The Contribution of Lipid Layer Movement to Tear Film Thinning and Breakup

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PURPOSE. To investigate whether the tear film thinning between blinks is caused by evaporation or by tangential flow of the tear film along the surface of the cornea. Tangential flow was studied by measuring the movement of the lipid layer.

METHODS. Four video recordings of the lipid layer of the tear film were made from 16 normal subjects, with the subjects keeping their eyes open for up to 30 seconds after a blink. To assess vertical and horizontal stretching of the lipid layer and underlying aqueous layer, lipid movement was analyzed at five positions, a middle position 1 mm below the corneal center, and four positions respectively 1 mm above, below, nasal, and temporal to this middle position. In addition, in 13 subjects, the thinning of the tear film after a blink was measured.

RESULTS. The total upward movement could be fitted by the sum of an exponential decay plus a slow steady drift; this drift was upward in 14 of 16 subjects (P = 0.002). Areas of thick lipid were seen to expand causing upward or downward drift or horizontal movement. The velocity of the initial rapid upward movement and the time constant of upward movement were found to correlate significantly with tear film thickness but not with tear-thinning rate.

CONCLUSIONS. Analysis indicated that the observed movement of the lipid layer was too slow to explain the observed thinning rate of the tear film. In the Appendix, it is shown that flow under a stationary lipid layer cannot explain the observed thinning rate. It is concluded that most of the observed tear thinning between blinks is due to evaporation. (Invest Ophthalmol Vis Sci. 2009;50: 2747–2756) DOI:10.1167/iovs.08-24159

Dry eye disorders can be caused by reduced production of aqueous tears and/or increased evaporation due to a deficient lipid layer.1 In both of these conditions, tear film breakup is more rapid than normal.2 Breakup can be observed either as dark spots in the fluorescein-stained tear film,3 or, noninvasively, by distortions in the reflected image of a grid.4 The noninvasive method may evaluate a somewhat different process than breakup, but not with tear-thinning rate.

Several types of tear film breakup have been described. In some cases, breakup can be related to specific aspects of the tear film. For example, tear breakup in the region of the menisci is represented by the formation of the “black line,”5–6 leading to ocular surface damage. The initial thinning is due to “pressure-gradient flow” related to the low pressure in the menisci,5,8 whereas final thinning and dry spot formation may be related to evaporation.9 Another type of breakup is due to partial blinks and occurs at the site where the upper lid reaches its lowest descent.10 In other cases, breakup may be related to elevations on the corneal surface.11–13

Other types of breakup may occur in any region of the cornea14 and their cause is less evident. Types have been classified as circular “dots,” linear “streaks,” and irregular “pools.”15 Some theories of such general cases of breakup are based on the idea that the posterior substrate of the aqueous layer becomes hydrophobic, causing spontaneous dewetting.16,17 Although the time course of tear thinning was not explicitly analyzed, these models seem to imply an accelerated, rapid thinning at the moment when the underlying substrate becomes hydrophobic. We will consider an alternative theory of breakup based on the proposal that steady thinning, caused mainly by evaporation, eventually causes the tear film to thin so much that fluorescein-stained or noninvasive breakup occurs.

It is important to note that tear film thinning at any position can be analyzed in terms of local properties such as tear thickness and tear surface shape (e.g., third equation in the Appendix) and local movement of the lipid layer.18 Tear thinning can be influenced by distant events such as tear flow into the menisci, but these distant events act by changing local conditions. Thus, tear film thinning can be analyzed in terms of local conditions without the need for knowledge of distant events.

Tear movement and its contribution to thinning can be analyzed as two components. First, there can be movement of both the lipid layer and the underlying aqueous layer. For example, surface tension gradients can cause movement of the lipid layer, and viscous drag then causes movement of the underlying aqueous layer.18 This concurrent lipid and aqueous movement is what was considered in the main, experimental part of the study. Second, there can be movement of the aqueous layer, even when the overlying lipid layer is stationary. The contribution of this component to tear movement and thinning, caused by gravity and the ellipsoidal shape of the cornea, was considered in the theoretical analysis in the Appendix.

