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More than meets the eye – Estimating blinking shear rates

Key Words: viscosity, shear thinning, ophthalmic formulation, dry eye drops, non-Newtonian, Carreau-Yasuda model, Cross model, blinking, shear rate estimation

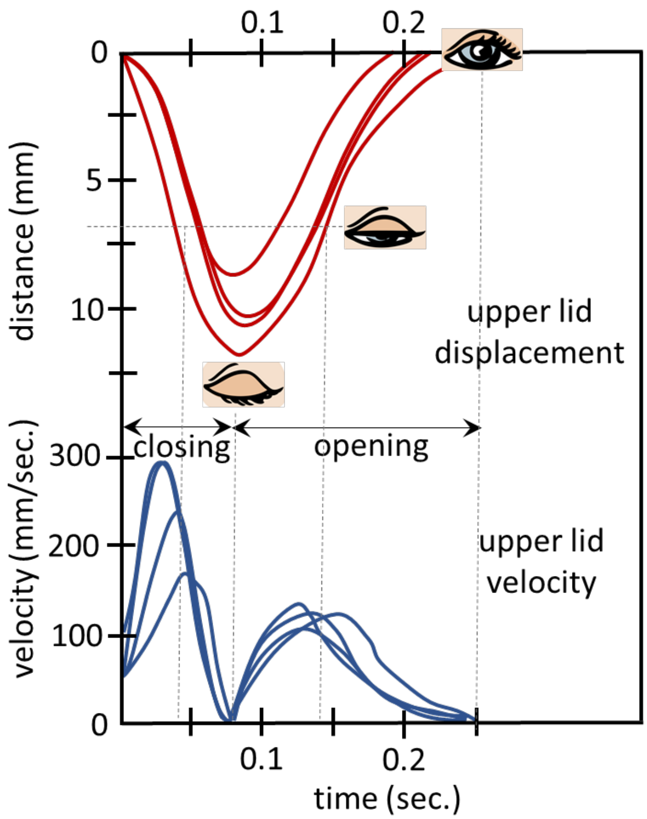
Goal: The second application note in this series considers the environment after the eye drops are inserted. The motion of the eyelid during the blink cycle will shear the tear film fluid which has been modified by the addition of the eye drops. The shear rate range of this process is estimated from published eyelid velocity profiles and tear film thickness measurements. The estimate confirms that the viscosity versus shear rate data for seven over the counter dry eye products was measured in the appropriate range and relevant to the blinking process.

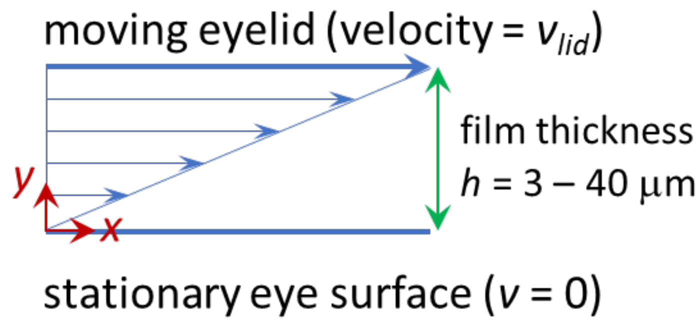
Introduction

It is always important to understand application details so that the most relevant viscosity data can be measured. This is especially true for non-Newtonian or shear rate dependent formulations such as the eye drop products. The next step to consider in the performance assessment is the blink cycle. Although the gravity driven drainage over the eye surface at the time of application is a low shear process, the shear rates imposed by the blink are generally assumed to be orders of magnitude higher. Published measurements for eyelid velocity profiles and tear film thicknesses are used to estimate the range of shear rates that may occur during the blink cycle. This approximate shear rate range is then compared to the viscosity data collected for the seven commercially available eye drops formulated for the treatment of dry eye. The comparison confirms that the data was measured over the appropriate shear rate range for the application with model fits providing viscosity estimates for the extreme conditions where required.

Shear Rate Analysis

Eyelid movement during the blink cycle and tear film thickness have both been measured under a variety of circumstances (refs 1-3). **Figure 1** (left) contains a schematic that mimics the upper eyelid displacement and velocity through the entire blink cycle which includes both the closing and opening phases. Although commonly characterized by a single value, the shear rate during the blink is not constant and ranges from zero at the turnaround points to some maximum value. This maximum can be highly variable depending on the specific patient, their current activity, and level of fatigue.





h (mm)	Peak v_{lid} (mm/sec)	$\dot{\gamma}_{max}$ (sec^{-1})
0.003	300	100,000
0.040	150	~4000

Figure 1: Schematic of upper eyelid displacement and velocity versus time during the full blink cycle (*left*). Approximate velocity profile within fluid tear film used for shear rate calculation (*top right*). Maximum shear rate range (*bottom right*).

A simplified view of the fluid film sheared between the upper eyelid and the surface of the eye is presented in **Figure 1** (*top right*). The no-slip boundary condition is assumed at both interfaces, which means that fluid is moving at the same velocity (v) as the adjacent surface. A shear rate ($\dot{\gamma}$) can be calculated with the following equation.

$$\dot{\gamma} = \frac{\partial v}{\partial y} = \frac{v_{lid}}{h}$$

The shear rate is a function of the variable eyelid velocity (v_{lid}) and the fluid film thickness (h). Measurements of the tear film thickness cover a very broad range from about 3 to 40 μm (ref 2). Values at the lower end are more commonly accepted even after accounting for a modest 20 – 30 % increase in thickness after the insertion of eye drops (ref 3). The peak lid velocity reaches a maximum of about 150 – 300 mm/sec during the closing phase (ref 1). Therefore, the maximum shear rate ($\dot{\gamma}_{max}$) experienced during the blink cycle can range from about 4000 to 100,000 sec^{-1} (**Figure 1**, *bottom right*).

