TECHNICAL NOTE

Computation of the osmotic water permeability of perfused tubule segments

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The development of *in vitro* perfusion of isolated segments of the nephron [1] has made the evaluation of tubular functions more precise than was previously possible. The measurement of fluid and solute transport rates is more accurate as the perfusion rate and the composition of the bath and perfusion solutions can be better controlled. These techniques have been used to measure the water permeabilities of different nephron segments [2–5].

The hydraulic conductivity is calculated by the following formula:

$$L_p = \dot{V}_r / \sigma S \overline{\Delta\pi} \qquad (1)$$

where $\dot{V}_r$ is the reabsorbed volume per minute (positive for water leaving the lumen); S, the area of the membrane; σ, the reflection coefficient of the solute; and $\overline{\Delta\pi}$ is the integrated mean difference between the osmotic pressures of the bath (π_b) and of the luminal fluid (π). Several approximations of $\overline{\Delta\pi}$ have been used. Grantham and Orloff [2] have used the arithmetic mean of the osmotic pressure differences:

$$\Delta\pi_a = (\Delta\pi_i + \Delta\pi_f) / 2. \qquad (2)$$

The subscripts i and f represent the values of the variables, respectively, at the perfusing and collecting ends. Kokko [3] and Abramow [4] have used a logarithmic mean:

$$\Delta\pi_1 = \exp\left[(\ln\Delta\pi_i + \ln\Delta\pi_f) / 2\right]. \qquad (3)$$

Schafer and Andreoli [5] approximate $\overline{\Delta\pi}$ by the following formula:

$$\Delta\pi_S = \pi_b - \exp\left[(\ln\pi_i + \ln\pi_f) / 2\right]. \qquad (4)$$

In the present paper, we present an equation which allows the exact computation of L_p and $\overline{\Delta\pi}$ when $\sigma = 1$. It will be shown that calculations of L_p based

either on the arithmetic or on the logarithmic means may give values which are significantly different from the exact analytical solution. The need to take into account the nonlinear osmotic pressure profile has been recognized previously for the *in vivo* measurement of the water permeability of glomerular [6, 7] and peritubular [8] capillaries. In these more general derivations, hydrostatic pressures were considered in addition to osmotic pressures; the resulting differential equation could only be solved by numerical methods. In the case of perfused tubules, the osmotic pressures are orders of magnitude greater than the hydrostatic pressures; the latter can thus be neglected. With this approximation, the equation can be solved analytically.

Description of the model. The tubule segment is approximated by a cylinder of length, L; the x coordinate is aligned along the cylinder's axis; the surface, S, of the segment has a uniform L_p. We assume that π_b is constant (bath perfectly mixed) and that π varies only axially. When $\sigma = 1$, as assumed in this study, the solute mass flow in the cylinder, $\dot{V}C$, is constant ($\dot{V}$ is the waterflow per minute and C the osmolality of the luminal fluid). The effect of unstirred layers is neglected.

The volume of water reabsorbed per minute in a small annular segment of length, dx, is equal to the change in the volume flow rate between points x + dx and x. According to Eq. 1,

$$d\dot{V} / dx = L_p S (\pi - \pi_b) / L. \qquad (5)$$

As π is proportional to C, we can write $\pi_b = RT C_b$ and $\pi = RTC = RT C_i \dot{V}_i / \dot{V}$, where C_b is the osmolality of the bath; R, the ideal gas constant; and T, the absolute temperature. Eq. 5 becomes

$$d\dot{V} / dx = R T L_p S (C_i \dot{V}_i / \dot{V} - C_b) / L; \qquad (6)$$

after separating the variables, both sides of Eq. 6 can be integrated using standard formulas [9]; the following solution is found:

$$L_p = \frac{1}{RT\,S\,C_b^2}\,[C_b\,(\dot{V}_i - \dot{V}_f) + C_i\,\dot{V}_i\,[ln\,(C_b$$

$$- C_i)\,\dot{V}_i - ln\,(C_b\,\dot{V}_f - C_i\,\dot{V}_i)].$$

$$(7)$$

Despite the apparent complexity of this formula, it can be used conveniently with any scientific calculator. The exact integrated mean osmotic pressure difference, $\overline{\Delta\pi}$, can be calculated using Eq 1.

