UNIVERSITY OF CAMBRIDGE Department of Chemical Engineering and Biotechnology

Investigating silicone oil emulsification in eye chamber models

By

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This thesis is submitted for the degree of Doctor of Philosophy

Declaration

This thesis is the result of my own work and includes nothing which is the outcome of work done in collaboration except as declared in the preface and specified in the text. It is not substantially the same as any work that has already been submitted before for any degree or other qualification except as declared in the preface and specified in the text. It does not exceed the prescribed word limit for the Engineering Degree Committee.

Material in Chapter 3 and 4 has been published in Wang *et al.* (2020), and accepted at the *Journal of Biomechanical Engineering*. This dissertation is 53744 words in length, and contains 105 figures and 28 tables.

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Abstract:

Investigating silicone oil emulsification in eye chamber models

The emulsification of silicone oil in intraocular liquid is an unwanted complication occurring after retinal detachment repair. The repair surgery consists of removing most of the intraocular liquid and replacing it by a tamponade fluid. Silicone oils with dynamic viscosities in the range 1-5 Pa s are often used as tamponades due to their high biocompatibility and chemical stability. Emulsification of the oil can occur during the tamponade stay in the eye chamber and the droplets can potentially lead to loss of or impairment of vision. The aim of the project is to establish the mechanisms by which the silicone oil emulsifies and understand the different factors involved in this phenomenon.

Two potential emulsification mechanisms have been studied using experimental investigations. A 3D model of the eye chamber, driven by a stepper-motor reproducing the eye geometry and saccadic motion, was developed to study the first hypothesis of bulk emulsification at the interface between oil-aqueous phases. The stability of the interface was investigated over an extensive range of experimental scenarios, supported by analytical and numerical calculations. The addition of surfactant to the aqueous phase modelled the effect of surface-active molecules on the interfacial properties. Low viscosity ratio, low interfacial tension and strong inertial motion resulted in large deformation of the oil-aqueous interface but did not result in interface breakup and droplet formation. Bulk emulsification was therefore excluded as the mechanism causing the oil droplets formation.

The second hypothesis concerned the stability of the three-phase contact line (TPCL) between the two liquid phases and the retinal surface. Hydrophobic silane coatings on flat solid substrates were used as a first approximation of the retina. The TPCL motion and stability was studied on uncoated and coated substrates. Above a critical substrate speed, the drag of the TPCL by the substrate led to a transition from partial to complete wetting of the liquid, leaving an oil film on the surface. The presence of printed silane features affected the dewetting of the TPCL and led to the destabilization of the oil film into shorter oil strands pinned to the feature. The shape of the oil strands depended on the surface energies and contact angles, and the oil strand length and

width increased with increasing substrate velocity and feature width. However, none of the pinned droplets detached from the features under the motions accessible by the set-up and by the stepper motor device.

The bulk emulsification hypothesis was reported to be the mechanism responsible in much of the literature on this topic. The experimental findings reported here indicate that surface-driven emulsification is more likely to be responsible of oil droplet formation. Confirmation of the hypothesis requires further investigation to establish which physiological and flow conditions will promote detachment of SiOil droplets from surface features.

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Nomenclature

Roman

Parameter	Description	Units
A	Saccade amplitude	rad
ΔA	Change in interfacial area	m²
As	Cross section	m²
b	Radius of a spherical cap	m
Во	Bond number	-
С	Height of a spherical cap	m
С	Concentration	mol L ⁻¹
Са	Capillary number	-
Ca _c	Critical Capillary number	-
d	Aqueous film thickness	m
D	Saccade duration	S
D _{drop}	Drop diameter	m
D _{oil}	Oil strand width	m
f	Surface area fraction	-
F	Body force vector	N m ⁻³
. <i>F</i> _B	Buoyancy force per unit length	N m ⁻¹
F _C	Surface tension force per unit length	N m ⁻¹
$F_{\rm D}$	Drag for per unit length	N m ⁻¹
Fr	Froude number	-
g	Gravitational acceleration constant	m s⁻²
g	Gravitational acceleration vector	m s⁻²
G	Dimensionless number group	-
G′	Storage modulus	Ра
<i>G''</i>	Loss modulus	Ра
G _c	Dimensionless number group	-
G_{c}	Dimensionless number group	-
ΔG_{f}	Gibbs free energy change for emulsion formation	J
h	Liquid film thickness	m
Н	Channel height	m
K	Equilibrium constant for adsorption of the surfactant at the liquid/liquid interface	-