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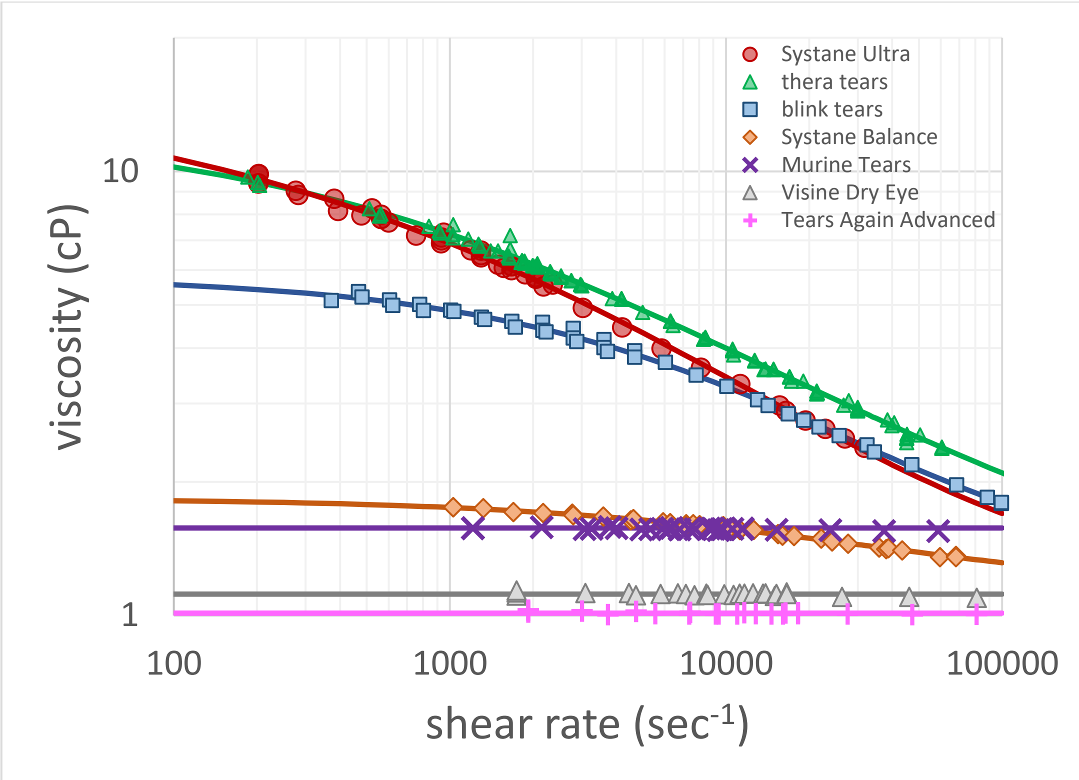

Figure 2: Viscosity versus shear rate for products listed in **Table 1**. Model fits and Newtonian values are presented as solid lines.

Discussion

Simplifying the shearing process of the tear film and utilizing parameters published in the literature made it possible to approximate shear rates relevant to the blink cycle. The shear rate range can then be used to define the best viscosity measurement protocol to assess the eye drop formulations. The shear rate during the blink will approach zero as the lid reverses and reach a maximum of 4000 – 100,000 sec^{-1} during the closing portion. Ideally, viscosity should be measured from the zero-shear limit (η_o) to the upper bound of 100,000 sec^{-1}.

The viscosity versus shear rate data for the commercially available eye drop formulations is presented in **Figure 2**. The appropriate range is nearly achieved for the non-Newtonian samples. For the formulations where it is not, models commonly used for polymer solutions or particle dispersions fit the data well and can be used to estimate the extreme values (i.e. Carreau-Yasuda and Cross). These viscosity values are presented in **Table 1** for each product tested. Even when there is a significant difference in the low shear regime, the shear thinning formulations begin to merge as the upper bound for $\dot{\gamma}_{max}$ is reached.

Product	η_o (cP)	η (cP)		Model	Formulation
		4K (s^{-1})	100K (s^{-1})		

Systane®Ultra	**16**	**4.6**	**1.7**	Carreau-Yasuda	Hydroxypropyl guar
thera tears®	**12**	**5.2**	**2.2**	Carreau-Yasuda	Sodium carboxymethyl cellulose
blink®tears	**5.8**	**4.0**	**1.8**	Carreau-Yasuda	Sodium hyaluronate
Systane®Balance	**1.8**	**1.7**	**1.3**	Cross	Mineral oil in water emulsion + hydroxypropyl guar
Murine Tears®	**1.6**	**1.6**	**1.6**	Newtonian	Polyvinyl alcohol
Visine®Dry Eye	**1.1**	**1.1**	**1.1**	Newtonian	Hydroxypropyl methylcellulose
Tears Again®Advanced	**1.0**	**1.0**	**1.0**	Newtonian	Liposomes

Table 1: Dry eye drops tested including major formulation component(s) and model fit information.

Concluding Remarks

Estimating shear rates during the blink cycle from eyelid velocity and tear film thickness measurements indicate that the process is not well characterized by a single value. Rather, it involves a broad range beginning at the zero-shear limit and extends to an upper bound as high as 100,000 sec^{-1}. Knowing how to estimate shear rates from the application parameters is critical to measuring relevant viscosity data of non-Newtonian samples that can support performance prediction. This is often achievable with a simplified view and information readily available in the literature. Stay tuned for our next installment to learn how the shear rate dependent viscosity can be correlated to performance.

References

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