Discussion. To illustrate the differences between the different methods, L_p was calculated for several values of $\dot{V}_r$ from Eq. 1, with $\overline{\Delta\pi}$ being given the values $\Delta\pi_a$, $\Delta\pi_i$ and $\Delta\pi_s$; L_p was also calculated from Eq. 7. $\dot{V}_i$, π_b, π_i and the surface area of the luminal membrane, S, are given realistic values (data are from Kokko [3]). The results of the simulation are shown in Fig. 1.

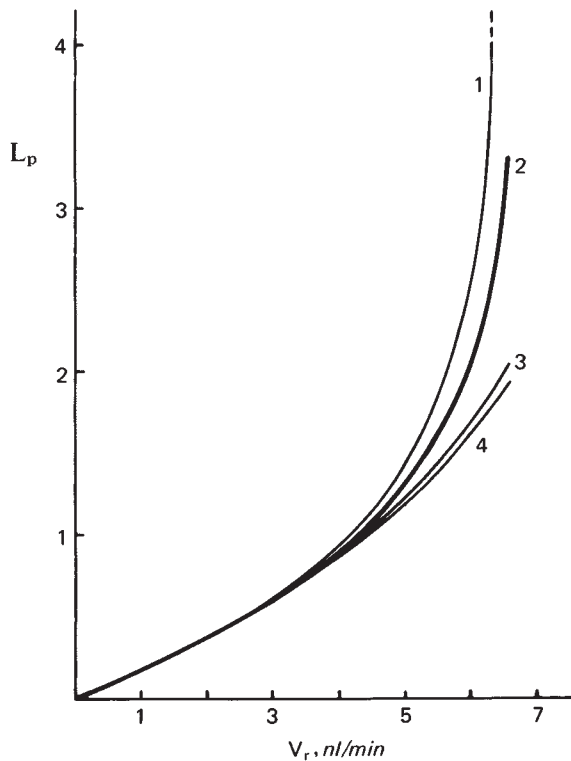For low values of $\dot{V}_r$, π hardly changes along the

Fig. 1. *Comparison between the values of Lp calculated by the different methods discussed in the text.* Data are taken from Kokko [3]: $\dot{V}_i = 28.1$ nl/min, $\pi_b = 407$ mOsm/kg H_2O, $\pi_i = 309$ mOsm/kg H_2O and $S = 4.18 \times 10^{-4}$ cm². $\dot{V}_r$ cannot exceed 6.766 nl/min; this value corresponds to osmotic equilibration at the collecting end. On the abscissa, $\dot{V}_r$ varies between 0 and 6.6 nl/min. Curve 1 corresponds to the logarithmic mean, Eq 2; curve 2 to the "exact" solution, Eq. 7; curve 3 to the arithmetic mean, Eq. 3; and curve 4 to Eq. 4. L_p is expressed in ml sec^{-1} atm^{-1} cm^{-2} × 10^{-4}.

tubule segment and the four methods give essentially identical results. However, for higher values of $\dot{V}_r$, π_i and π_f are very different and the values of L_p differ strongly. The model shows that $\dot{V}_r$ cannot exceed a finite value which corresponds to osmotic equilibration at the end of the tubule segment: $\pi_b = \pi_f$. When this condition obtains, an increase of L_p does not increase $\dot{V}_r$.

It is apparent that, under conditions approaching osmotic equilibration, the accuracy of the determination of L_p becomes unsatisfactory, since a small experimental error in the determination of $\dot{V}_r$ gives a huge error on L_p.

In conclusion, we think that the calculation of L_p based on Eq. 7 should be preferred to the methods currently in use. The latter have no theoretical basis. In addition, we have drawn the attention on the necessity of carrying out experimental determinations of L_p under conditions sufficiently remote from osmotic equilibration at the collecting end of the perfused segment.

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