experiment, T the temperature, R the gas constant, and V the volume of one compartment. The parameter ω is related to ω^* by the expression

$$\omega = \omega^* + c_s L_p\, \sigma\,(1 - \sigma)$$

where c_s is the logarithmic mean of the concentrations in the two compartments. The two salt permeabilities differed by no more than 2 percent in any of the experiments reported here.
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Genetic Control of Drug Levels in Man: Antipyrine

Abstract. *Antipyrine was administered to identical or monozygotic twins and to fraternal or dizygotic twins. Individuals with identical genotypes (monozygotic twins) exhibited significantly less variability in antipyrine half-life than did genetically different individuals (dizygotic twins). Therefore variations in antipyrine metabolism appear to be determined genetically rather than environmentally. In the 36 twins tested, antipyrine half-lives varied between 5.1 and 16.7 hours. No significant correlation occurred between half-lives for phenylbutazone and antipyrine in the 28 twins who received both drugs.*

Large differences among individuals in the half-lives of phenylbutazone (*1*) and dicumarol (*2*) have been reported, but the basis for this variability remains obscure. Variability in the metabolism of antipyrine has been described in rats and in man (*4*).

This study extends previous observations of the half-life of phenylbutazone in human twins (*5*). Large variations in normal individuals not receiving other drugs depend on genetic rather than environmental factors (*5*). Since phenylbutazone is bound almost entirely to albumin (*1*), the results could not exclude individual differences in binding to albumin or in catabolism of albumin (*5*). Antipyrine was selected as the second drug because structurally it resembles phenylbutazone, both being phenylpyrazolon derivatives, but it is bound only 10 percent by albumin (*6*). Since renal excretion of antipyrine is negligible (*4*), variability in half-life suggests difference in metabolism—that is, in levels of the hepatic microsomal enzyme that hydroxylates antipyrine (*4*).

The subjects were 18 pairs of volunteer twins from the Washington, D.C., area; determined by blood grouping, nine twinships were identical and nine were fraternal. The subjects included 14 pairs who participated in an earlier study of phenylbutazone (*5*). All 36 volunteers were Caucasian, over 21 years of age, and in good health; they had not received drugs for several weeks before administration of antipyrine. The individual identical twins of six of the nine pairs studied lived in different households, so that in this respect similarity of the external environment seems an unlikely explanation for the results in identical twins.