J. Membrane Biol. 63, 93–98 (1981)

The Journal of
Membrane Biology

Potassium Transport across Rabbit Descending Colon *in Vitro*: Evidence for Single-File Diffusion through a Paracellular Pathway

Michael Fromm* and Stanley G. Schultz

Department of Physiology and Cell Biology, University of Texas Medical School at Houston, Houston, Texas 77025

Summary. The results of previous studies indicate that the bidirectional fluxes of K across short-circuited rabbit descending colon are attributable to passive diffusion through paracellular pathways and that this route is ten times more permeable to K than to Na and Cl. However, transepithelial diffusion potentials in the presence of large transepithelial Na and K concentration differences are much lower than those predicted by the "constant field equation" and appear to be inconsistent with this high K selectivity.

The results of the present studies, designed to resolve this apparent contradiction, indicate that:

(a) The ratios of the bidirectional transepithelial fluxes of K determined over a wide range of combined chemical and electrical potential differences conform reasonably well with those predicted by the Ussing flux-ratio equation.

(b) The permeability coefficient of K (P_K), determined from the net fluxes in the presence of concentration differences and from unidirectional fluxes under short-circuit conditions, decreases with increasing K concentration; in the presence of low K concentrations, P_K is approximately ten-times P_{Na}, but it approaches P_{Na} in the presence of high K concentrations. P_{Na} is not affected under these conditions.

These results provide an explanation for the failure to observe large transepithelial diffusion potentials in the presence of large transepithelial Na and K concentration differences. In addition, these results are consistent with the notion that K diffuses across this preparation through two parallel pathways, one that does not discriminate among K, Na and Cl (a "free-solution" shunt) and another that is highly K selective and involves an interaction with one, or at most two, sites along the route.

Key words: Colon, K transport, paracellular pathway, single-file diffusion

* *Present address:* Institut für Klinische Physiologie, Freie Universität Berlin, 1000 Berlin 45, F.R. Germany

Previous studies dealing with K fluxes across rabbit descending colon *in vitro* have indicated that: (i) under short-circuit conditions, the net K flux, J_K, does not differ significantly from zero (Frizzell, Koch & Schultz 1976; Frizzell & Schultz, 1978; Frizzell & Turnheim, 1978); and (ii) the apical or mucosal membrane appears to be essentially impermeable to K (Frizzell & Jennings, 1977; Schultz, 1981). On the basis of these and other observations, we concluded that transepithelial K movements take place predominantly or exclusively via paracellular pathways and that the overall permeability of this route to K is at least ten times greater than its permeability to Na and Cl (Frizzell et al., 1976). Subsequently, Wills, Lewis and Eaton (1979) questioned that notion on the basis of the observation that when the NaCl in the mucosal bathing solution alone was replaced with KCl (the serosal solution containing 136 mM Na), thereby creating large concentration differences for K and Na across the tissue, the resulting transepithelial diffusion potentials were always less than 10 mV; this value is much lower than the diffusion potential of approximately 53 mV that would be expected if the permeability of the shunt pathway to K is ten times greater than its permeabilities to Na and Cl. These findings of Wills et al. (1979) have been confirmed in this laboratory.

The present studies were undertaken in an effort to resolve this apparent contradiction.

Materials and Methods

Adult New Zealand white rabbits (2–4 kg) were sacrificed by intravenous injection of pentobarbital. A segment of descending colon was removed, opened along the mesenteric border, rinsed free of intestinal contents and stripped of the underlying musculature and connective tissues as described by Frizzell et al. (1976). Four segments of tissue from the same animal were mounted in the short-circuit apparatus described previously (Schultz & Zalusky, 1964).

The standard bathing solution contained (mM): Na, 140; Cl, 124; HCO_3, 21; K, 5.0; HPO_4, 2.4; H_2PO_4, 0.6; Ca, 1.2; Mg,

0022-2631/81/0063-0093 $01.20

1.2; and glucose, 10. This solution had a pH of 7.4 when gassed with a mixture of 95% O_2-5% CO_2 at 37 °C.

