

## Emulsification of silicone oil and eye movements

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**Purpose:** Emulsification is an inherent problem of silicone oil used in vitreoretinal surgery. It has been shown that silicone oil can be made more resistant to emulsification and easier to inject by adding high molecular weight components (5 or 10% 423kD polydimethylsiloxane) to normal 1,000mPa.s silicone oil. We hypothesize that this might also reduce the movement of oil within an eye.

**Methods:** A model eye chamber made of surface-modified polymethylmethacrylate was driven by a computer and a stepper motor to mimic saccadic eye movement. Seven silicone oils with different shear and extensional viscosities were tested. Two sets of eye movements were used: (amplitude 9°, angular velocity 390°/s, duration 50ms and amplitude 90°, angular velocity 360°/s, duration 300ms). The movements were captured and analysed by video recording.

**Results:** The angular velocity of an oil bubble relative to the eye chamber appears to form an exponential relationship with its shear viscosity. Depending on the thickness of the film of aqueous between the eye wall and the oil bubble, the shear rate was estimated to be between 6 and 14 x 10<sup>4</sup>s<sup>-1</sup>. The addition of 10% of 423kD polydimethylsiloxane to 1,000mPa.s silicone oil significantly reduced the peak relative velocity compared with the base oil of 1,000mPa.s but not 5,000mPa.s.

**Conclusion:** The addition of high molecular components to a base oil increases its extensional and shear viscosity. Whilst the extensional viscosity affected the ease with which the oil could be injected, our results showed that it was the shear viscosity that determined the relative velocity between the oil and the wall of the vitreous cavity, and thus the propensity to emulsify.

## Introduction

Emulsification is an inherent problem with long-term silicone oil tamponade and is associated with other complications such as glaucoma, inflammation and proliferative vitreoretinopathy<sup>1</sup>. Recent *in vitro* experiments have shown that the addition of a high molecular weight component (HMWC) [5% or 10% of 423kD polydimethylsiloxane (PDMS)] to 1,000mPa.s silicone oil made the resultant blend as resistant to emulsification as 5,000mPa.s silicone oil<sup>2</sup>. We have also shown that compared to oils with the similar shear viscosities, oil blends with high molecular additives are significantly quicker to inject<sup>3</sup>.

By adding high molecular weight components, the extensional viscosities of the oil blends were increased at high strain rates. The extensional viscosity of silicone oil is believed to be important in determining its readiness to breaking off and form droplets<sup>4</sup>. At present, we do not know what amount of shear stress occurs during normal saccadic eye movements at the oil-aqueous interface. To the best of our knowledge, no one has studied the movement of a silicone oil bubble inside an eye or estimated the shear forces that might cause emulsification.

We devised a model eye chamber that can mimic eye movements in order to estimate the shear rates that the different oils and oil blends are subjected to. Physicists refer to the viscosity of a fluid as its ability to diffuse momentum<sup>5</sup>. Emulsification of silicone oil inside an eye would depend on eye movement generating the shear, which in turn depends on the relative velocities between the oil and the wall of the vitreous cavity. When the eye rotates, the oil inside would also move but to varying degrees dependent

on its ability to diffuse of momentum, in other words its viscosity. One could imagine the oil bubble as being made up of layers, each moving with a different velocity. The layer closest to the retina would move almost at the same velocity as that of the eye, whilst a layer of oil further away would move slower because of inertia. Thus there would be a gradient of velocities within the oil. Low viscosity oil will have a sharp gradient and high viscosity oils will have a gentle gradient. In these circumstances, the addition of high molecular weight PDMS, in which the large polymer molecules could span the layers, might lead to a reduction in the gradient. If that was the case, the shear rate might be reduced because the relative velocity at the interface between the oil and the eye might also be reduced. Thus our hypothesis is that the addition of high molecular components reduces the relative velocity between the oil and the wall of the vitreous cavity. To test this hypothesis we devised the following experiments.