Tear thinning between blinks can be analyzed in terms of three contributions19: (1) outward flow of water (i.e., evaporation); (2) inward flow into the epithelium or contact lens; and (3) “tangential flow” along the surface of the cornea or contact lens. The first two contributions can generate thinning over all the tear film surface, whereas the tangential flow typically causes a redistribution of tear thickness (i.e., flow out of one area causes thinning), but the redistributed tears cause thickening in other areas where there is a net inflow. No evidence of mechanism 2 was obtained,19 and there is evidence of a small outward flow from cornea to tear film, which tends to cause an increased tear thickness.20 Therefore, evap-
oration and tangential flow were the contributions to tear film thinning considered in this study.

Nichols et al.19 have used interferometry to measure the rate of thinning of the precorneal and prelens tear films over a period of ~20 seconds after a blink. Apart from the first 2 seconds after a blink, when there is an upward drift of the tear film,16,21 there was a steady, linear, thinning of the tear film with no obvious accelerated, rapid thinning that might be expected from sudden dewetting of an underlying hydrophobic substrate. (In this respect, it may be noted that evidence against Holly’s theory of a hydrophobic corneal surface16 has been presented by Tiffany.22,23) Thinning rates were quite variable and were sometimes as high as ~20 μm/min, which is much higher than reported evaporation rates that are equivalent to ~1 μm/min.24,25 These rapid thinning rates were fast enough to explain observed breakup times; for example, with an initial thickness of 3 μm and a thinning rate of 20 μm/min, the tear film would thin to zero thickness in 9 seconds, which is comparable to observed noninvasive breakup times.26

The rate of tear thinning was often rather slow (~1 μm/min), but in other measurements, the thinning rate was much more rapid—up to ~20 μm/min as just mentioned. Because the slow thinning rates correspond to reported measurements of evaporation rate,24,25 we suggested that slow thinning corresponded to evaporation, whereas rapid thinning corresponded to another mechanism (e.g., tangential flow). However, a problem with the latter suggestion is that, as noted above, tangential flow generally causes a redistribution of the tears but not overall thinning and so may contribute to the variability of thinning rate, but less to the average thinning rate.

The main purpose of this study was to evaluate the contributions of evaporation and tangential flow to thinning of the precorneal and prelens tear film between blinks. It is argued that tangential flow of the aqueous tears is largely determined by the movement of the lipid layer, which can be studied by the imaging method of Doane27 together with a cross correlation method for measuring lipid motion.28 In this way, the contribution of tangential flow to tear film thinning can be derived and compared with measurements of the total thinning rate of the tear film, which includes the effect of evaporation as well as tangential flow.

METHODS

Imaging Interferometry

A simplified diagram of the optical system, which is a modified version of Doane’s interferometer,27 is given in Figure 1. Light from a compact tungsten-halide source, S, is reflected from a glass plate beam splitter, B, and the source is imaged at the center of curvature of the cornea by the large aperture, f/0.8, lens, L1. Light therefore strikes the cornea at normal incidence and so is reflected straight back along its path so that a further image of the source is formed near the center of L2, the objective lens of a video camera (V is the video sensor). The video camera is focused on infinity, so that the tear film is in focus when it lies in the focal plane of L2. Uncompressed video recordings were made at 30 images per second with an exposure duration of 30 ms; video resolution was 650 × 494 pixels. The filter, F, was a long-pass infrared filter (RG780; Schott, Duryea, PA), thus avoiding possible reflex tear stimulation from high-lumiance stimuli. A more detailed diagram and description of the optical system, including a second narrow-spectral-band beam and video camera, ocular alignment system, and fixation point have been presented previously.29

Experimental Studies

The study adhered to the principles of the Declaration of Helsinki and approval was granted by the Biomedical Institutional Review Board of the Ohio State University. Informed consent was obtained from all participants after explanation of the procedure. Sixteen subjects (mean age, 30 ± 9 [SD] years, 9 women) with good ocular health, no systemic diseases, and no dry eye symptoms, participated in the studies. After alignment of the subject, video recordings were made for 30-second periods, with subjects asked to blink ~1 second after the start of the recording and then try to keep their eyes open for the remaining time. Four such recordings of the precorneal lipid layer were made from the right eye of each subject, with a 3-minute recovery period between each recording. One of these video recordings was chosen for the analysis of lipid movement, based on good focus and good contrast of detail in the lipid layer, absence of large saccades, and lack of obstruction of the measurement areas by eye lashes.