In experiments where the concentrations of K in the two bathing solutions differed, isosmolarity was maintained either by lowering the Na concentration and/or the addition of choline as described in the Results section and Tables 1 and 2. In the experiments performed under short-circuit conditions, where the K concentrations in both bathing solutions were equal and varied over the range 2–125 mM, the Na concentration in both solutions was constant at 20 mM and isosmolarity was maintained by the addition of the appropriate amount of choline; when K = 125 mM, Cl was replaced with SO_4 plus mannitol inasmuch as the preparation deteriorated rapidly in the presence of 125 mM KCl.

The electrical potential differences arising from the use of asymmetric solutions ("junction potentials") and the fluid resistance between the voltage-sensing electrodes were determined in each experiment for all combinations of solutions used. After mounting the tissues, clamp voltages were adjusted so that the true transepithelial electrical potential difference was established within ±1 mV. All clamp voltages were corrected "instantaneously" for changes in fluid resistance when bathing solutions were changed. Fluid resistances ranged 22–28 $\Omega \cdot cm^2$, and tissue resistances, corrected for the fluid resistance, averaged 171 ± 10 $\Omega \cdot cm^2$; the variation among tissues in the same experiment was always less than 25%.

Unidirectional K fluxes were determined using ^{42}K (New England Nuclear). Samples were withdrawn at 10-min intervals beginning 30 min after the addition of the isotope to ensure the achievement of a steady-state, and each unidirectional flux across a *single* tissue represents the mean of 4–5 determinations. The appearance of tracer in the unlabeled solution was linear with time during the measuring period, indicating that a steady state had, in fact, been achieved.

In one series of experiments, the unidirectional fluxes of Na from the serosal to the mucosal solution were determined simultaneously with unidirectional K fluxes as described previously (Frizzell & Schultz, 1978).

Results are expressed as the mean ± the standard error of the mean; differences were analyzed using the Student t test and a value of $P < 0.05$ was considered significant.

Results

Bidirectional K Fluxes in the Presence of Chemical and Electrical Potential Differences

The first series of experiments was designed to determine whether the bidirectional transepithelial K fluxes conform to the Ussing flux-ratio equation (Ussing, 1949) over a wide range of *combined* electrical and chemical potential differences. Three sets of experiments were performed. In the first set (I) the K concentration of the mucosal solution alone, $[K]_m$, was reduced from 5 to 2 mM by replacing 3 mM KCl with choline-Cl and the bidirectional K fluxes were determined when the transepithelial electrical potential difference, ψ^{ms}, was clamped at +50, +30, 0, −30 and −50 mV.[1] The second set (II) differed only in that the mucosal solution contained 47 mM K and 98 mM Na and the serosal solution contained 125 mM K and 20 mM Na so that the sum of Na *plus* K in both solutions remained 145 mM. In the third set (III), the mucosal solution contained 47 mM K, 20 mM Na and 78 mM choline whereas the serosal solution contained 125 mM K and 20 mM Na.

Thus, the difference between set I and sets II and III is that whereas the concentration *ratio* of K across the tissue is essentially the same (i.e., $([K]_m/[K]_s) = 0.4$) the transepithelial K concentration *difference* in set I was 3 mM while the transepithelial K concentration *difference* in sets II and III was 78 mM. The difference between sets II and III is that in the former the Na concentration in the bathing solutions differed whereas in the latter it was equal at 20 mM.

The results of these studies are given in Table 1, where J_K^{ms} is the unidirectional flux of K from the mucosal solution to the serosal solution, J_K^{sm} is the unidirectional flux in the opposite direction, and J_K is the net flux given by $J_K^{ms} - J_K^{sm}$.

The observed ratio of (J_K^{ms}/J_K^{sm}) is plotted against the ratio predicted by the Ussing flux-ratio equation (Ussing, 1949) in Fig. 1 clearly, there is reasonable agreement between the observed and predicted ratios over a 40-fold range. There appears to be a systematic departure from the line of identity when $\psi^{ms} = +30$ mV and +50 mV, for which we have no explanation at this time. There is certainly no evidence for active K secretion as reported by others (Yorio & Bentley, 1978; Wills & Biagi, 1980); if anything, the departures from the line of identity are consistent with a nondiffusional absorptive component.