l _{dd}	Drop spacing	m
$l_{\rm m}$	Interfacial length during saccadic motion	m
lo	Interfacial length at rest	m
$l_{\rm S}$	Segment length	m
l_{SS}	Segment spacing	m
Δl^*	Length ratio	-
L	Latency time	S
\overline{L}	Characteristic length	m
L^*	$L_{\rm c}/\lambda_{\rm m}$	-
L_{c}	Capillary length	m
L_{\min}	Minimum wavelength	m
n	Unit normal vector	-
Oh	Ohnesorge number	-
Р	Pressure	Pa
Q	Water flow rate	m³ s⁻¹
r	Radial direction in the spherical polar coordinate	m
$ ilde{r}$	Surface roughness ratio of the wetted area	-
R	Radius	m
Ŕ	Universal gas constant (molar basis)	J·K ^{−1} ·mol ^{−1}
Re	Reynolds number	-
ΔS^{conf}	Change in configurational entropy	J K ⁻¹
t	Time	S
t	Unit tangent vector	-
Т	Temperature	K
T , T	Stress tensor	N m ⁻²
T_{s}	Saccade period	S
и	Velocity	m s ⁻¹
u	Velocity vector	m s ⁻¹
$\Delta u_{\rm c}$	Critical velocity difference	m s ⁻¹
u_{arphi}	Dimensionless azimuthal velocity	-
u_{arphi}^{*}	Azimuthal velocity	m s ⁻¹
U		
	Velocity	m s ⁻
\overline{U}	Velocity Characteristic velocity	m s ⁻¹

U_{TPCL}	Velocity of the three-phase contact line	m s⁻¹
V^*	Dimensionless averaged steady streaming velocity	-
\overline{V}	Averaged steady streaming velocity	m s⁻¹
$\overline{V}_{\mathcal{Y}}$	Averaged velocity in the <i>y</i> -direction	m s⁻¹
\bar{V}_z	Averaged velocity in the <i>z</i> -direction	m s⁻¹
W	Feature width	m
W	Channel width	m
We	Weber number	-
Wo	Womersley number	-
x	x-coordinate, Cartesian coordinate	m
X	Unit vector, Cartesian coordinate	-
у	y-coordinate, Cartesian coordinate	m
У	Unit vector, Cartesian coordinate	-
Ζ	z-coordinate, Cartesian coordinate	m
Z	Unit vector, Cartesian coordinate	-
Z _c	Position of the three-phase contact line	m
z _{eq}	Static meniscus rise height	m
z _m	Minimum height of the liquid-liquid interface	m
Z_{SS}	Steady state position of the meniscus	m

Greek

Parameter	Description	Units
α	Volume fraction of the aqeuous phase	-
β	Angle of inclination	rad
γ	Interfacial tension between two fluids	N m ⁻¹
γo	Interfacial tension without surfactant	N m ⁻¹
γ^{d}	Dispersive component of the surface energy	N m ⁻¹
$\gamma^{ m p}$	Polar component of the surface energy	N m ⁻¹
Ý	Shear rate	S ⁻¹
Γ^{∞}	Surface excess concentration	mol m ⁻²
δ	Lens indent depth	m
$\delta_{ m Stokes}$	Stokes boundary layer thickness	m
ϵ	$\lambda_{\rm m}/L_{\rm c}$	-
ζ	Angle	rad