Analysis of Lipid Movement

Both vertical and horizontal movement were analyzed by finding maxima of cross-correlation functions between succeeding images.28 Advantages and limitations of this method have been discussed.28 A custom program was developed for this analysis. Vertical movement was analyzed in the three rectangular areas shown in Figure 2a at the center of the image and 1 and 2 mm below the center; each area was 1.4 mm × 0.7 mm. Figures 2b–e are enlarged images of the top rectangle, which have been high-pass filtered to emphasize local contrast detail. Figures 2b and 2d correspond to the image in Figure 2a, whereas Figures 2c and 2e correspond to an image obtained 0.1 second later. It can be seen that the lipid layer had moved to the upper right in that interval. This movement was estimated by finding the best match between the first image, f(x, y), and the second image after displacing it by an amount δx, δy, i.e., g(x + δx, y + δy); all dimensions, x, δx, y, and δy were specified in pixels. The best match was found by finding the values of δx and δy that maximize the cross-correlation function

\[ C(\delta x, \delta y) = \sum_x \sum_y f(x, y) g(x + \delta x, y + \delta y) \]  

where the summation is over all pixels in the integration area given by the solid rectangle, A, in the first image (Fig. 2b) and the corresponding displaced rectangle, A’, in the second image (Fig. 2c). This formula was found to be nonoptimal; for example, if there is a bright region extending off the top of both regions, the second image area may be shifted upward more than optimally to increase the contribution of this bright region. We therefore modified the calculation as follows:

\[ C(\delta x, \delta y) = \sum_x \sum_y f(x - \delta x/2, y - \delta y/2) g(x + \delta x/2, y + \delta y/2) \]
which was found to be less affected by the artifact. Typical areas used in this modified calculation are illustrated by the dashed rectangles, $A_1$ and $A_2$, in Figures 2d and 2e. For odd values of, say, $\delta x/2$, the values of $x - \delta x/2$ and $x + \delta x/2$ were rounded up by half a pixel to form integer values. The position of the maximum along, say, the $\delta x$ dimension was interpolated by fitting an inverted parabola through the maximum and two surrounding values ($\delta x - 1$, $\delta x + 1$) and calculating the maximum position for this parabola with subpixel accuracy. The analysis was usually performed on sequential images. However, the analysis program detected blurring caused by saccadic eye movements, which would cause inaccurate movement estimates—in this case, lipid movement—was calculated from cross-correlation between an image before the saccadic movement and an image after the movement. Total horizontal and vertical movements, $X(t)$ and $Y(t)$, were derived from

$$X(t) = \sum \delta x$$

$$Y(t) = \sum \delta y$$

where the summation is over all times up to time $t$. Immediately after the blink, rapid upward movement of the lipid layer caused blurring of the image, which made the cross-correlation analysis of equation 2 inaccurate; therefore, analysis started a short time after the blink, on average after 0.22 seconds.

Comparison of vertical movement in the top and bottom rectangles in Figure 2a provides information about the potential contribution of the tangential flow of tears to tear film thinning in the region between these rectangles. For example, if there is more upward movement at the top rectangle than at the bottom rectangle, it would contribute to

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**FIGURE 2.** To illustrate the cross-correlation method for measuring movement of the lipid layer. (a) Image of the lipid layer showing top, middle, and bottom measurement areas (rectangles). (b) Image of the area in the top rectangle in (a) after high-pass spatial filtering. (c) Corresponding filtered image at 0.1 second later, showing that lipid has moved to the upper right. (cA') Dashed area gives the best match to the original area in (bA), derived from cross-correlation. (d, e) Images of the area in the top rectangle in (a) as in (b) and (c). (dA1, eA2) Dashed areas correspond to matching areas using a modified cross-correlation method.
RESULTS

Figure 3a shows upward movement of the lipid layer for a period of 8 seconds after a blink, calculated from equation 3b, and averaged for the 16 subjects. (A period of 8 seconds was used to avoid inclusion of any subsequent blinks and because the fixation of some subjects became less stable after this time). The upward movement at the center of the cornea is slightly greater than that at 2 mm below the center. Rapid upward motion occurs initially, followed by a slow upward drift. The dotted lines are fits to the upward movement data using the sum of an exponential decay plus a steady upward drift,

\[ y = a[1 - \exp(-t/t_0)] + bt \]  