The net fluxes of K, given in Table 1, are plotted as functions of ψ^{ms} in Fig. 2. When $[K]_m = 2$ mM and $[K]_s = 5$ mM, the relation between J_K and ψ^{ms} is almost linear. However, when $[K]_m = 47$ mM and $[K]_s = 125$ mM, this relation is decidedly nonlinear; the rationale for the curve fitted to these data points will be discussed below.

The values of the transepithelial K permeability coefficient, P_K, when $\psi^{ms} = 0$, can be determined from the relation

$$P_K = J_K/([K]_m - [K]_s).$$

For the experiments in sets I, II and III, P_K (in cm/hr) averaged 0.15 ± 0.2, 0.015 ± 0.006, and 0.012 ± 0.003, respectively. Thus, when $[K]_m = 47$ mM and $[K]_s = 125$ mM [sets II and III)], P_K is approximately one-tenth of that observed when $[K]_m = 2$ mM and $[K]_s = 5$ mM [set I]; the value of P_K observed in set I does not differ significantly from that reported by Frizzell et al. (1976) (0.12 ± 0.02 cm/hr).

[1] ψ^{ms} was clamped at these values in a pseudo-random order. In each instance, the first clamping-voltage was repeated at the end of the experiment (e.g., $\psi^{ms} = +50$, 0, −50, +50 mV; or $\psi^{ms} =$ 0, −30, +30, 0 mV). In no instance did the fluxes obtained during the first clamping period differ significantly from those obtained during the final (time-control) period.

Table 1. Bidirectional K fluxes in the presence of transepithelial electrochemical potential differences

Compositions (mM)			n	Fluxes	ψ^{ms}				
	M	S			+50 mV	+30 mV	0 mV	−30 mV	−50 mV
[K]	2	5		J_K^{ms}	0.13±0.02	0.17±0.02	0.22±0.02	0.26±0.03	0.37±0.04
[Na]	140	140	14	J_K^{sm}	1.34±0.09	1.05±0.13	0.66±0.05	0.27±0.03	0.19±0.02
[Choline]	3	0		J_K	−1.21±0.10	−0.89±0.13	−0.44±0.05	−0.02±0.04	0.17±0.05
[K]	47	125		J_K^{ms}	0.99±0.06	1.23±0.10	1.86±0.07	2.83±0.22	5.67±0.86
[Na]	98	20	6	J_K^{sm}	8.56±1.0	5.83±0.49	3.04±0.44	1.90±0.19	1.87±0.24
[Choline]	0	0		J_K	−7.57±1.0	−4.60±0.50	−1.18±0.45	0.93±0.29	3.81±0.90
[K]	47	125		J_K^{ms}	1.16±0.18	1.12±0.11	2.01±0.16	3.83±0.21	6.62±0.91
[Na]	20	20	6	J_K^{sm}	7.84±0.46	5.02±0.42	2.96±0.19	2.19±0.32	1.95±0.19
[Choline]	78	0		J_K	−6.68±0.49	−3.90±0.43	−0.95±0.25	1.64±0.38	4.67±0.93

M and S designate the mucosal and serosal solutions; all fluxes are in μeq/cm² hr; n is the number of experiments at each point in the grid.