## **Materials**

Seven silicone oils were tested in this study. All oils were kindly donated by Fluoron GmbH (Ulm, Germany). Their compositions, the labelled and the actual measured shear viscosities are listed in Table 1. There was a silicone oil with very low viscosity of around 5mPa.s. Siluron 2000™ was a blend made by adding 5% of the 423kD PDMS to a base oil of 1,000mPa.s. The additive 423kD PDMS has a shear viscosity of 1,000,000mPa.s. Siluron 2000™ had a shear viscosity of around 2000mPa.s. It was designed to be more resistant to emulsification due to the fact that it had a high extensional viscosity under high shear strain. Blend A was made by mixing 55% 1,000mPa.s with 45% 5,000mPa.s silicone oil. It also had a shear viscosity of around

2000mPa.s. Because Blend A did not have a high molecular weight component (HMWC), its extensional viscosity under shear strain would be roughly midway between its component 1,000mPa.s and 5,000mPa.s base oils<sup>4</sup>. Blend B was made by adding 10% of the 423kD PDMS to a base oil of 1,000mPa.s. Lastly, an oil with shear viscosity 12,500mPa.s was also included in this study. The extensional viscosities of all the oils under different shear strain rates have been previously published<sup>4</sup>.

These oils were chosen to test our hypothesis in two ways. Firstly, we wanted to determine if adding the HMWC decreased the shear rate. We will be comparing silicone oil 1,000mPa.s with and without HMWC. However, we appreciate that adding the HMWC increased not only the extensional viscosity but also the shear viscosity of the resultant blend. Secondly, therefore we wanted to test if oils with the same shear viscosity but with different extensional viscosity would behave differently. We compared Siluron 2000<sup>TM</sup> with Blend A, both with similar shear viscosity of around 2000mPa.s and likewise, Blend B with silicone oil 5,000mPa.s.

## **Methods**

### Eye chamber

The eye chambers that we used were described previously. Briefly, the eye model chambers were cylindrical with an internal diameter of 20mm, a length of 20mm and a volume approximately of 6.3ml<sup>6</sup>. The chambers were made of polymethylmethacrylate. We rendered the surface hydrophilic by coating it with protein<sup>7</sup>. This was achieved by using 0.1g/ml non-fat milk powder (Brand: Nestle, Carnation) in 1X phosphate-buffered saline; the protein was allowed to adsorb for one hour. Five millilitres of each silicone

oil was injected into the chambers and the remaining space topped up with phosphate-buffered saline coloured with trypan blue. We took great care to ensure that the chamber contained no air bubbles.

### Simulation of eye movements

We developed a mechanical system to generate motion. The system consists of a stepper motor (C4/MD2 Step Motor System, Arrick Robotics, USA), a shaft encoder (Baumer Electric, Switzerland) and a data acquisition device (National Instruments, USA). An adapter was fashioned to affix the eye model chamber to the shaft of the stepper motor. The motion was therefore rotational and in one plane only. A computer and a dedicated programme were used to control the stepper motor. It was possible using the software to send instructions to execute repetitive motions. The shaft encoder enabled us to record the angular displacement, velocity and acceleration of the actual motion being executed.

The most frequent human saccades have amplitudes below  $15^\circ$ , with a maximum angular velocity from  $300^\circ/\text{s}$  to  $400^\circ/\text{s}$  and a duration of around  $50\text{ms}$ <sup>8,9</sup>. With our mechanical system, we instructed the system to execute 2 different sets of motion: (amplitude  $9^\circ$ , angular velocity  $390^\circ/\text{s}$ , duration  $50\text{ms}$ ) and (amplitude  $90^\circ$ , angular velocity  $360^\circ/\text{s}$ , duration  $300\text{ms}$ ), with the aim of mimicking the stereotyped velocity profiles observed in healthy, adult humans<sup>10,11</sup>.