(4)

where \(a\), \(t_0\), and \(b\) were adjusted to give least-squares fits to the data. This equation provides reasonable fits to the data, judging by correlation coefficients of \(r^2 = 0.996\) at both positions. At the center of the cornea, the time constant of the exponential decay, \(t_0\), was 0.564 seconds, and the total upward movement from the exponential decay, \(a\), was 2.19 mm. Because the analyses started 0.22 seconds after the blink on average (see the Methods section), it can be estimated that the total movement, \(a_{total}\) would have been 3.25 mm, including this initial period after the blink; the corresponding value of \(a_{total}\) at 2 mm below the corneal center was 2.92 mm. The steady upward drift, \(b\), was 0.051 and 0.056 mm/s at the center of the cornea and 2 mm below, respectively; both upward drifts were significant (Wilcoxon signed rank test, \(P = 0.002\)), but there was no significant difference between the two values of \(b\).

Figure 3b shows average horizontal movement at positions 1 mm nasal and temporal to the central area over the same 8-second period. There is a slight nasalward movement that is slightly greater at the 1-mm nasal position (linear regression slope of 0.051 mm/s versus 0.044 mm/s at 1 mm temporal). The movement at either the nasal or temporal position was not significantly different from zero (Wilcoxon signed rank test, \(P = 0.26\) and 0.24, respectively). It was notable that although there was relatively little horizontal movement (less than \(1\) mm) in most subjects, two subjects showed nasal movement of over 2 mm and one showed temporal movement of nearly 2 mm.

The rapid upward movement (exponential decay) in Figure 3a has been analyzed in previous studies,\(^{18,21}\) but we are not aware of any report of the slower steady upward movements (\(bt\) in equation 4) or of considerable horizontal movements. Figure 4a is an example of upward movement that shows a particularly large steady upward movement of \(b = 0.130\) mm/s at the center of the image, more than 2.5 times the average value of 0.051 mm/s in Figure 3a. Figure 4b shows the corresponding lipid image at the beginning (time 0 seconds) of the movement plot in Figure 4a. This image is notable for brighter areas (e.g., marked by an asterisk), near the bottom of the cornea, corresponding to increased lipid thickness.\(^{30}\) Figure 4c shows the lipid image at the end (time 8 seconds) of Figure 4a; the thick lipid present inferiorly in Figure 4b had expanded greatly (compare the lipid spot marked by asterisks in Figs. 4b and c) causing an extensive upward drift of the lipid layer (the contrast in Fig. 4c has been enhanced to show the low contrast lipid pattern better). Figure 5a shows an unusual case in which the steady movement was downward (\(b\) negative). Only 2 of the 16 subjects showed this downward movement and this subject showed the greater downward movement. Figure 5b is the final image (\(t = 8\) seconds in Fig. 5a) and shows a bright area corresponding to increased lipid thickness developed under the upper lashes (asterisk) which was seen expanding and hence pushing the lipid down. Figure 6a shows the relatively large horizontal movement in the temporal direction in the one subject already mentioned. Figure 6b shows that, in the first image of this recording, there was a brighter region (asterisk) over the nasal cornea, corresponding to thicker lipid, which was seen to expand during the 8-second period of Figure 6a, pushing the central lipid layer in a temporal direction. The dotted curve shows that this movement could be fit quite well \((r^2 = 0.979)\) with an exponential decay having a time constant of 1.29 seconds. In one of the two cases of large horizontal movement in the nasal direction, a bright region of lipid was
correspondingly observed over the temporal cornea, but in the other case, the movement appeared to be associated with a piece of debris on the temporal cornea. The slow movement associated with thick lipid areas in Figures 4 to 6 are presumably driven by surface tension gradients—the surface tension in the thick lipid spots being lower than in the surrounding areas, thus causing expansion of these thick spots.18