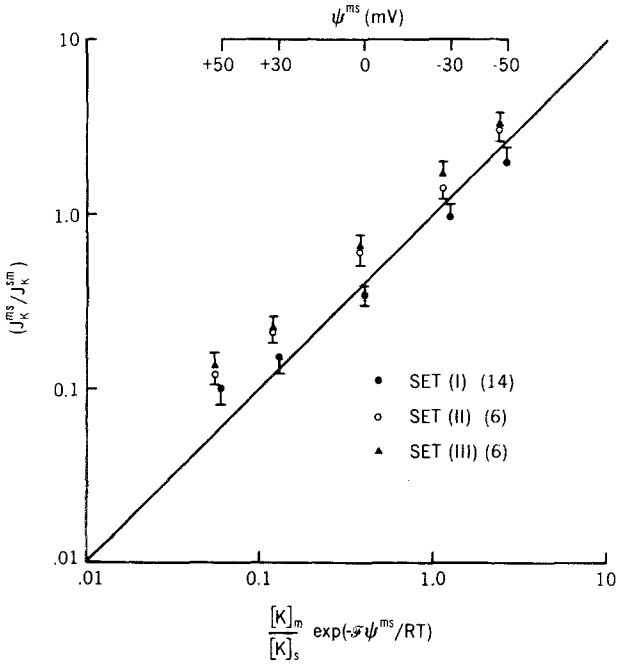

Fig. 1. The observed flux-ratio (J_K^{ms}/J_K^{sm}) on the ordinate *vs.* the flux-ratio predicted by the Ussing equation on the abscissa in the presence of combined chemical and electrical potential differences. The clamping voltages corresponding to each set of data points are shown above

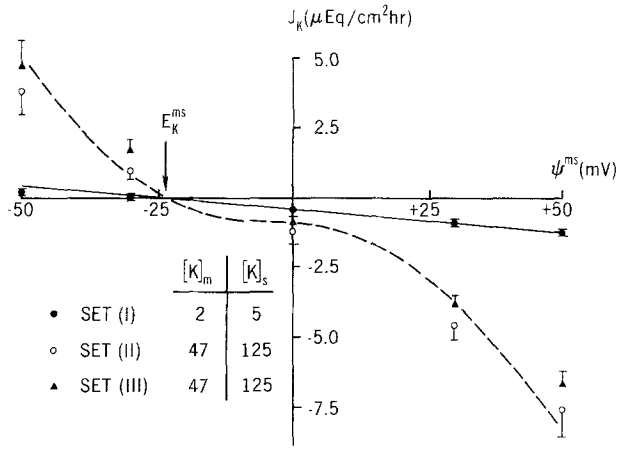

Fig. 2. The net flux of K, J_K, as a function of ψ^{ms} from the data given in Table 1. The dashed curve was drawn by eye with the sole constraint that it pass through the "reversal potential," E_K^{ms}, as discussed in the text

In order to determine whether the decrease in P_K observed in the presence of high K concentrations is specific or whether it can be attributed to some nonspecific effect on the tissue (e.g., cell swelling and narrowing of the paracellular spaces), a series of experiments was performed in which the bidirectional fluxes of K were determined in the presence of two concentration differences and the unidirectional flux of Na from the serosal solution to the mucosal solution, J_{Na}^{sm}, was determined simultaneously on the same tissues. In these experiments, ψ^{ms} was clamped at 0 mV. These results are given in Table 2.

Clearly, the data obtained in this series for J_K^{ms}, J_K^{sm} and J_K are in excellent agreement with those given in Table 1. Once again, there was a tenfold decrease in P_K in the presence of the higher K concentration. However, P_{Na} given by ($J_{Na}^{sm}/[Na]_s$) did not differ significantly under these conditions and is in reasonable agreement with the value of 0.01 cm/hr reported by Frizzell et al. (1976).

Thus, we conclude that the decrease in P_K cannot be attributed to an entirely nonspecific effect of high K concentrations on the tissue. Because there is good reason to believe that the bidirectional K fluxes and the serosa-to-mucosa flux of Na are largely restricted to the paracellular route, we can further conclude that the permeability of this pathway to K, but not to Na, is concentration-dependent.

Table 2. Simultaneous K and Na fluxes when the transepithelial electrical potential difference is clamped at zero

	Compositions (mM)			
	M	*S*	*M*	*S*
[K]	2	5	47	125
[Na]	140	140	20	20
[Choline]	3	0	78	0
J_K^{ms}	0.20 ±0.03		1.99 ±0.10	
J_K^{sm}	0.61 ±0.05		2.92 ±0.18	
J_K	−0.41 ±0.05		−0.93 ±0.21	
J_{Na}^{sm}	2.24 ±0.25		0.25 ±0.02	
P_K	0.132±0.018		0.012±0.003	
P_{Na}	0.016±0.002		0.013±0.001	

Fluxes are in μeq/cm² hr; *P* in cm/hr; values are the results of experiments on 6 tissues.

