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Effect of tear additives on the shear stress and normal stress acting on the ocular surface

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Abstract

Based on lubrication theory, an elastohydrodynamic model of the human tear film is presented. Using this model we investigate the effect altering the viscosity of the tears has on the stresses acting on the cornea during a blink. In order to model the compliant cornea and eyelid surface, a mattress model is employed. This model is then coupled with the lubrication model of the tear film leading to a one-dimensional nonlinear partial differential equation governing the fluid pressure in the lubrication film. The differential equation is solved numerically using a finite-difference scheme. The results indicate that typical tear additives will lead to an increase in the shear stress acting on the cornea. This in turn may effect the shedding rates of corneal epithelial cells. The model is also of use in predicting the drag force the eyelid exerts on a contact lens and in assessing how tear additives may effect the movement and rotation of the contact lens.

Introduction

During blinking the human upper eyelid acts as a wiper which deposits and redistributes the tear film in order to ensure the development of a clean and optically smooth surface. However a condition known as dry eye may result in cases where the tear film fails to be fully deposited on the cornea or the tear film ruptures prematurely after a blink. Aspects of modelling the deposition and thinning processes can be found in [7] and [6].

A common treatment for dry eye is to add a tear additive which has the effect of increasing the viscosity of naturally occurring tears. This has two effects on the behaviour of the tear film. Firstly an increase in viscosity will cause an increase in the deposited tear film thickness. Secondly an increase in viscosity will slow the subsequent thinning and ultimate rupture of the tear film. However viscous enhancing additives will lead to an increase in the shear stresses exerted on the corneal surface during a blink. This may ultimately have an adverse effect on the health of the corneal surface since the rate of shedding of epithelial cells on the cornea is related to the magnitude of the shear forces [10]. The aim of this paper is to investigate how increasing the tear film viscosity effects the shear forces using a recently developed mathematical model of the eyelid wiper [5].

Eyelid wiper

The eyelid wiper is defined as the area of the eyelid which is "in contact with" or "wipes" the ocular surface during the blinking action [9]. The under-surface of the upper eyelid is lined with epithelium. However, the epithelium on the eyelid wiper region is found to differ from the rest of the eyelid and is known as *stratified squamous epithelium* [9]. Since this form of epithelium is often found on tissue that experiences frequent rubbing [9] conclude that it defines the wiper region.

The under-surface of the eyelid has been studied by everting the upper eyelid [3, 1, 9] after a vital staining dye has been applied to the surface (e.g. lissamine green or rose bengal). Eyelids stained in this way reveal a common feature referred to as Marx's line, which is a stained line that extends along the entire length of the eyelid. Figure 1 shows an everted upper eyelid that we stained with lissamine green dye and a stained region can clearly be seen. Based on the measurements of [3] and [1], the width of the line is approximately 0.1 mm.

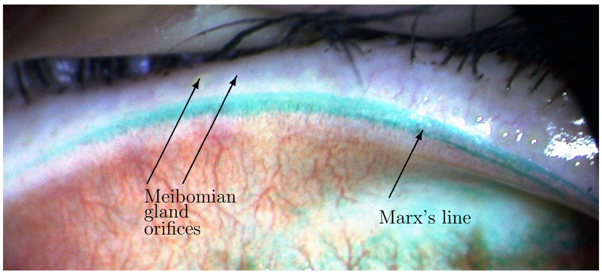

Figure 1: Lissamine green staining of upper eyelid. The width of the stained region is $\sim 0.1\,\mathrm{mm}$.

One interpretation of Marx's line is that it is the site of the lubrication region during blinking. In this lubrication region higher normal stresses and shear stresses are generated compared to the stresses on the adjacent tissue and this may lead to cell damage and hence staining. Another important finding of [9] is that patients with dry eye syndrome often have more severe staining of the eyelid wiper (lid wiper epitheliopathy) when compared with patients who do not report dry eye symptoms. This may indicate that the lubrication film is very thin or incomplete resulting in solid to solid contact and hence high surface shear forces.

Elastohydrodynamic model of eyelid

The model, as reported here, is described in more details in [5]. The lid wiper geometry shown in Figure 2. Lubrication analysis will be applied to the region $-w/2 < x < w/2$ which can be thought of as the lubrication or "contact" region. The region $x > w/2$ is referred to as the reservoir. In the reservoir, the pressure is assumed to be constant and it is also assumed that an unlimited flux of tear fluid can enter or leave this region. At $x = -w/2$ we will take the pressure at this boundary to correspond to the pressure under the tear film meniscus which is assumed to remain constant. We restrict the analysis to one dimension and consider the single dimension running vertically along the centreline of the ocular surface from the lower to upper eyelid. Hence any variations in the z-direction are ignored.