θ	Contact angle	rad
$ heta_{ m adv}$	Advancing contact angle	rad
$ heta_{ m app}$	Apparent contact angle	rad
$ heta_{ m app}^{ m W}$	Wenzel apparent contact angle	rad
$ heta_{ m app}^{ m CB}$	Cassie-Baxter apparent contact angle	rad
$ heta_{ m d}$	Dynamic contact angle	rad
$ heta_{ m e}$	Static equilibrium contact angle	rad
$ heta_{ m m}$	Microscopic contact angle	rad
$ heta_{ m rec}$	Receding contact angle	rad
θ	Polar angle in spherical polar coordinates	rad
κ	Curvature	m⁻¹
λ	Viscosity ratio	-
$\lambda_{ m m}$	Microscopic length scale	m
μ	Dynamic viscosity	Pa s
ν	Kinematic viscosity	m² s ⁻¹
ρ	Density	kg m⁻³
σ	Surface tension	N m⁻¹
τ	Shear force per unit surface area	N m ⁻²
$ au_{ m max}$	Maximum shear stress at wall	Ра
$ au_{rarphi}$	Dimensionless shear stress in the azimuthal direction	-
$ au^*_{r arphi}$	Shear stress in the azimuthal direction	Ра
arphi	Azimuthal angle, spherical polar coordinates	rad
Ø	Level of fill	-
ω	Fourier frequency	-
ω^{*}	Dimensionless frequency	-
arOmega	Angular velocity	rad s ⁻¹
$arOmega_{ m max}$	Maximum angular velocity	rad s⁻¹

Acronyms

Acronym	Meaning
СА	Contact angle
CFD	Computational fluid dynamics
CMC	Critical micelle concentration
DTS	Decamethylcyclopentasiloxane/tetrakis(trimethylsilyloxy)silane
IFT	Interfacial tension
OTS	Octadecyltrichlorosilane
PDMS	Polydimethylsiloxane
PFCL	Perfluorocarbon liquid
PIV	Particle imaging velocimetry
PMMA	Poly(methyl methacrylate)
PVD	Posterior vitreous detachment
RBF	Round-bottom flask
SiOil	Silicone oil
TPCA	Three-phase contact angle
TPCL	Three-phase contact line

Chapter 1 Introduction

The retina is the inner layer of the eye wall and is made up of photo-receptor cells which generate nerve signals when they sense light. The brain interprets these signals as vision. Retinal detachment is a serious eye condition where the inner neurosensory retina detaches from the underlying retinal pigment epithelium (RPE). The most common type of retinal detachment happens with retinal tears and is known as the rhegmatogenous retinal detachment. The detachment is usually treated via surgery involving two simultaneous steps: (i) removal of the vitreous humour, which is a viscoelastic aqueous fluid in the eye, and (ii) injection of a vitreous substitute, also called a retinal tamponade, to occlude the tears. An additional step of laser treatment or cryotherapy is needed to produce a biological adhesion between the neurosensory retina and RPE.

Viscous silicone oils (SiOils) are commonly used as retinal tamponade. These possess good optical transparency, high chemical and thermal stability, and good biocompatibility. The SiOil remains in the eye for a period lasting from a few weeks to several months depending on the surgeon's recommendation. Because of its movement within the eye and optical side effects (due to its higher refractive index) the oil is usually removed once the retina is fully stable. In addition, if the oil is not removed it can emulsify. Clinical studies have reported the presence of micron-sized oil droplets in the eye between 1 and 12 months after surgery (Toklu *et al.*, 2012), and the difficulty in detecting the onset of emulsification in clinical examinations (Federman and Schubert, 1988). This complication is clinically significant due to the risk of the oil droplets blocking the drainage system of the eye, leading to secondary glaucoma and thereby further loss of vision (Tode *et al.*, 2016).

Many of the studies in the literature have attributed droplet formation to a bulk emulsification mechanism, where the droplets result from the break-up of the interface between the SiOil and the vitreous humour, due to the shear forces generated at the interface by movement of the eye (de Silva, Lim and Schulenburg, 2005; Chan, *et al.*, 2011). However, this widely cited hypothesis is still not fully understood and has not been proven experimentally. Investigating the dynamics of two fluids inside the eye chamber subject to the eye's saccadic motion will allow the factors influencing emulsification to be identified. Understanding the mechanisms that lead to the formation of oil droplets is required to minimise, and potentially avoid, emulsification.

This chapter introduces the relevant medical background to understand retinal detachment and the surgical procedure of retinal tamponade injection.

1.1 Retinal detachment

1.1.1 Eye anatomy

The eye is the sensory organ responsible for vision. The human eye is approximately spherical, with a diameter of about 24 mm along the visual axis and 23 mm along the vertical axis. Figure 1.1 shows a cross section of the eye. It consists of three chambers. The anterior chamber is located between the cornea and the iris. The posterior chamber lies behind the iris and surrounds the lens. The lens is suspended to the ciliary body by ligaments called zonule fibres (Bassnett, 2021). Both chambers are continuous and are filled with aqueous humour, a dilute protein solution produced continuously by the ciliary body epithelium, that flows from the posterior chamber into the anterior chamber while providing nutrients (Siggers and Ethier, 2012).