Table 3. Unidirectional K fluxes under short-circuit conditions

	2 mM	5 mM	15 mM	45 mM	125 mM
$\bar{J}_K$ (μeq/cm²hr)	0.22 ±0.02	0.39 ±0.06	0.70 ±0.13	1.66 ±0.31	3.39 ±0.60
P_K (cm/hr)	0.110	0.078	0.046	0.035	0.027

$\bar{J}$ is the average of six unidirectional fluxes at each concentration.

Bidirectional K Fluxes Under Short-Circuit Conditions

In the studies described above, P_K was calculated from the net flux in the presence of a transepithelial K concentration difference when $\psi^{ms}=0$ mV. This final series of studies was carried out under short-circuit conditions and bidirectional K fluxes were determined when *both* bathing solutions contained 2, 5, 15, 47 or 125 mM K.[2] P_K was calculated from the average of the unidirectional fluxes at each concentration.

The results are given in Table 3 and illustrated in Fig. 3. Clearly, there is a large decrease in P_K over the range K = 2 mM to K = 15 mM and a smaller, but significant, decline thereafter.

Conclusions

The results of these studies appear to resolve a conflict in the literature and disclose an interesting and unexpected property of the pathway(s) for K diffusion across rabbit descending colon, *in vitro*.

[2] In each tissue, fluxes were determined in the presence of 3–4 different K concentrations applied in pseudo-random order. In each instance, the first concentration was repeated at the end of the experiment (e.g., [K]=15, 2, 47, 15 mM; or [K]=2, 47, 125, 2 mM). In no case did the fluxes determined during the first period differ significantly from those determined during the final (time-control) period.

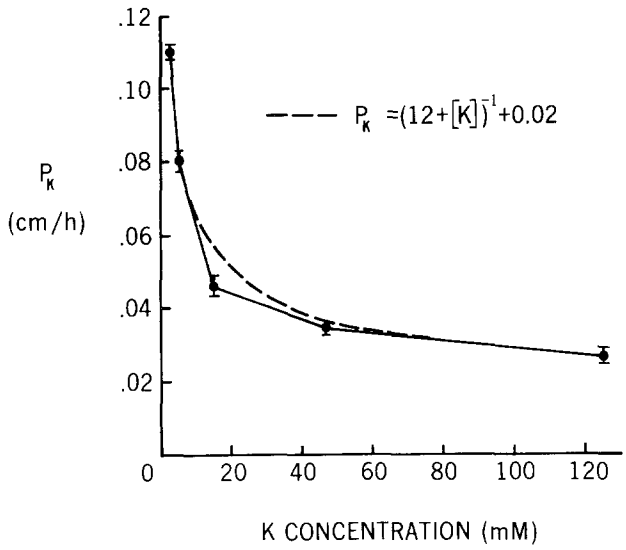

Fig. 3. P_K *vs.* the K concentration in both bathing media determined from the unidirectional fluxes of ^{42}K under short-circuit conditions. The dashed curve, given by the equation $P_K=[(12+K)^{-1}+0.02]$ passes through all points but one

Let us first summarize our reasons for believing that transepithelial K movements across this preparation are restricted, within the limits of experimental error, to paracellular routes. First, under short-circuit conditions (in the absence or presence of aldosterone), J_K does not differ significantly from zero (Frizzell et al., 1976; Frizzell & Schultz, 1978; Frizzell & Turnheim, 1978). Second, although cell K rapidly exchanges with ^{42}K in the serosal bathing solution, exchange with ^{42}K in the mucosal solution is extremely slow; after 1 hr only 5% of cell K exchanges with ^{42}K in the mucosal solution and this is likely to be an overestimate inasmuch as during this time some ^{42}K must have gained access to the serosal solution via the paracellular (junctional) route and could have been taken up across the basolateral membranes (Frizzell & Jennings, 1977; Schultz, 1981). Third, electrophysiological studies have shown that the electrical potential difference across the apical membrane is not significantly affected by sudden changes in the K concentration in the mucosal solution (Y. Suzuki and S.G. Schultz, *unpublished observations*). Fourth, K secretion can be elicited by the addition of amphotericin B to the mucosal solution (Frizzell & Schultz, 1978), supporting the notion that the absence of K secretion under control conditions is due to the fact that, normally, the apical membrane is essentially impermeable to that cation. Finally, the present results disclose reasonable agreement over a wide range between the observed flux-ratio and that predicted by the Ussing flux ratio equation for a strictly diffusional process.