Elastic model

The undeformed ocular surface is assumed to be a smooth flat surface and the undeformed eyelid wiper profile is modelled as a parabola in the lubrication region. The lubrication film thickness, $h(x,t)$, is given by

$$h(x,t) = h_0(t) + \frac{x^2}{2R} + \Delta h(x,t), \qquad (1)$$

where $h_0(t)$ is the minimum of the undeformed lip wiper, R is

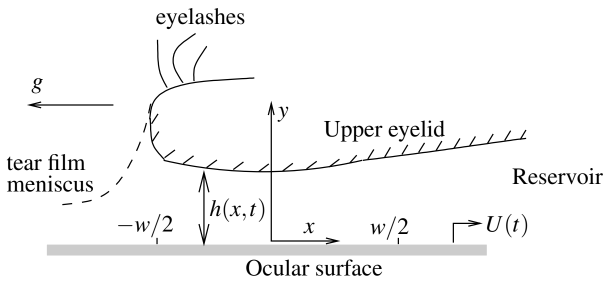

Figure 2: Eyelid wiper geometry and coordinate system. A lubricating tear film of thickness $h(x,t)$ exists between the ocular surface and upper eyelid. Note diagram is not to scale.

the radius of curvature of the undeformed lid wiper and $\Delta h(x,t)$ is the total deformation due to deformations in both the cornea and the wiper surface. It is noted here that it is only the total deformation at a given x-coordinate which is of importance when solving the hydrodynamic problem and not the details of where the deformations are occurring.

In order to maintain a positive hydrodynamic force in the y-direction the geometry of the wiper and the ocular surface under the wiper region must change between an opening blink and a closing blink. A possible mechanism by which this could occur is if the wiper and cornea are compliant. In order to simplify the analysis deformations of the surfaces are modelled using a "mattress foundation" model (also called the Winkler model). In the mattress model the elastic surfaces are modelled as a series of independent springs each having an elastic modulus K (Nm^{-3}) so that the deformation of a given surface, $\Delta h(x,t)$, at point x is given by

$$\Delta h(x,t) = \frac{p(x,t)}{K}. \tag{2}$$

Since we are allowing for deformations in both the eyelid wiper and ocular surfaces the constant K appearing in (2) can be interpreted as the *equivalent* stiffness of the system and is given by

$$K = \left(\frac{1}{K_c} + \frac{1}{K_w}\right)^{-1},$$

where where K_c and K_w are the individual stiffness of the cornea and the wiper surface, respectively.

Hydrodynamic model

Here a model for the tear film dynamics is developed based on the standard thin film approximations.

Using the lubrication approximations the momentum equations describing the flow are

$$\frac{\partial p}{\partial x} = \mu \frac{\partial^2 u}{\partial y^2} \tag{3}$$

$$\frac{\partial p}{\partial y} = 0 \tag{4}$$

where y is the coordinate normal to the ocular surface, ρ is the fluid density, μ is the fluid viscosity and $u(y)$ is the fluid velocity in the x direction. In (3) the effect of gravity has been ignored since over the length scales of interest the pressures produced by gravity are insignificant. Solving (3) and (4) and applying the no-slip boundary condition at the solid boundaries ($y = 0$ & $y = h$) gives

$$u = \frac{1}{2\mu}\frac{\partial p}{\partial x} y(y-h) - U\left(\frac{y}{h} - 1\right), \tag{5}$$

where $U = U(t)$ is the velocity of the upper eyelid. Taking into account the lubrication approximations, flow conservation of mass requires that

$$\frac{\partial Q(x,t)}{\partial x} = -\frac{\partial h(x,t)}{\partial t}, \tag{6}$$

where $Q(x,t)$ is the volume flux. Integrating the velocity profile (5) gives

$$Q(x,t) = \frac{-h^3}{12\mu}\frac{\partial p}{\partial x} + \frac{1}{2}Uh. \tag{7}$$

Hence the equation governing the film thickness evolution is given by

$$\frac{\partial}{\partial x}\left[\frac{-h^3}{12\mu}\frac{\partial p}{\partial x} + \frac{1}{2}Uh\right] = -\frac{\partial h}{\partial t} \tag{8}$$

and is known as the Reynolds lubrication equation. It is valid for either a moving or stationary eyelid where $U = 0$ for the stationary case.