Figure 1.1: Schematic vertical cross-section of the eye

The back of the eye consists of the vitreous cavity, the retina, the choroid and the sclera. It is generally assumed to be spherical in shape and is symmetric around the visual axis (Meskauskas, Repetto and Siggers, 2012). The vitreous chamber is filled with vitreous humour: a transparent, viscoelastic, gel-like fluid that maintains the eye shape. It is approximately 98–99 wt.% water with trace amounts of hyaluronic acid, glucose, ions and collagen (Siggers and Ethier, 2012). The humour is contained within the vitreous membrane that is attached to the retina.

The retina is approximately 0.5 mm thick and lines the inside of the back of the eye (Remington, 2012). It is comprised of 10 layers composed of different cell types, with the two outer layers being the photoreceptor layer and the retinal pigmented epithelium (RPE) (Kolb, 1995). The photoreceptive layer contains the light sensitive cells that absorbs light and converts it into a neural signal that is transmitted to the brain along the optic nerve. The RPE is a monolayer of pigmented cells that separates the retina from the choroid, and helps maintaining the photoreceptor layer (Strauss, 2005).

1.1.2 Posterior vitreous detachment

While the aqueous humour is considered to be a Newtonian fluid with a similar viscosity to saline (Johnson et al., 1989), the vitreous humour exhibits viscoelastic behaviour as a result of the hyaluronic acid and collagen present (Siggers and Ethier, 2012). As the eye ages, the vitreous humour is known to liquefy and become more Newtonian, with lower apparent viscosity (Los et al., 2003; Stefánsson, 2009). The vitreous chamber can shrink and pull the vitreous membrane away from the inner surface of the retina, resulting in a condition known as posterior vitreous detachment (PVD). When PVD occurs, retinal tears can form in up to 35% of patients (Ramovecchi, Salati and Zeppieri, 2021). Vitreous humour can then pass through the torn region and collect in the space between the neurosensory retina and its underlying RPE. The vitreous pushes the retina away from the RPE, leading to retinal detachment. This is known as the rhegmatogenous retinal detachment.

It is hypothesized that the forces generated by subsequent motion of the eye can lead to further detachment of the retina. When the tear or the detachment happens in the inferior part of the retina (lower half of the eye with respect to the visual axis), it is called an inferior detachment (or inferior break), whereas a superior break involves a tear or detachment in the upper part.

1.1.3 Eye motion

The human eye rotates in all three directions and the movement is controlled by the extraocular muscles. There are different types of eye movement, with the most typical being the eye saccade. A saccade is a rapid rotation of the eyeball to redirect the visual axis to a new direction and is performed a large number of times on a daily basis (Becker and Fuchs, 1969). Following each saccade pulse, the eye remains stationary at its new position before undergoing another saccade. The pause between two saccades is called the saccadic latency. The saccadic eye movement is defined by several parameters: the angular displacement or saccade amplitude, *A*; the direction of the motion; the duration of the saccade pulse, *D*; the angular velocity, Ω ; and the latency time between saccades, *L*. Most saccades are completed within a few tens of milliseconds, and the latency time varies, with an average value of 200 ms (Becker and Fuchs, 1969). Figure 1.2 shows a typical saccadic motion with an amplitude of 11°, a peak angular velocity of 420 °/s ($\Omega_{max} = 7.3$ rad/s), and a duration of about 40 ms.



Figure 1.2: Example of (a) the angular displacement – time profile and (b) associated angular velocity profile recorded for a healthy human eye. Saccade parameters: $A = 11^{\circ}$, $\Omega_{max} = 420^{\circ}/\text{s}$, D = 40 ms. Reproduced from Chan *et al.* (2011). Labels Ω_{max} , *L*, *D* and *A* are explained in the text.

Saccadic motions generate intraocular fluid movements in the vitreous chamber which can add additional shearing forces at the point of retinal detachment. Repetto *et al.*,

(2011) suggested that this additional shearing could lead to larger tears and fluid ingress under the retina.