All of these findings are consistent with the notion that, normally, transepithelial K movements are diffusional and by-pass the absorptive cells.

Frizzell et al. (1976) calculated P_K from the bidirectional fluxes of K under short-circuit conditions as well as from the relation between J_K^{sm} and ψ^{ms} when the latter was clamped at +50, 0, and −50 mV; in all experiments, both bathing solutions contained 5 mM K. They concluded that, under these conditions, P_K was at least ten times greater than the value of P_{Na} determined from measurements of J_{Na}^{sm} assuming that this movement is, for the most part, also paracellular. As discussed above, Wills et al. (1979) questioned this conclusion on the grounds that transepithelial diffusion potentials observed in the presence of large transepithelial difference in Na and K concentrations were much smaller than those which would be predicted if P_K were much larger than P_{Na}. We have confirmed the observation of Wills et al. (1979) over a wide range of transepithelial Na and K gradients; in all instances, the observed diffusion potentials were less than 10 mV regardless of the size or orientation of these gradients.

However, when diffusion potentials (bionic or multi-ionic) are used to estimate membrane permeabilities, the implicit assumption is that the permeabilities are not affected by the experimental manipulation and, in particular, that the permeabilities are concentration-independent. In the case of a complex barrier, concentration-independent permeabilities are likely to be the exception rather than the rule (Adrian, 1969). The results of the present studies indicate conclusively that P_K is strongly dependent upon concentration. In the presence of low K concentrations (2–5 mM), P_K is much greater than P_{Na} but it declines very sharply and approaches P_{Na} with increasing K concentration. These findings are consistent with, and provide a reasonable explanation for, the failure to find large diffusion potentials in the presence of large transepithelial K (and Na) concentration differences.

We now explore, briefly, the simplest model for transepithelial K diffusion consistent with our observations. The two pivotal observations that must be accommodated by any such model are: (i) the observed flux ratio, (J_K^{ms}/J_K^{sm}) conforms reasonably well with the predictions of the Ussing flux-ratio equation; and (ii) P_K decreases with increasing K concentration. The simplest model consistent with these two findings is one in which every K ion crossing the membrane in either direction must interact with (bind to) a single site in its path. Complete, formal descriptions of this so-called two-barrier, one-site model derived employing the Eyring rate theory have been given elsewhere (Hille, 1975; Schultz, 1980). The essential predictions of this model, for the present purposes, are:

(a) The permeability coefficient determined from unidirectional fluxes under short-circuit conditions will decrease hyperbolically (i.e., the unidirectional flux saturates) with increasing concentration (*see* Eq. (2.44) in Schultz, 1980). The dashed curve illustrated in Fig. 3 conforms to the equation $P_K=[(12+[K])^{-1}+0.02]$ (cm/hr) and is consistent with a model in which K diffuses through a simple pathway in which P_K is independent of concentration (=0.02 cm/hr) and a parallel pathway in which it must interact with a single site. This notion will be discussed further below.