Figure 7a shows a plot of time constant, $t_0$ (equation 4), as a function of median PCTF thickness for the 13 subjects whose tear film thickness was measured (see the Methods section). A significant correlation ($r^2 = 0.378, P = 0.025$) was found between time constant and tear thickness. (The solid line is the linear regression through the data points; however, this line is an approximate fit, as an exact analysis should take account of the variability of both thickness and time constant values.31) Initial upward velocity, $v_0$, immediately after the blink was derived from the formula

$$v_0 = \frac{a_0}{t_0}$$  \hspace{1cm} (5)

where $a_0$ is amplitude of the exponential decay (cf., $a$ in equation 4) extrapolated back to the time of the blink. Figure 7b is a plot of initial upward velocity, $v_0$, as a function of PCTF thickness. Again there is a significant correlation ($r^2 = 0.412, P = 0.018$).

The mean thinning rate for the 13 subjects was 4.98 μm/min. There was no significant correlation between the thinning rate and either time constant, $t_0$, or initial upward velocity, $v_0$.

**DISCUSSION**

A major goal of this study was to evaluate the contribution of tangential flow to the thinning of the PCTF between blinks. It

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**FIGURE 4.** (a) Total upward movement of the lipid layer, at the center of the cornea for a subject with a relatively large upward drift ($r^2 = 0.992$). (b) Appearance of the lipid layer at the beginning time of (a), $t = 0$. (b, c, asterisks) A thick lipid spot over the inferior cornea. (c) Appearance after 8 seconds showing that the thick lipid spot in (b) expanded considerably.

**FIGURE 5.** (a) Total vertical movement of the lipid layer, at the center of the cornea for a subject with a downward drift ($r^2 = 0.968$). (b) Appearance of the lipid layer at the end of the analysis, $t = 8$. Asterisk: a thick lipid spot over the superior cornea.
was assumed that tangential flow is laminar \( \text{18} \); thus, if the velocity of the lipid layer is \( v \), the velocity of the tear film decreases linearly from \( v \) at the lipid surface to 0 at the corneal surface, so that the mean velocity is \( v/2 \). The contribution of tangential flow to tear film thinning at any position can be derived by considering flow across the borders of a small element (e.g., square) surrounding that position. If there is more outward flow across some borders than inward flow across the other borders, then the tear film thins. This thinning can be considered to be the sum of two contributions: “tear stretching” and “wedge movement.” These are illustrated in Figure 8, where the hatched tear film is shown to the left of the corneal surface in each plot. For simplicity in explanation, it will be considered that all movement is vertical. “Tear stretching” (Figs. 8a, 8b) occurs when lipid velocity is nonuniform while tear thickness may be uniform; for example if the lipid upward velocity, \( v \), (and hence mean tear film velocity, \( v/2 \)) is greater at the upper edge of the square than at the lower edge, indicated by the arrows in Figure 8a, thinning occurs, as shown in Figure 8b (where dashed lines indicate the original position of the tear film in Fig. 8a). Thinning by “wedge movement” (Figs. 8c, 8d), occurs when the tear film is wedge-shaped while the velocity of the lipid layer may be uniform; for example, if the tear film is thicker at the upper edge of the square than at the lower edge (Fig. 8c), then the volume of outward flow of tears across the upper edge is greater than the inward flow across the lower edge and thinning occurs, as shown in Figure 8d.

Considering first tear stretching, the average data of Figure 3a show somewhat greater upward movement at the center of the cornea compared with 2 mm below the center. This difference is due to the rapid exponential component rather than the slow upward drift. The total rapid (exponential) movements at the center and 2 mm below were 3.23 and 2.92 mm. As discussed earlier, the corresponding average movements of the aqueous layer are estimated to be half these values: 1.615 and 1.46 mm. There should therefore be a net outflow of tears corresponding to 1.615 to 1.46 = 0.155 mm; this is approximately 7.8% of the 2-mm separation between upper and lower measurement areas, and thus the PCTF may be expected to thin by this amount, on average, during the rapid, exponential movement of the lipid layer. Examples of such thinning have been presented previously.\( \text{19} \) Because this rapid thinning occurs immediately after a blink, but not later, its contribution to breakup, which normally occurs at a considerably later time, is likely to be minimal.