1.2 Vitrectomy and retinal tamponade

1.2.1 Surgical procedure

In most cases, retinal detachment, if untreated, will lead to blindness of the eye. Retinal detachment requires surgical repair to re-attach the retina and seal any tears present.

Retinal detachment has been treated by vitreoretinal surgery, also called vitrectomy. Vitrectomy involves removing the vitreous humour and replacing it by a substitute (see Figure 1.3). The substitute, known as a retinal tamponade or vitreous substitute, is a fluid (liquid or gas). It occludes the retinal tear(s) during the re-attachment process. Although the surgical procedure consists of replacing all the vitreous by the tamponade fluid, there will always be some aqueous phase present in the vitreous chamber. The aqueous humour is generated by the ciliary body epithelium, and flows from the posterior chamber into the anterior and vitreous chambers (Siggers and Ethier, 2012).



Figure 1.3: Schematic representation of the (a) direct-exchange between removal of the vitreous humour, V, and injection of a denser-than-water silicone oil, S, (b) treatment of the detachment/tear(s) by laser photocoagulation or cryotherapy

In the case of rhegmatogenous retinal detachment, the surgeon includes a step of laser coagulation or cryotherapy, to seal the retinal tears and/or help the scarring and adhesion of the retina. The sealing of the retinal tears takes about two weeks to form. This treatment step introduces additional damage to the retina and surrounding areas

(Soman and Banerjee, 2003). Jain *et al.* (2008) showed experimentally that the retinal lesion size increased linearly with laser beam power and logarithmically with laser pulse duration. The diameter of the lesions reported varied from 100 to 500 μ m.

An encircling scleral buckle is sometimes used as a complementary technique to assist in closure of the retinal tears - especially if they are in the lower part of the eye (inferior). One example is an encircling buckle which is tightened around the whole perimeter of the eye and shortens the eye radius (see Figure 1.4). This assists by pushing retinal breaks in the lower part of the eye into the internal tamponade to help ensure closure. The reduction of the eye radius may also reduce the shear stress and the traction on the retinal wall (Ghoraba *et al.*, 2012).





1.2.2 Retinal tamponades

The choice of the tamponade fluid depends on the patients' condition, the location of the detachment, and the length of time that the tamponade is required to remain in the eye. Tamponades in common use include gases such as air and gaseous perfluorocarbons, and liquids such as SiOils and perfluorocarbon liquids (Soman and Banerjee, 2003). Table 1.1 compares the relevant physico-chemical properties of three retinal tamponades in clinical use with related aqueous solutions.
Fluids properties	Aqueous solutions			Retinal tamponades			
	Water	Saline	Aqueous Humour	Vitreous Humour	SiOil	PFCL	Gas
Density (kg/m ³)	997	1006	1010	1005 - 1009	967 - 975	1750 - 2020	< 1.3
Refractive index (-)	1.33	-	-	1.33	1.3 - 1.4	1.27 - 1.34	-
Surface tension (mN/m)	72	-	-	48 (liquid phase)	20	14	-
Interfacial tension (against water, mN/m)	-	-	-	-	40	50	70
Viscosity (mPa s)	0.89	1	1	Visco- elastic	1000 - 5000	1 - 8	-
Molecular weight (g/mol)	18	-	-	-	20,000 - 100,000	400 - 800	20 - 200
рН	7.0	7.4	7.0-7.4	7.0 - 7.4	-	-	-

 Table 1.1: Comparison of some physico-chemical properties of retinal tamponades and aqueous solutions at 25°C. Values are taken from the references cited in this section.

The essential requirements for a retinal tamponade are biocompatibility, non-toxicity and transparency. The refractive indices in Table 1.1 lie between 1.2 and 1.4, which is close to that of the vitreous humour (1.33) (Soman and Banerjee, 2003). During surgery, it is easier to detect the interface between the tamponade and the humour if their refractive indexes differ. However, a large difference in refractive index would result in poorer vision for the patient. The location of the tear or detachment determines the density to be used: some surgeons deploy denser tamponades for inferior breaks.

