SUPPLEMENTARY MATERIAL

In-Vivo Corneal Oxygen Uptake During Soft-Contact-Lens Wear

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Appendix B. POS Directly Applied to Soft Contact Lens

Measurement of oxygen uptake into the cornea with SCL wear can be obtained by placing the POS directly onto the lens rather than by removing the lens and placing the POS onto the cornea. However, the underlying quantitative model is more involved. This appendix presents the requisite analysis.

Fig. B1 shows expected transient oxygen partial-pressure profiles upon placing the Clark-electrode probe onto the SCL. The main difference between Fig. B1 and Fig. 1 of the text is the presence of the SCL between the POS membrane and the cornea. \( x = -L_L \) in Fig. B1 corresponds to the membrane/SCL interface, \( x = 0 \) corresponds to the SCL/anterior cornea interface, and \( x = L \) specifies the posterior cornea/anterior chamber interface. Oxygen concentration at the electrode surface \( (x = -L_L - L_m) \) is zero because of the limiting-current condition.

Dashed profiles in Fig. B1 correspond to early time when the probe is first placed onto the SCL and for which the measured electrode current does not reflect oxygen tension. Once pseudo-steady state is achieved for times exceeding \( L_m^2 / D_m \), tension profiles in the membrane are linear (solid lines for \( P_m(t,x) \) in Fig. B1), and the pre-calibrated POS signal corresponds to oxygen tension at the anterior lens surface (filled circles at \( x = -L_L \) in Fig. B1). Remaining features of Fig. B1 are similar to those for Fig. 1 described in the text.

We desire to obtain the flux of oxygen into the anterior cornea during steady SCL wear from the POS measurement. That is, we must relate the measured tensions, \( P_L(t,-L_L) \), at pseudo-
steady state in Fig. B1 to the initial oxygen flux into the cornea $J_o(0)$. For the covering membrane where there is no oxygen reaction, application of Fick’s second law in the pseudo-

![Diagram](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933469/)  

**Figure B1.** Qualitative illustration of transient oxygen tension profiles upon placing the POS onto a SCL worn on the cornea. Solid curves represent transient oxygen-tension profiles in the covering membrane, $P_m(t,x)$, of thickness, $L_m$, the SCL, $P_L(t,x)$, of thickness, $L_L$, and the cornea, $P(t,x)$, of thickness, $L$. The initial steady-state oxygen profile before POS emplacement is demarked by $P_L(0,x)$ and $P(0,x)$. Dashed curves show the early time profiles before membrane pseudo-steady state is established. Filled circles along the membrane/anterior SCL interface at $x = -L_L$ represent the measured POS tension data. The dashed line with an arrow denotes progression of time.

steady state gives $P_m(t,x)$, the local oxygen partial pressure in the membrane:
\[ P_m(t,x) = P_L(t, -L_L) \left( 1 + \frac{x + L_L}{L_m} \right) \]  

(B1)

where \( x \) is the 1D rectilinear coordinate and \( L_m \) is the thickness of the membrane. Eq. B1 holds only when the membrane is at pseudo-steady state, or for measurement times longer than \( L_m^2 / D_m \).

In the SCL, diffusion of oxygen follows Fick’s second law

\[ \frac{\partial P_L(t,x)}{\partial t} = D_L \frac{\partial^2 P_L(t,x)}{\partial x^2} \]  

(B2)

where \( D_L \) is the diffusivity of oxygen in the cornea and \( L_L \) is the lens thickness. For the cornea, oxygen mass conservation demands that

\[ k \frac{\partial P(t,x)}{\partial t} = Dk \frac{\partial^2 P(t,x)}{\partial x^2} - k_i P \]  

(B3)

where \( k \) and \( D \) are the partition coefficient and diffusivity of oxygen in the cornea, respectively, and \( k_i \) is the first-order oxygen-consumption rate constant or the zero-tension slope of the Monod rate expression. In the present analysis, we average these parameters over the three layers of the cornea.

To obtain oxygen uptake with contact-lens wear from the POS-measured tensions, we seek solution to Eqs. B1 – B3. Initial conditions for Eqs. B2 and B3 are the initial steady profiles in the cornea and SCL obtained in Appendix A with a fixed anterior SCL partial pressure \( P_o (= 155 \text{ mm Hg for open eye}) \). These are given in Eqs. A1 and A2 of Appendix A. Boundary conditions are that the oxygen tension at the electrode surface is zero, that the partial pressure
and flux of oxygen at the membrane/SCL and SCL/epithelium interfaces are continuous, and that
the endothelium/anterior-chamber interface is fixed at $P_{AC} (= 24 \text{ mm Hg})$

$$P_m(t, -(L_L+L_m)) = 0, \quad (B4)$$

$$P_m(t, -L_L) = P_L(t, -L_L), \quad (B5)$$

$$D_m k_m \left( \frac{\partial P_m(t, -L_L)}{\partial x} \right) = D_L k_L \left( \frac{\partial P_L(t, -L_L)}{\partial x} \right), \quad (B6)$$

$$P_L(t,0) = P(t,0), \quad (B7)$$

$$D_L k_L \left( \frac{\partial P_L(t,0)}{\partial x} \right) = D k \left( \frac{\partial P(t,0)}{\partial x} \right), \quad (B8)$$

and

$$P(t,L) = P_{AC}, \quad (B9)$$

Eq. B4 reflects the limiting-current condition of zero oxygen concentration at the cathode.63-65