Considering now the slow component of lipid movement, \( bt \) in equation 4, the lipid velocity, \( b \), was similar at both the center of the cornea and 2 mm below, 0.051 and 0.056 mm/s; corresponding average velocities of the aqueous layer, \( b/2 \), would be 0.0255 and 0.028 mm/s. This should contribute a net inflow of tears of 0.028 − 0.0255 = 0.0025 mm/s, and hence the PCTF should thicken at a rate of 0.125%/s given the 2-mm separation between the measurement areas. By a similar calculation, it can be shown that the difference in horizontal (nasal) movements at the 1-mm nasal and temporal positions would be predicted to cause thinning at a rate of 0.175%/s. Combining effects from vertical and horizontal flows predicts an overall thinning rate of 0.05%/s. Summarizing the tear-stretching contributions, the rapid exponential movement may make some contribution to tear thinning but is over before tear breakup occurs. The slower, steady thinning is unlikely to make a detectable contribution to tear film breakup.
How much can wedge movement (Figs. 8c, 8d) contribute to tear thinning and breakup during the slow upward movement (bt) of the lipid layer? Omitting any rapid exponential transient during the first 2 seconds after a blink, the observed thinning rate averaged 4.98 µm/min or 0.083 µm/s. It has been reported that the PCTF distribution is sometimes in the form of a wedge that is thicker over the superior cornea. Suppose that the tear film is a wedge, with a thickness difference between the center of the cornea and 2 mm below of \( \delta b \mu m \). The mean upward velocity at the corneal center and 2 mm below was \( v = 0.0535 \) mm/s, so the expected average rate of movement of the aqueous layer is half of this or \( v/2 = 0.0268 \) mm/s. Consider the cross-sectional area of the tear film between the center of the cornea and 2 mm below. This cross-sectional area is reduced at the rate of \( \delta b \cdot v/2 \). If this wedge movement is the cause of tear thinning, this formula, \( \delta b \cdot v/2 \), should equal the observed thinning rate, 0.083 µm/s multiplied by the 2-mm separation between the measurement areas. Equating these two values of rate of cross-sectional area reduction, gives a thickness difference, \( \delta b \), of 6.2 µm between the center of the cornea and 2 mm below, a thickness gradient of 3.1 µm/mm. This is highly improbable; for example, if the tear thickness 2 mm below the cornea was the minimum possible, zero, the thickness at the center of the cornea would be predicted to be 6.2 µm, which is greater than the average observed thickness. Thickness gradients of approximately 10% of the above figure have been observed indicating that wedge movement could contribute about this percentage of tear film thinning.

Figures 4 and 5 illustrate how the slow lipid movement, \( bt \) in equation 4, may be driven by expansion of thick lipid layers respectively below and above the central cornea. Berger and Corrsin modeled the rapid upward movement of the lipid layer after a blink (exponential function in equation 4) by assuming that surface tension was inversely related to the concentration of a surfactant; the lipid layer provides much of the surfactant properties of the PCTF, so surface tension is generally inversely related to lipid thickness. The low surface tension in regions of thick lipid allow these regions to be stretched by surrounding regions of higher surface tension, thus giving rise to the slow movements observed in Figures 4 and 5. The horizontal, temporally directed movement shown in Figure 6 is similarly related to an expanding region of thick lipid over the nasal cornea. It is not clear why these movements should be slower that the rapid exponential movements that are always seen after a blink; perhaps the relatively thick lipid areas, such as those shown in Figures 4 to 6, take longer to reach equilibrium. It may be noted that although, immediately after a blink, the lipid layer is sometimes clearly thicker inferiorly, this does not always seem to be evident; in the latter case, perhaps the surface tension gradient is due to a concentration gradient in polar lipids (lower concentration superiorly) causing a gradient in the interfacial tension of the lipid–aqueous interface, and hence in the overall surface tension of the tear film.

Figure 7 shows that the exponential time constant of the rapid upward movement after a blink is negatively correlated with tear film thickness, while the initial upward velocity is positively correlated. Figure 9 helps to provide an explanation of these findings, based on the analysis of Berger and Corrsin. The lipid layer is modeled as a spring, anchored at the upper and lower lids, and which, just after a blink, is stretched more over superior than over inferior cornea (Fig. 9a). The spring tends to return to its equilibrium position (Fig. 9b), but its return is slowed by the viscosity of the aqueous tears, shown by pistons in sloppy fitting cylinders. The viscous drag of the aqueous layer is inversely proportional to its thickness, so a thicker tear film provides less drag (sloppier pistons in Fig. 9), leading to a higher velocity (for a given surface-tension gradient) and quicker return to equilibrium (reduced time constant). These predictions are verified in Figure 7.