Gases such as air and perfluorocarbons are used as vitreous substitutes. They exert high tamponade forces due to the large difference in density compared to water. When

injected into the eye chamber, intraocular gas, such as sulfur hexafluoride or perfluoropropane, undergoes an initial expansion phase due to the diffusion of the nitrogen from the surrounding tissue fluid compartment into the gas. Then, the gas slowly diffuses out of the eye (Kanclerz and Grzybowski, 2018). In general, gases exert a tamponade force for up to a few weeks, depending on the gas (Soman and Banerjee, 2003). Gases are thus suitable for short-term treatment.

Perfluorocarbon liquids (PFCLs) such as perfluoro-n-octane or perfluorodecalin are used owing to their high density (density of 1.6 - 2.1 relative to saline (Remington, 2012)). PFCLs are synthetic analogues of hydrocarbons, containing C-F bonds instead of C-H bonds. They are optically transparent and immiscible with aqueous solutions. They have low viscosity (1 - 8 mPa s at 25°C) (Peyman *et al.*, 1995) which facilitates their injection and removal from the vitreous chamber. However, clinical studies have shown that the immune system was activated after 1 to 2 weeks of PFCL being present in the eye, causing ocular inflammation (Yu *et al.*, 2014). PFCL is mainly used to push the retina back to the RPE, and then is replaced by another tamponade fluid such as SiOil during the surgery.

Silicone oil and its derivatives are good long-term tamponades. SiOil was first introduced by Paul Cibis, an ophthalmologist and surgeon, in 1962 (Cibis et al., 1962). John Scott, eye surgeon at Addenbrooke's hospital (Cambridge, UK), later extended the work of Cibis and improved the surgical techniques employed in the repair of retinal detachment (Scott, 1998). SiOils used in retinal surgery are synthetic polymers of polydimethylsiloxane (PDMS). PDMS is transparent, inert and hydrophobic. The viscosity used clinically ranges from 1 to 5 Pa s with the higher viscosity oil often poses challenges in injection and removal during the vitrectomy surgery. The viscosity of the oil increases with the polymer chain length. The larger and the more monodisperse the polymer molecular weight, the better the biocompatibility of a SiOil (Barca, Caporossi and Rizzo, 2014). Its biocompatibility was debated until the Silicone Study clinically investigated the relative merits of SiOils over gas tamponades in 1992 (Lean et al. and McCuen et al., 1992). PDMS has a density around 970 kg/m³ and is used for superior retinal detachment. Adequate oil level of fill is imperative to ensure sufficient intraocular tamponade forces to push the retina back to the eye. Denser SiOils also called "heavy SiOil" can be obtained either by substituting the methylfunctional groups of PDMS by fluorinated groups, or by blending PDMS with liquids of higher density (Caramoy *et al.*, 2010, 2015; Williams *et al.*, 2010). The work presented here focuses on PDMS, *i.e.* SiOils less dense than water.

1.2.3 Silicone oil emulsification and other complications

SiOil can usually remain in the vitreous chamber for months without inducing ocular inflammation or toxicity. Recent work by Dresp (2020) analysed 12 different medical brand SiOils using GC-MS and found the presence of oligosiloxanes at levels ranging from 0.1 to 491 ppm. Dresp reported that the presence of those impurities could cause visual toxicity and side effects on the retinal surface. The effect of these lower molecular weight molecules on the retinal surfaces requires further clinical study.

SiOil is also chemically inert, except in the case of contact with PFCL after a surgical exchange of PFCL by SiOil. Some clinical studies have shown that PFCL is soluble in SiOil and can change the property of the oil by making it 'sticky' and adherent to the retina (Veckeneer *et al.*, 2008; Romano *et al.*, 2012). This adhesion of the oil may also increase the difficulty of removing it from the eye.

In addition, several studies have reported the presence of SiOil droplets in both the posterior (Chan, Cheung, *et al.*, 2015) and anterior (Savion *et al.*, 1977) compartments of the eye (see Figure 1.5). The detected droplets had diameters ranging from 1 to 50 μ m, with 1 μ m the lower limit of the detection techniques (Ichhpujani, Jindal and Jay Katz, 2009). It is challenging to know the onset time of emulsification because of the difficulty in detecting individual small droplets in the vitreous chamber. Emulsification is usually detected when many droplets have already formed and migrated into the anterior chamber via the intraocular fluid circulation. Depending on their density relative to the aqueous humour, those droplets could either cream or sediment in the anterior chamber. A few studies have found SiOil droplets adhered to the surface of the lens (Sharma, Sudan and Gaur, 2003; Hu and Peng, 2018).