The system is converted into ordinary differential equations and boundary conditions by
Laplace transform.74, 75 Eqs. B1 – B3 become, respectively,

$$\overline{P}_m(s,x) = \overline{P}_L(s,-L_L) \left( 1 + x/(L_m + L_L) \right), $$

$$s \overline{P}_L(s,x) - P_L(0,x) = D_L \frac{\partial^2 \overline{P}_L(s,x)}{\partial x^2}, \quad (B11)$$

and

$$s \overline{P}(s,x) - P(0,x) = \frac{D}{k} \frac{\partial^2 \overline{P}(s,x)}{\partial x^2} - \left(k_i/k\right)\overline{P}(s,x). \quad (B12)$$
where \( s \) is the Laplace variable, overbars on the partial pressures indicate Laplace space, and \( P_L(0,x) \) and \( P(0,x) \) are given in Eqs. A1 and A2.

Corresponding boundary conditions for Eqs. B4 – B9 in the Laplace domain are

\[
\bar{P}_m(s,-(L_L + L_m)) = 0, \quad (B13)
\]

\[
\bar{P}_m(s,-L_L) = \bar{P}_L(s,-L_L), \quad (B14)
\]

\[
D_m k_m \left( \frac{\partial \bar{P}_m(s,-L_L)}{\partial \chi} \right) = D_L k_L \left( \frac{\partial \bar{P}_L(s,-L_L)}{\partial \chi} \right), \quad (B15)
\]

\[
\bar{P}_L(s,0) = \bar{P}(s,0), \quad (B16)
\]

\[
D_L k_L \left( \frac{\partial \bar{P}_L(s,0)}{\partial \chi} \right) = Dk \left( \frac{\partial \bar{P}(s,0)}{\partial \chi} \right), \quad (B17)
\]

and

\[
\bar{P}(s,L) = P_{AC} / s. \quad (B18)
\]

Since the initial oxygen flux into the electrode is given by \( J_m(0) = -D_m k_m P_o / L_m \) and since \( J_o(0) \) obeys Eq. 1, solution to Eq. B10 evaluated at \( x = -L_L \) is

\[
\bar{P}_m(s,-L_L) = \frac{-J_m(0) \left( \frac{L_m}{D_m k_m} \right) + J_o(0) \left( \frac{L_L}{D_L k_L} \right)}{s \left( 1 + \left( \frac{D_m k_m L_L}{D_L k_L L_m} \right) \Lambda \sqrt{D_L / s L_L^2} \right)} \quad (B19)
\]

where
\[
\Lambda = \frac{(D_L k_L L_m / D_m k_m L_L) \sqrt{\left(\frac{D_L}{D_m} \frac{L_L^2}{L_m^2}\right) (s + k_1)}}{(D_L k_L L_m / D_m k_m L_L) \sqrt{\left(\frac{D_L}{D_m} \frac{L_L^2}{L_m^2}\right) (s + k_1)}} \tanh \left(\frac{L_L^2 (s + k_1)}{D_m} \right) \cosh \left(\frac{L_m^2 s}{D_L} \right) + \sinh \left(\frac{L_m^2 s}{D_L} \right) \tanh \left(\frac{L_L^2 s}{D_L} \right) + \cosh \left(\frac{L_L^2 s}{D_L} \right)
\]

(B20).

Appendix C demonstrates that the solution to Eq. B19 is of the form

\[
P_L(t, -L_L) = P_L(\infty, -L_L) + \sum_{n=1}^{\infty} A_n e^{-\alpha_n t}
\]

where \(P_L(\infty, -L_L)\) is the final steady oxygen partial pressure at the membrane/anterior SCL interface, and \(\alpha_n\) and \(A_n\) are constants that contain the desired rate constant \(k_1\) to evaluate oxygen uptake with SCL wear in Eq. 1. The complexity of Eq. B19, however, precludes full inversion into the time domain. Fortunately, the constant parameters appearing in the exponential terms in Eq. B20, \(\alpha_n\), can be obtained using the theorem of residues\textsuperscript{74,75} as outlined in Appendix C. The remaining parameters in Eq. B20, \(A_n\), are not required in our analysis. From Appendix C, we find that

\[
\alpha_n = \left( b_n^2 + \varphi^2 \right) D / L^2 \quad n \geq 1
\]