Yokoi et al. demonstrated that initial upward velocity of the lipid layer after a blink is significantly and positively correlated with the radius of curvature of the lower meniscus; tear film thickness is expected to be proportional to meniscus radius, so this result implies that velocity should be positively correlated with tear thickness, in agreement with the results of Figure 7b and the model of Figure 9. Goto and Tseng measured the “spread time” of the tear film, the time taken for the lipid layer to reach a stable position after a blink. This spread time would be expected to be roughly proportional to our time constant, \( t_w \), in equation 4. The spread time was increased in aqueous tear deficiency, which is to be expected from Figure 7a and the model of Figure 9, if tear thickness was reduced in their patients.

Returning to the major conclusion of this article, that tangential flow is generally too slow to explain most of the observed thinning of the tear film between blinks, the findings imply that evaporation is the main cause of tear film thinning and breakup. However, most measured values of evaporation rate are lower than our observed mean thinning rate of 4.98 µm/min. We have argued that evaporation in “free-air” conditions, when ambient air currents remove the humid layer of air in front of the cornea, is generally more rapid than in experimental measurements using preocular chambers.
chambers block room air currents, so that a thick humid layer of air builds up in front of the cornea, forming a resistant barrier to evaporation.\textsuperscript{20} However, in the ”ventilated chamber” method of measuring evaporation,\textsuperscript{36,37} air currents are directed over the cornea, a method that is more similar to natural free-air conditions and yields evaporation rates more similar to the thinning rates that we measure by interferometry.\textsuperscript{20}

If tear film thinning is mainly due to evaporation rather than tangential flow, this has implications for the interpretation of tear film breakup\textsuperscript{36} using fluorescein. Evaporation should reduce the thickness of tears without reducing the amount of fluorescein per unit area of cornea. Thus, the reduced fluorescence seen in most cases of tear film breakup is probably not due to the absence of fluorescein. The concentration of fluorescein should increase in inverse proportion to the reducing tear thickness. It thus seems possible that the dimming of fluorescence that is observed during breakup is usually due to ”concentration quenching,” the reduced efficiency of fluorescence that occurs when fluorescein concentration exceeds approximately 0.1%.\textsuperscript{38} In certain special cases of tear film breakup, such as near the tear meniscus, over corneal surface elevations, and after partial blinks, tangential flow may make a relatively large contribution initially, with final thinning caused by evaporation.\textsuperscript{7,12,39–42}

Whereas this study has considered thinning due to aqueous tear movement caused by lipid movement, it is theoretically possible for tangential flow of the aqueous tear film to occur even if the lipid layer is stationary. In the Appendix, it is shown that gravity and also a pressure gradient between central and peripheral cornea, due to the ellipsoidal shape of the cornea, make only a minor contribution to observed tear film thinning. Thus, combining the results of the theoretical analysis in the Appendix with the experimental studies of lipid layer movement supports the hypothesis that tangential flow of the tear film generally makes only a minor contribution to tear film thinning, implying that evaporation is typically the main cause of tear thinning and breakup.

**APPENDIX**

In this article, the contribution to tear film thinning from tangential flow of tears associated with lipid movement was considered. We now consider how, even in the absence of lipid movement, the internal flow of the aqueous layer could cause tear film thinning.

We first consider the local thinning caused by the nonuniform curvature of the average cornea, with the corneal shape as described by Read et al.\textsuperscript{43} The cornea can be considered an axisymmetric ellipsoid of the form

\[
\frac{z^2}{a^2} + \frac{r^2}{b^2} = 1
\]

in the circular cylindrical coordinate system \((r, \phi, z)\) where \(r\) is the radius, \(\phi\) is the azimuthal angle, and \(z\) is the elevation, with constants \(a\) and \(b\). The surface is independent of \(\phi\).