Alternatively, an equation governing the pressure can be obtained by substituting (1) and (2) into (8) giving

$$\frac{\partial}{\partial x}\left[\frac{-\left(h_0 + \frac{x^2}{2R} + \frac{p}{K}\right)^3}{12\mu}\frac{\partial p}{\partial x} + \frac{1}{2}U\left(h_0 + \frac{x^2}{2R} + \frac{p}{K}\right)\right] = -V(t) - \frac{1}{K}\frac{\partial p}{\partial t}, \tag{9}$$

where

$$V(t) = \frac{\partial h_0}{\partial t}, \tag{10}$$

is the velocity of the undeformed eyelid wiper normal to the undeformed ocular surface. The two boundary conditions on (9) are

$$p(-w/2,t) = p_{\mathrm{m}} \qquad \text{and} \qquad p(w/2,t) = p_{\mathrm{r}}, \tag{11}$$

where p_{m} is the pressure in the meniscus and p_{r} is the pressure in the reservoir and both are taken to be constants. investigation.

The shear stress acting on the ocular surface is

$$\tau|_{y=0} = -\frac{1}{2}\frac{\partial p}{\partial x}h - \frac{\mu U}{h}, \tag{12}$$

and the shear stress acting on the lid wiper is

$$\tau|_{y=h} = -\frac{1}{2}\frac{\partial p}{\partial x}h + \frac{\mu U}{h}. \tag{13}$$

The first term appearing on the right hand side of (12) and (13) is due to the "Poiseuille" component of the flow and the second term is due to the "Couette" component of the flow.

Eyelid force

Since $V(t)$ is unknown in (9) a further equation is required to solve for the film pressure, $p(x,t)$. This is obtained by specifying the normal force the eyelid applies to the ocular surface at an instant in time. Neglecting the inertia of the eyelid this gives the constraint equation

$$\int_{-w/2}^{w/2} p\,dx = \frac{F_l(t)}{s}, \tag{14}$$

where $F_l(t)$ is the normal force the eyelid exerts towards the ocular surface, s is the arc length of the eyelid.

Eyelid velocity

During an opening phase of the blink the upper lid moves primarily in the vertical direction. Using high speed video we have measured the vertical displacement of the upper eyelid during a blink for a single subject. The data was differentiated to give the experimental eyelid velocity and a the following piecewise curve fit is used to represent the eyelid velocity in ms^{-1}:

$$U(t)=\begin{cases}0.3511\left[1-\tanh^2(57.56t-3.833)\right],\ t<0.0786\\ 6.353(t-0.1002)\exp\left[-22.82(t-0.1002)\right],\ t\geq 0.0786.\end{cases} \tag{15}$$

Viscosity of tears and tear additives

The tear film has been described as having a tri-laminar structure [4]. It can be considered essentially as an aqueous layer sandwiched between two much thinner films. These thinner films comprise a lipid layer on the surface of the aqueous layer and a mucus layer between the cornea and aqueous layer. The aqueous layer is approximately 10μm thick while the lipid and mucin layers are less than $0.1\,\mu$m thick. Hence tear film fluid properties are usually taken to correspond to pure water and the viscosity is taken to be $1.3\times10^{-3}\,\mathrm{Nsm}^{-2}$. The measurements of [11] suggest that human tears may be shear-thinning although under sufficient shear the viscosity of tears is found to be close to that of water.

The viscosity of 10 different commercial tear additives has been measured by [8] and they found values of viscosity ranging from 2.34×10^{-3} to $23.6\times10^{-3}\,\mathrm{Nsm}^{-2}$ (i.e. up to 18 times the viscosity of natural tears).

Summary of model parameters

Table 1 summarises all the other model parameters used in the numerical calculations. For a discussion on the choice of the model parameters the reader is referred to [5].

Parameter	Value	Units
K	8.33×10^{9}	Nm^{-3}
w	0.375	mm
R	0.5	mm
F_l	0.03	N
s	33	mm
p_m	-125	Nm^{-2}
p_r	0	Nm^{-2}

Table 1: Model parameter values used in calculations unless stated otherwise. Note p_m and p_r are relative to atmosphere.

Numerical method

To solve (9) a finite-difference method is implemented. The spatial derivatives are discretized using second order centred differences. The solution is advanced in time using a semi-implicit method and hence the nonlinear terms are evaluated at the current time level, whereas the linear terms are treated at the future time level. The system is then reduced to a linear system of algebraic equations which are solved using the linear algebra package LAPACK.