(B22)

where the eigenvalues \(b_n\) are calculated by trial-and-error from
\[
\frac{b_n Dk L_m}{D_n k_n L_n} + \sigma_n \begin{bmatrix} \sigma_n^{-1} \sin \sigma_n + \frac{D_n k_n L_n}{D_m k_m L_m} \cos \sigma_n \\ \sigma_n^{-1} \cos \sigma_n - \frac{D_n k_n L_n}{D_m k_m L_m} \sin \sigma_n \end{bmatrix} \tan b_n = 0 \quad n \geq 1 \quad (B23)
\]

and

\[
\sigma_n^2 = \alpha_n L_n^2 / D_L. \quad (B24)
\]

As in the main text and in our previous effort, we apply Eq. B21 only at later time where \( P_L(\infty, -L_L) \) can be neglected and where only the first term in the series need be retained, giving an identical form to Eq. 3 but now for the oxygen tension at the membrane/SCL interface

\[
\ln P_L(t, -L_L) = \ln A_i - \alpha_i t \quad (B25)
\]

Thus, the negative slope on a semi-logarithmic graph of measured tension \( P_L(t, -L_L) \) versus time at longer times gives \( \alpha_i \). Hence, Eqs. B23 and B24 need be solved only for \( n = 1 \) to give \( b_1 \). The first-order oxygen-consumption rate constant, \( k_1 \) then follows from Eq. B22. Finally, \( k_1 \) is used in Eq. 1 to establish oxygen uptake flux into the cornea, \( J_o(0) \).

**Appendix C: Inversion of Laplace Domain from Theorem of Residues**

Eq. B19 is written in the form \( \overline{P}_L(s, -L_L) = E(s, -L_L) / H(s) \), where \( H(s) \) is established as a polynomial of at least one degree greater than \( E(s, 0) \). The singular points (poles) of \( \overline{P}_L(s, -L_L) \) are thus identified by the zero-roots of \( H(s) \). Because \( \overline{P}_L(s, -L_L) \) is analytic except at the poles (see Eq B19), the inverse transform is given by the theorem of residues.
where $\rho_n(t)$ is the residue of $\bar{P}_L(s,-L_L)$ at the pole $s_n$. Since the poles of $\bar{P}_L(s,-L_L)$ are simple (i.e., all roots of $H(s)$ are distinct), residues are given by

$$\rho_n(t) = \frac{E(s_n,-L_L)}{dH(s_n)/ds} e^{s_L t}, \quad (C2)$$

where $dH(s_n)/ds$ is the derivative of $H(s)$ evaluated at the pole $s_n$.

Because of the complexity of Eq. A19, obtaining $dH(s_n)/ds$ is onerous. Fortunately, we need only the poles $s_n$ to determine the relationship between $\alpha_l$ and metabolic rate constant, $k_l$. We calculate the poles $s_n$ by setting $H(s) = 0$. We obtain one root at $s_o = 0$ and roots at $s_n (n \geq 1)$ for which $1 + \left(\frac{D_m k_m L_m}{D_L k_L L_L}\right) \Lambda(s_n) \sqrt{\frac{D_L}{s_n L_L^2}} = 0$. This result justifies the form of Eq. B20.

To proceed, we rewrite the poles $s_n$ as

$$\sqrt{L_L^2 (s_n + k_l^{-1})} / D = ib_n$$

where $i = \sqrt{-1}$ and $b_n$ are the eigenvalues to be determined. With much algebra, this expression simplifies to

$$\left[ \left(\frac{D_L k_L L_m}{D_m k_m L_L}\right) \cos \sigma_n + \sigma_n^{-1} \sin \sigma_n \right] b_n \sigma_n^{-1} \left(\frac{D k_m L_m}{D_L k_L L_L}\right) \cos \sigma_n - \left[ \left(\frac{D_L k_L L_m}{D_m k_m L_L}\right) \sin \sigma_n - \sigma_n^{-1} \cos \sigma_n \right] \sin \sigma_n = 0 \quad (C3)$$

where $\sigma_n^2 = \left(\frac{D L_L^2}{D_L L_L^2}\right) \left(\varphi^2 + b_n^2 \right)$ with $\varphi^2 = k_L L_L^2 / Dk$. After elimination of the Thiele modulus in Eq. C3 using Eq. B22, we arrive finally at the desired result in Eq. B23 where now $\sigma_n^2 = \alpha_n L_L^2 / D_L$. Given the membrane, lens, and corneal diffusive and thickness properties,
along with the experimental semi-logarithmic negative slope, $a_i$, Eq. B23 is solved for the eigenvalue $b_i$. Upon obtaining $b_i$, Eq. B22 is used to find the metabolic rate constant, $k_i$, embedded in the Thiele modulus. Finally, Eq. 1 is used to quantify the corneal-oxygen-uptake rate during SCL wear.

References