### Measurements of angular displacement and angular velocity to estimate shear rate

A digital camera that took 30 frames per second was used to capture the motion of the eye chamber and the oil contained within. We recorded the maximum angular

displacements of the oil bubble (Fig.1) and calculated the relative velocity between the wall of the model eye chamber and the oil bubble. The shear rate was dependent on this relative velocity and the thickness of the film of aqueous between the oil bubble and the chamber wall such that:

$$\text{shear rate} = v/h$$

where  $v$  is the relative velocity between the eye chamber wall and the oil bubble

and  $h$  is the thickness of the film of aqueous between them.

An image analysis programme, Image J software (National Institutes of Health, Bethesda, Maryland) was used to analyse the photographs to measure the angular displacement (Fig. 1) and the velocity of the bubble and the eye chamber.

### Statistical Method

Unpaired t-tests were performed using GraphPad Prism software.  $p$  values  $<0.05$  were considered to be statistically significant. In the experiments with  $9^\circ$  movement,  $n = 15$ . In the experiments with  $90^\circ$  movement,  $n = 8$ . All values in the graphs are shown as mean  $\pm$  SD.

## Results

### First set of motion: amplitude of 9°, velocity of 390°/s and duration of 50ms

The angular displacement versus time and angular velocity versus time profiles of the simulated saccadic eye movement are presented in Fig. 2a and 2b. The shape of these plots resembled those of human saccades data that were obtained from a healthy adult executing saccades of a similar amplitude, recorded using infrared oculography (Fig. 2c and 2d). Within the limitation of the stepper motor, this was the best simulation that we could achieve.

Maximum Angular Displacement: Silicone oil 12,500mPa.s had the largest while 5mPa.s oil had the smallest angular displacement (Fig. 3a). There seemed to be an exponential relationship between the shear viscosity of the oil and its angular displacement (Fig. 3b). There was a significant difference between the maximum displacements of the two oils with the HMWC when compared with base silicone oil 1,000mPa.s. The maximum displacement of Blend B was statistically greater than that of 5,000mPa.s oil ( $p = 0.0355$ ) whereas the maximum displacement of Siluron 2000™ was not statistically different to that of Blend A ( $p = 0.919$ ).

Angular velocity: The duration of motion was 50ms. We could not reliably measure the angular velocity of the oils using our camera as it only captured 1 frame per 33ms.

### Second set of motion: amplitude of 90°, velocity of 360°/s and duration of 0.3s

Maximum displacements: The results turned out to be similar to the above (Fig. 4a). Silicone oils with additives had significantly higher maximum angular displacements than the base oil 1,000mPa.s. There was no statistical difference between the maximum angular displacements of 5,000mPa.s oil and Blend B ( $p = 0.4864$ ) or between that of Siluron 2000™ and Blend A ( $p = 0.7973$ ). When we plotted the maximum angular displacements against the shear viscosity of the oils, we found a relationship that was exponential (Fig. 4b).

Angular velocities: Figure 5a shows a plot of the angular velocities of the eye chamber and the oil bubbles. The velocity of the chamber was set to reach 360° per second in about 0.03 sec. This velocity was maintained for 0.23 sec, and the chamber came to a stop in about 0.03 sec. The plots of angular velocities for all the oils showed a rise and a fall. The velocity was highest for the silicone oil 12,500mPa.s and lowest for silicone oil 5mPa.s. The angular velocity of silicone oil 1,000mPa.s was lower than that of Blend A, Siluron 2000™, 5,000mPa.s oil and Blend B. There was little difference that separated the angular velocity of any of the latter 4 oils.

Figure 5b gives the plot for the relative angular velocities of different oils. With the exception of the silicone oil 5mPa.s, all the plots showed two peaks. The first peak occurred just after the eye chamber reached its peak velocity and the second peak occurred after the eye chamber started to slow to a stop. The plots illustrate the different ability of oils to diffuse momentum. Silicone oil 5mPa.s has the highest relative angular velocity when the chamber was moving and the lowest when the chamber was stopping, whereas silicone oil 12,500mPa.s had

the lowest relative velocity when the chamber was moving and the highest when the chamber was stopping. Silicone oil 1,000mPa.s behaved in a fashion between these two extremes. There was little to separate the velocities of the 4 oils: Blend A, Siluron 2000™, silicone oil 5,000mPa.s and Blend B. Figure 6a shows the peak relative angular velocities of the different oils; the plot (Fig. 6b) shows an exponential relationship between the peak relative velocity and the shear viscosity.