(b) The current-voltage relations predicted by this model are, in general, described by a family of hyperbolic sine functions and, thus, have an antisymmetric shape with maximum currents or maximum conductances at extreme voltages (Hille, 1975; Hall, Mead & Szabo 1973; Kohler & Heckmann, 1979; Hladky, 1974). When the concentrations on both sides of the membrane are equal, these curves are antisymmetric about the origin. The dashed curve shown in Fig. 2 was drawn by eye to provide a reasonable description of the experimental data with the restriction that the value of ψ^{ms} when $J_K=0$ (the "reversal potential") is given by $(RT/F)\ln(0.4)=24$ mV; this is the sole thermodynamic constraint on any strictly diffusional system. The solid line through the points when $[K]_m=2$ mM and $[K]_s=5$ mM (set I) conforms to this restriction.[3] Obviously, other curves could be drawn through the experimental data so that we do not wish to emphasize the quantitative aspects of the curve chosen; nonetheless, it should be clear that the data are distributed antisymmetrically about the axes as predicted by a two-barrier, one-site model. These data certainly cannot be fit by the current-voltage relation predicted by the Goldman-Hodgkin-Katz flux equation (Goldman, 1943; Hodgkin & Katz, 1949) which assumes a constant (concentration- and voltage-independent) permeability coefficient.

We now inquire: Could a more complex system such as a multisite, single-file diffusion pathway satisfy these data? The limiting observation with regard to this question is the conformity of the data with the Ussing flux ratio equation. As discussed by many, but most recently by Kohler and Heckmann (1979), the general form of the flux ratio equation for single-file diffusion through a pore is (using our notation):

$$(J_K^{ms}/J_K^{sm})=[([K]_m/[K]_s)\exp(-F\psi^{ms}/RT)]^n$$

where n is *related* to the number of "sites" or K ions in single-file within the pore. If there are m sites, then the minimum and maximum values of n are

[3] This finding adds to the body of evidence that transepithelial K transport across this preparation is strictly diffusional.

$m-1$ and m, respectively. Now, it can be readily shown that for any integral value of n greater than 1, the experimental data plotted in Fig. 1 would depart markedly from the predicted values. Thus, our experimental data, according to this analysis, are most consistent with a single-site pore but could be satisfied by a pathway that can accommodate two K ions in single-file diffusion. A model that involves the obligatory single-file diffusion of more than two K ions per pore would seem to be excluded.

As pointed out above, the analysis of the data illustrated in Fig. 3 suggests that there are two parallel pathways for K diffusion across this epithelium; one in which P_K is strongly concentration dependent and another in which P_K is constant at a value (in these studies) of 0.02 cm/hr. As indicated in Table 2, P_{Na} averaged approximately 0.014 cm/hr. It is of interest that the ratio of the free solution mobilities of Na and K, $\lambda_{Na}/\lambda_K=0.7$, is in excellent agreement with the ratio of P_{Na} to the K permeability of the concentration-independent pathway. Further, Frizzell et al. (1976) demonstrated that P_{Na}/P_{Cl} for the passive conductive pathway(s) across this preparation is equal to the free-solution mobility ratio $\lambda_{Na}/\lambda_{Cl}$. Taken together, these findings suggest the presence of a nonselective paracellular pathway that does not discriminate between Na, K and Cl (a "free-solution" shunt)[4] in parallel with a concentration-dependent K selective pathway. Clearly, additional studies are necessary to test this notion.

Finally, as discussed elsewhere (Schultz, 1981), under physiological conditions mammalian colon, *in vivo*, secretes K and the rate of secretion is increased by mineralocorticoids such as aldosterone. We have argued that, for the cases of *in vivo* rat and *in vitro* rabbit colon, K secretion is a passive process driven by the transepithelial electrical potential difference which, in turn, is the result of active Na absorption (Frizzell & Schultz, 1978; M. Fromm & U. Hegel, *unpublished observations*). If this argument is correct[5], the presence of a K-selective paracellular pathway is ideally suited to subserve this physiological function and the concentration-dependence of P_K would serve as a negative-feedback regulatory mechanism that could prevent excessive K secretion by this "passive" process.

[4] The "free-solution" shunt could be, in part, due to "edge damage." Barry, Diamond and Wright (1971) have suggested the presence of such a shunt in rabbit gallbladder which develops with time after mounting the tissue and a similar finding has been reported for frog gallbladder (Moreno & Diamond, 1975).