At each time step (9) must be solved subject to the boundary conditions (11) and the constraint equation (14). The constraint equation gives an equation for the unknown $V(t)$ appearing in (9) and this is solved using a root bracketing method which is implemented using the GSL "Brent-Dekker method" [2].

The value of $h_0(t+\Delta t)$ is found using

$$h_0(t+\Delta t)=h_0(t)+V(t)\,\Delta t,$$

where Δt is the time step.

Results

Figures 3 and 4 show the pressure distribution under the eyelid wiper and the shear stress acting on the ocular surface, respectively, at three times during a complete blink cycle. These times correspond to a stationary eyelid immediately before a blink ($t=0.05$ s), at the time of maximum closing speed ($t=0.13$ s) and at the time of maximum opening speed ($t=0.21$ s). The pressure and shear stress profiles are presented for two values of viscosity ; $\mu=1.3\times10^{-3}$, which is based on the viscosity of water and represents the value for a normal tear, and $\mu=13\times10^{-3}$, which represents a typical value for a tear additive [8].

At $t=0.05$ s the eyelid is stationary ($U=0$) and the pressure profiles are symmetric about $x=0$ (squeeze film profile). There is very little difference between the pressure profiles for the two values of viscosity when the eyelid is stationary. When the eyelid is moving ($t=0.13$ and $t=0.21$ s) a difference in the pressure profiles for different values of viscosity is evident and for the higher viscosity fluid the pressure is distributed over a larger area. The shear stress acting on the ocular surface is significantly higher for the more viscous fluid. The maximum shear stress generated during the blink is found to increase by approximately a factor of 2.5. Referring to equation (12) the increased shear stress can be explained by a corresponding increase in the film thickness for the more viscous fluid which has the effect of increasing the pressure gradient term in (12).

Tear additives with viscosity up to 18 times that of water were measured by [8] and at this highest value of viscosity the maximum shear stress during a blink is found to increase by a factor of approximately 3.7. However the normal stress, p, is less affected and the maximum normal stress generated during a blink, for this value of viscosity, increases by only $\approx 5\%$ when compared to water.

Integrating the shear stress profiles gives the resultant drag force (per unit span of wiper) acting on the ocular surface during a blink and this is shown in Figure 5. As with all of the results presented in this paper, this drag force is representative of the drag experienced at the central part of the eyelid, where the eyelid velocity is greatest. It therefore also corresponds to the maximum drag force experienced across the span of the eyelid. The drag magnitude is greatest at the maximum closing speed ($\approx t=0.13s$) and comparing the results for the two values of viscosity it can be seen from Figure 5 that the higher viscosity fluid leads to a factor of 3 increase in the maximum drag magnitude.

In Figure 6 the local maxima of the drag magnitude $|D|_{\max}$ are plotted for the range of viscosity measured by [8]. The closing phase of a blink takes approximately 0.1 s whereas the opening phase takes approximately 0.3 s, hence for a given value of viscosity the value of $|D|_{\max}$ during closing is higher. It can be seen from Figure 6 that undiluted tear additives can lead to an increase in maximum drag of up to a factor of 5. It should be noted that it is the increase in the stresses that are important when assessing cell damage whereas the drag force is of more importance when assessing contact lens stability.

Conclusions

The use of tear additives which have values of viscosity greater than natural tears will lead to a significant increase in the shear

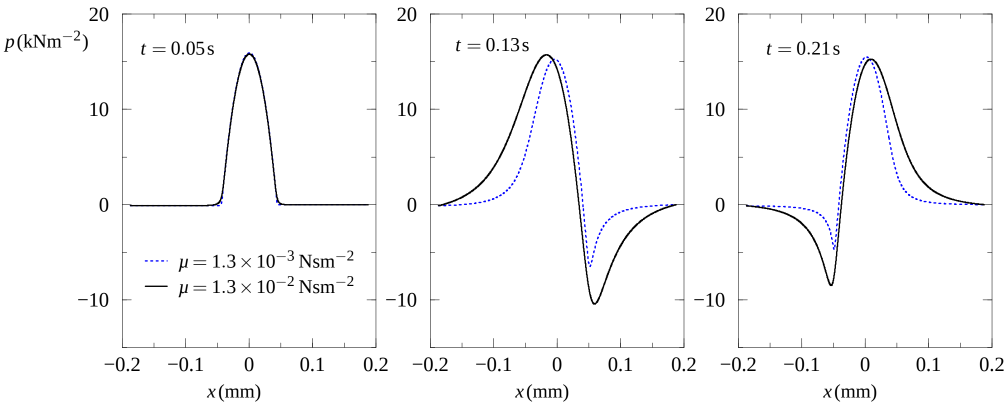

Figure 3: Pressure profiles during a blink. The $t = 0.05\,\mathrm{s}$ frame represents a stationary eyelid immediately before the beginning of a closing blink, $t = 0.13\,\mathrm{s}$ represents the time at maximum closing speed and $t = 0.21\,\mathrm{s}$ represents the time at maximum opening speed.