## Discussion

Emulsification of silicone oil observed in patients is a dispersion of oil droplets in aqueous. In the anterior chamber, these droplets can be seen by gonioscopy<sup>12</sup> and if extensive, can manifest as an “inverted hypopyon”<sup>13</sup>. The inner surface of the eye wall is made up of the retina and the crystalline lens anteriorly. Depending on the thoroughness of the vitrectomy, there might be a variable amount of cortical vitreous attached to the retina and to the lens posteriorly. We have demonstrated in the past that the vitreoretinal surface was hydrophilic and we have also shown that its surface property could be mimicked by protein-coated PMMA<sup>7</sup>. We justified the use of our eye model chamber made of this material in a number of previous static studies<sup>14,15,16</sup>. Being hydrophilic, the vitreoretinal surface should not make direct contact with an intraocular oil bubble. Instead, there should be a thin layer of aqueous interposed between the oil and the retina. Using optical coherence tomography, Winter et al measured the thickness of the aqueous film between a bubble of perfluorocarbon liquid

and the retina to be between 5 to 10 microns<sup>17</sup>. We envisaged that emulsification of silicone oil occurs because of the shear stress applied across a similarly thin film of aqueous. Although there is no published value on the actual thickness of this film, this information is nonetheless important as the shear stress is determined by it, such that the thinner this film of aqueous the greater the shear stress. In this study, we attempted, using a dynamic model, to study the shear rate. Our hypothesis is that the addition of high molecular weight additives would reduce the relative velocity between the eye chamber and the oil and therefore would also reduce the shear rate. By implication, the energy available for dispersion of silicone oil would also be diminished.

Rheologists describe viscosity as a measure of the ability to diffuse momentum; a liquid with high shear viscosity is more able to diffuse momentum than one with low shear viscosity. In the dynamic study with 90° motion, 5mPa.s silicone oil clearly demonstrated this phenomenon. It seemed to remain more still (because of inertia) when the chamber rotated. It was also quicker to stop moving when the chamber stopped (Fig. 5). Low shear viscosity oils had low angular displacement with simulated saccadic movement. With silicone oil 12,500mPa.s the reverse was demonstrated: it had the highest angular displacement with saccadic movement; it tended to move more with the eye chamber; it also carried on moving once the chamber stopped. In terms of absolute velocities, the trend was clear; the higher viscosity oils had higher angular velocity and vice versa.

However, in terms of shear rate, it was the relative velocity between the oil and eye chamber that mattered. For a given thickness of aqueous film, the peak relative velocity reflected the maximum shear rate. The addition of 10% of the 423kD PDMS did

significantly reduce the peak relative velocities compared to that of 1,000mPa.s oil. Our hypothesis is therefore supported. The addition of 5% of the 423kD HMWC also reduced the peak relative velocities but not significantly so. The experiment demonstrated a general trend: that the higher the shear viscosity, the lower the peak relative velocity. The 5mPa.s oil had the highest peak relative velocity; silicone oil 125,000mPa.s had the lowest with silicone oil 1,000mPa.s somewhere in between the two extremes. Comparing oils with a similar shear viscosity, we found that Blend A had a significantly higher peak relative velocity than Siluron 2000™. This could be explained by the fact that Blend A did have a slightly lower shear viscosity than Siluron 2000™. There was no significant difference between silicone oil 5,000mPa.s and Blend B. In terms of peak relative velocity (that determines the shear stress) it was the shear viscosity that was the main determining factor. Adding HMWC only succeeded in increasing the shear viscosity. Comparing oils with similar shear viscosity but different extensional viscosity revealed that increasing extensional viscosity did not succeed in reducing the peak relative velocity.