For our purposes, it is convenient to write the surface in the form

\[
z = a \sqrt{1 - \frac{r^2}{b^2}} = f(r).
\]

Using lubrication theory to derive an equation for the thin film thickness \(b(r, t)\) on this ellipsoid gives\textsuperscript{44}

\[
\frac{\partial b}{\partial t} + \frac{1}{\mu} \frac{1}{r} \frac{\partial}{\partial r} \left[ b^3 \frac{\partial}{\partial r} \left( 2H \right) \right] = 0.
\]

where \(\sigma\) is the surface tension, \(\mu\) is the viscosity, and \(H\) is the mean curvature of the cornea. This equation assumes a tear film surface that is laden with a strong surfactant that renders it tangentially immobile.\textsuperscript{9} The effect of the curvature of the cornea is significantly larger than that of the tear film thickness variation, allowing us to neglect the contribution from the film thickness itself. A general result has been given\textsuperscript{45}; details of the application to the corneal surface will be published elsewhere by some of the current authors.

The task remains to provide the term for the curvature of the corneal surface \(2H\) (twice the mean curvature) in terms of our ellipsoidal surface. It is the sum of the radial curvature \(\kappa_r\) and the azimuthal curvature \(\kappa_\phi\), which may be written as\textsuperscript{45}

\[
2H = \kappa_r + \kappa_\phi = \frac{\frac{\partial^2 f}{\partial r^2}}{1 + \left( \frac{\partial f}{\partial r} \right)^2}^{3/2} + \frac{\frac{\partial f}{\partial r}}{r \left[ 1 + \left( \frac{\partial f}{\partial r} \right)^2 \right]^{3/2}}.
\]
Lipid Layer Movement and Tear Thinning

Evaluating these expressions gives

\[ 2H = \frac{-1}{R} \left( \frac{2 - \frac{r^2}{b^2} \left( 1 - \frac{a^2}{b^2} \right)}{1 - \frac{r^2}{b^2} \left( 1 - \frac{a^2}{b^2} \right)^{3/2}} \right) \]

We will use the following properties: surface tension \( \sigma = 45 \) mN/m; density, \( \rho = 10^3 \) kg/m\(^3\); viscosity, \( \mu = 10^{-3} \) Pa \( \cdot \) s.

For the cornea, we have that \( R = 0.0078 \) m is the radius of curvature and \( Q = -0.19 \) is the corneal asphericity; then

\[ a = \frac{R}{1 + Q} \quad \text{and} \quad b = \frac{R}{\sqrt{1 + Q}}. \]

Using the expression for the curvature, the definitions of \( a \) and \( b \), and evaluating at \( r = 0 \) (the center of the cornea), we obtain

\[ \frac{\partial b}{\partial t} = \frac{2\sigma Qb^3}{5\mu R^2}. \]

Evaluating the right side with \( b = 4 \) \( \mu \)m, we find that \( \partial b/\partial t = -0.045 \) \( \mu \)m/min; for \( b = 3 \) \( \mu \)m we find \( \partial b/\partial t = -0.019 \) \( \mu \)m/min; and for \( b = 5 \) \( \mu \)m we have \( \partial b/\partial t = -0.09 \) \( \mu \)m/min. All these rates are small compared to our experimental measurement.

We now turn to the gravitationally driven motion where all other effects but viscosity are absent. For a thin fluid film, the equation under the lubrication approximation for the tear film thickness is given by

\[ \frac{\partial b}{\partial t} + \frac{pgb^2}{4\mu} \frac{\partial b}{\partial x} = 0. \]

Here the \( x \) coordinate points downward in the direction of gravity with acceleration \( g = 9.81 \) m/s\(^2\). The viscosity \( \mu \) and the density \( \rho \) are as already given, and \( b \) is chosen to be a representative film thickness. This equation is also for the tangentially immobile limit. We now use the rate of thinning from measurement on the corneal surface so that the only unknown in the equation is the slope \( \partial b/\partial x \). If the slope is an unreasonable value, then it is not a plausible mechanism for the observed thinning. Using \( b = 3 \) \( \mu \)m and \( \partial b/\partial t = -4.98 \) \( \mu \)m/min, we find \( \partial b/\partial x = -3.62 \) \( \mu \)m/mm. This slope is impossibly large, being approximately 10 times greater than observed values.

References