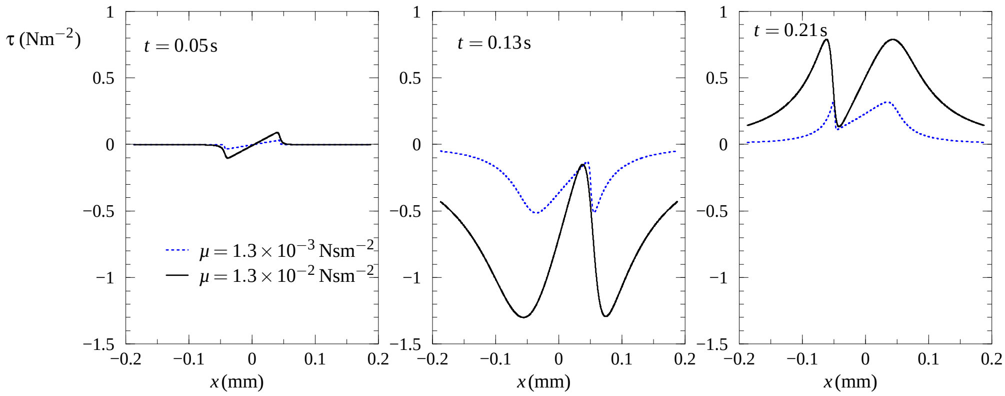

Figure 4: Shear stress acting on the ocular surface during a blink. The $t = 0.05\,\mathrm{s}$ frame represents a stationary eyelid immediately before the beginning of a closing blink, $t = 0.13\,\mathrm{s}$ represents the time at maximum closing speed and $t = 0.21\,\mathrm{s}$ represents the time at maximum opening speed.

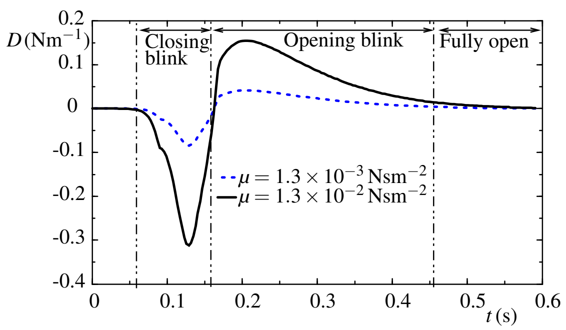

Figure 5: Drag per unit span (D) acting on ocular surface during a blink.

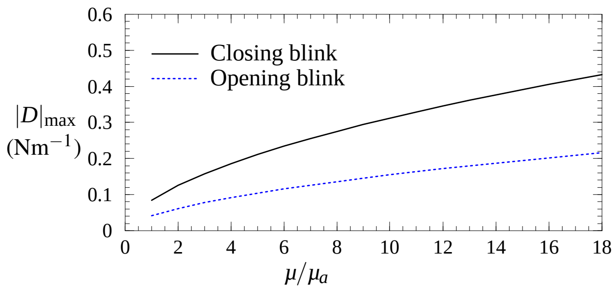

Figure 6: The maximum magnitude of drag (per unit span) acting on ocular surface during the closing phase of a blink and the opening phases of a blink as a function of tear fluid viscosity where μ_a is the viscosity of a normal tear (i.e. pure aqueous solution).

stress on the ocular surface during a blink. Using an elastohydrodynamic model of the tearfilm and eyelid wiper it is found that the tear additives can increase the drag force by up to a factor of 5. Increasing tear fluid viscosity increases the region over which the pressures in the lubrication film are significant. However the maximum and minimum pressures in the lubrication film are not significantly altered by viscosity. The direct effect of increasing tear viscosity is to increase the overall thickness of the lubrication film and this is turn increases the "Poiseuille" component of the shear stress (see equation 12). Further experimental or modelling work is required to determine whether or not the increased shear stress predicted here will have on adverse effect on the health of the epithelial cells of the wiper and cornea. It would also be interesting to determine if it is the normal stresses or shear stresses which are of primary importance to cell damage. Since this work has shown the effect on the normal stresses is far less pronounced than the effect on the shear stresses.

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