Previous studies on silicone oil emulsification relied on the use of large mechanical forces and the vigorous motion generated by vibrators or rotary devices<sup>4,18</sup>. They have shown that 5,000mPa.s silicone oil was more stable and less likely to emulsify compared to 1,000mPa.s<sup>19,20,21</sup>. It has always been puzzling to us how emulsification could happen in the human eye given that such violent movements do not occur. Our study tried to mimic human eye movements in terms of amplitude, velocity and duration. One weakness of the study is that we could not find a reliable way to measure the thickness of the aqueous film. Our study has shown for the first time that the peak

relative velocity of the oils closely approximated that of the peak velocity of the eye chamber. In other words, if the peak velocity of the eye chamber was  $360^\circ/\text{s}$ , then all the oils attained relative angular rotation velocities of between  $310$  to  $340^\circ/\text{s}$ . All oils irrespective of their shear viscosity had significant inertia such that with the mimicked movement of  $90^\circ$ , when the chamber reached maximum angular velocity, the oils remained more or less stationary. This is the single most important finding. Because the oil remained stationary whilst the eye chamber moved, relative movement occurred that gave rise to shear stress at the interface between the chamber and the oil. One could estimate the shear rate by making some assumptions for the thickness of the aqueous film. If we take the figure of  $10$  microns<sup>17</sup> and assume the peak relative velocity to be between  $310$  to  $340^\circ/\text{s}$  and the diameter of the eye to be  $2.3$  cm then the maximum shear rate would be between:  $6200$  to  $6800\text{s}^{-1}$ . The difference in the shear rate between  $5\text{mPa}\cdot\text{s}$  and  $12,500\text{mPa}\cdot\text{s}$  silicone oil would be as little as  $10\%$ . It is surprising to us that such little difference in shear rate could account for such difference in propensity to emulsify.

To prevent emulsification several strategies have been employed. The usual strategy has been to use oils with higher shear viscosity, that is  $5,000\text{mPa}\cdot\text{s}$  or above. As we have shown, using higher viscosity oil would reduce the peak relative velocity, thus the shear rate and the energy available to disperse the silicone oil. Once droplets break off from the main body of silicone oil, there also needs to be surfactants available to stabilise the small droplets, otherwise surface energy would drive them to coalesce back into larger bubbles. It has been shown that blood products could stabilise dispersed droplets<sup>22</sup>. Therefore the extent of any inflammation and the breakdown of

blood-ocular-barrier might be relevant. Thus, there are individual patient's parameters that might be confounding factors for emulsification. To date, there is no randomised clinical trial to show that 5,000mPa.s oil is more resistant to emulsification than 1,000mPa.s oil and there is no consensus amongst vitreoretinal surgeons as to which viscosity should be chosen. While clinical studies comparing silicone oils of different viscosities emphasized the differences in anatomical outcome<sup>23</sup>; they did not look specifically at emulsification<sup>24</sup>. The only consensus thus far has been to use highly "purified" oils with the lower molecular weights removed, as they do tend to cause emulsification<sup>16,25</sup>.

Although it seems preferable to use high viscosity oils to prevent emulsification, there are also compelling reasons to choose less viscous oils. With the advent of smaller gauge vitrectomy, surgeons want oils that are easier to inject and extract through smaller-bore instruments. The new proposed strategy to prevent emulsification is to add HMWC to 1,000mPa.s silicone oil. This increases the extensional viscosity which should make it more difficult for droplets to form. The addition of 5% and 10% 423kD PDMS to 1,000mPa.s oil gives the blend a shear viscosity close to 2000mPa.s and 5,000mPa.s respectively. Yet during injection, when shear strain was applied, the molecules line up thus making the blends quicker to inject. Our research question is therefore very timely. We asked whether the addition of high molecular components could also reduce shear rate. We have shown for the first time, the movement of the oil bubbles inside a model eye chamber and we have been able to measure the relative angular velocity. Simplistically, it could be said that oils with higher shear viscosity tended to move with the eye chamber and therefore tended to exhibit less relative movement or shear stress.