[5] Yorio and Bentley (1977) and Wills and Biagi (1980) have presented evidence for active K secretion across short-circuited segments of rabbit descending colon. However, in four separate studies between 1976–1980 involving different investigators and/or technical assistants (i.e., Frizzell et al., 1976; Frizzell & Schultz, 1978; Frizzell & Turnheim, 1978; and the present study), we have not detected a statistically significant level of K secretion by this tissue under short-circuit conditions, and all of our findings are consistent with a strictly diffusional process. We cannot offer a definitive explanation for these discrepant findings. Clearly, the tissue is "poised" to actively secrete K, and whether or not significant active secretion takes place will depend upon the permeability of the apical membrane to this cation (Schultz, 1981). Currently, we cannot speculate how, or if, this permeability is regulated.

References

Adrian, R.H. 1969. Rectification in muscle membrane. *Prog. Biophys. Mol Biol.* **19**:339–369

Barry, P.H., Diamond, J.M., Wright, E.M. 1971. The mechanism of cation permeation in rabbit gallbladder. *J. Membrane Biol.* **4**:358–394

Frizzell, R.A., Jennings, B. 1977. Potassium influx across basolateral membranes of rabbit colon: Relation to sodium absorption. *Fed. Proc.* **36**:360

Frizzell, R.A., Koch, M.J., Schultz, S.G. 1976. Ion transport by rabbit colon. I. Active and passive components. *J. Membrane Biol.* **27**:297–316

Frizzell, R.A., Schultz, S.G. 1978. Effect of aldosterone on ion transport by rabbit colon, *in vitro*. *J. Membrane Biol.* **39**:1–26

Frizzell, R.A., Turheim, K. 1978. Ion transport by rabbit colon: II. Unidirectional sodium influx and the effects of amphotericin B and amiloride. *J. Membrane Biol.* **40**:193–211

Goldman, D.E. 1943. Potential, impedance and rectification in membranes. *J. Gen. Physiol.* **27**:37–60

Hall, J.E., Mead, C.A., Szabo, G. 1973. A barrier model for current flow in lipid bilayer membranes. *J. Membrane Biol.* **11**:75–97

Hille, B. 1975. Ionic selectivity of Na and K channels of nerve membrane. *In:* Membranes—A Series of Advances. G. Eisenman, editor. Vol. 3, pp. 255–323. Marcel Dekker, New York

Hladky, S.B. 1974. Pore or carrier? Gramicidin A as a simple pore. *In:* Drugs and Transport Processes. B.A. Callingham, editor) p. 193. University Park Press, Baltimore

Hodgkin, A.L., Katz, B. 1949. The effect of sodium ions on the electrical activity of the giant axon of the squid. *J. Physiol. (London)* **108**:37–77

Kohler, H.H., Heckmann, K. 1979. Unidirectional fluxes in saturated single-file pores of biological and artificial membranes. I. Pores containing no more than one vacancy. *J. Theor. Biol.* **79**:381–401

Moreno, J.H., Diamond, J.M. 1975. Cation permation mechanisms and cation selectivity in "tight junctions" of gallbladder epithelium. *In:* Membranes—A Series of Advances. G. Eisenman, editor. Marcel Dekker, New York

Schultz, S.G. 1980. Basic Principles of Membrane Transport. Cambridge University Press, New York

Schultz, S.G. 1981. Potassium transport by rabbit descending colon *in vitro*. *Fed. Proc.* **40**:2408–2411

Schultz, S.G., Zalusky, R. 1964. Ion transport in rabbit ileum. I. Short-circuit current and Na fluxes. *J. Gen. Physiol.* **47**:567–584

Ussing, H.H. 1949. The distinction by means of tracers between active transport and diffusion. *Acta Physiol. Scand.* **19**:43–56

Wills, N.K., Biagi, B. 1980. Evidence for active K transport across rabbit descending colon. *J. Gen. Physiol.* **76**:12a

Wills, N.K., Lewis, S.A., Eaton, D.C. 1979. Active and passive properties of rabbit descending colon: A microelectrode and nystatin study. *J. Membrane Biol.* **45**:81–108

Yorio, T., Bentley, P.J. 1977. The permeability of the rabbit colon *in vitro*. *Am J. Physiol.* **232(1)**:*F5–F9*

Received 12 March 1981; revised 19 May 1981