This could be one explanation of why oils with higher viscosity have lower propensity to emulsify. The addition of HMWC did reduce the peak velocity. This however, might be simply due to the increase in corresponding shear viscosity.

### **Conclusion: which oil should we choose?**

We conclude from our study that the shear viscosity was the main factor that determined the maximum shear rate. From the plot between shear viscosity and peak relative velocity, it could be seen that 5,000mPa.s oil was already on the steep part of the exponential curve (Fig.6b). This suggests using oils of higher shear viscosity might not be that much more effective at reducing shear rate. There was no significant difference in the peak relative velocity between the between 12,500mPa.s oil and 5,000mPa.s oil whereas there was a significant difference between 5,000mPa.s oil and 1,000mPa.s oil. This finding concurred with other *in vitro* studies<sup>17,18</sup>. If we were indeed to choose oils with a shear viscosity of around 5,000mPa.s, it might be preferable to choose an oil blend of 10% 423kD PDMS in 1,000mPa.s oil rather than a normal 5,000mPa.s. The ease of injecting the former over the latter is sufficient to make it more attractive to some surgeons.

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## Legends

**Fig. 1** The measurement method of the maximum angular displacement. Fig. 1a showed the tamponade at rest and fig. 1b showed the tamponade at its maximum displacement. The line in each figure indicated the chord of the tamponade. By measuring the slope of the chord in fig. 1b the maximum angular displacement could be obtained. The aqueous was coloured by trypan blue and a black background was used to enhance the contrast between the tamponade and aqueous phase. The red mark on the chamber indicated the position of the eye model chamber.

**Fig. 2** The displacement-time (a) and velocity-time (b) graph of the simulated saccadic eye movement by the mechanical system. The displacement-time (c) and velocity-time (d) graph of a human saccade of similar amplitude, recorded from a healthy adult using infrared oculography.

**Fig. 3a** Maximum angular displacement with  $9^{\circ}$  motion (unpaired t-test, \*,  $p < 0.05$ ; \*\*,  $p < 0.01$ ; \*\*\*,  $p < 0.001$ ; Error bar =  $\pm$ SD)

**Fig. 3b** Plot of shear viscosity versus maximum angular displacement with  $9^{\circ}$  motion

**Fig. 4a** Maximum angular displacement with  $90^{\circ}$  motion (unpaired t-test, \*\*\*,  $p < 0.001$ ; Error bar =  $\pm$ SD)

**Fig. 4b** Plot of shear viscosity versus maximum angular displacement with  $90^{\circ}$  motion

**Fig. 5a** Angular velocity of eye chamber and different oils with  $90^{\circ}$  motion

**Fig 5b** Angular velocity of oil relative to the eye chamber with  $90^{\circ}$  motion

**Fig. 6a** Peak relative angular velocities of the different oils

**Fig. 6b** Plot of peak relative angular velocities versus shear viscosities

## Table

**Table 1** Compositions and the physical properties of various silicone oils

Silicone oil	Compositions	Shear viscosity at 25°C/mPa.s *
Silicone oil 5mPa.s	Cannot be provided by manufacturer	5
Silicone oil 1,000mPa.s	PDMS 1000 mPa.s (37kDa)	1030
Blend A	55% Siliicone oil 1,000mPa.s + 45% Silicone oil 5,000mPa.s	2141
Siluron 2000™	95% Siliicone oil 1,000mPa.s + 5% high molecular- weight PDMS (423kDa, 1,000,000mPa.s)	2189
Silicone oil 5,000mPa.s	PDMS 5000 mPa.s (65kDa)	4910
Blend B	90% Siliicone oil 1,000mPa.s + 10% high molecular- weight PDMS (423kDa, 1,000,000mPa.s)	5090
Silicone oil 12500mPa.s	Cannot be provided by manufacturer	12500

kDa, Kilo Dalton; PDMS, Polydimethylsiloxane

\* Data were provided by Hagedorn Nadine from Fluoron GmbH (Ulm, Germany) using oscillation rheology method

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