The migration of the oil droplets into the anterior chamber gives rise to other potential complications. The oil can block the trabecular meshwork, which is the drainage canal of the aqueous humour. A blockage can lead to a rise in intraocular pressure and the accumulation of waste products in the eye. The rise in the pressure leads to the risk of developing glaucoma (Siggers and Ethier, 2012).



Figure 1.5: Photography of a layer of silicone oil droplets floating in the upper portion of the anterior chamber (Montague, 2014)

1.3 Current limitations in silicone oil emulsification studies

In previous experimental studies, emulsification between the oil and aqueous phase is assumed to occur either at the bulk liquid-liquid interface or the three-phase contact line (TPCL) between the two liquids and the retinal surface. Some workers treat the aqueous phase as a thin film layer about 5 to 10 μ m thick on the hydrophilic retinal surface (Winter *et al.*, 2000). Others assume the presence of a TPCL between the two liquids and the retinal surface (Fawcett, Williams and Wong, 1994). Figure 1.6(a) shows a simplified model of the eye chamber filled with the aqueous and the tamponade phases, with the aqueous layer as a thin film of varying thickness on the retinal surface. Figure 1.6(b) represents a chamber model with the two liquid phases forming a contact line on the retinal surface.

The SiOil emulsification mechanism most often proposed in the literature is bulk emulsification (de Silva, Lim and Schulenburg, 2005; Chan, *et al.*, 2011 & 2014; Chen *et al.*, 2020). The oil droplets are formed from the break-up of the oil-aqueous interface, due to the shearing forces between the two liquids generated by the movement of the eye. The latest experimental studies found in the literature investigated the bulk emulsification hypothesis in a cylindrical model of the eye chamber under saccadic motion. However, the experiments only employed two different sets of saccadic conditions (Chan, Williams and Wong, 2014). No experimental studies to date have proved the bulk emulsification hypothesis in 3D *in-vitro* eye models representative of the real eye geometry and processes.



Figure 1.6: Simplified model of the vitreous chamber as a sphere with (a) the oil (L2) and the aqeuous film (L1) with *d* the local aqueous layer thickness; or (b) the presence of a three-phase contact line between the two liquids and the retina, with L1 denser than L2.

A recent mechanism proposed by Lu *et al.* (2019) suggested that the SiOil-aqueous TPCL moving along the retinal surface may pin to the retinal cells and give rise to droplet formation. The investigation was carried out with a microchannel device coated with retinal cells, and the three-phase contact line (2 Pa s oil/cell culture medium) was observed to pin to the cells when moving across the channel and leave a droplet on the pinning sites. However, the studies did not mention if the pinned drop eventually detached from the cells. This surface emulsification hypothesis requires further experimental investigation to characterise the effect of surface and liquid properties on the stability of three-phase contact line, and determine the conditions where the pinned droplets detach from the substrate under the shearing flow of the surrounding liquid phase.

1.4 Thesis objectives and scope

With the widespread use of SiOil tamponades, the need to understanding *in-vivo* emulsification process has increased. Establishing the mechanism that leads to interface breakup and understanding the main factors causing emulsification are needed to prevent its occurrence, and hence, improve the surgical outcomes.

The gaps in knowledge in this field lie in the lack of experimental eye models that accurately represent the eye chamber geometry and simulate the eye saccadic motion; the investigation of the SiOil emulsification mechanisms in these representative models; as well as a lack of analytical and numerical studies that investigate two-

phase flow dynamics in the eye. The aim of the thesis is to develop representative *invitro* eye chamber models and tuneable saccadic sequence motions to investigate the SiOil emulsification mechanisms. The objectives are:

- To develop a spherical eye model to study the bulk emulsification mechanism by considering hydrodynamics and surface science, and determine the conditions that promote interface instability
- (ii) To provide insights into one-phase and two-phase flow dynamics in eye model under saccadic motion
- (iii) To establish the main factors contributing to SiOil emulsification by considering bulk and interfacial properties
- (iv) To develop an experimental set-up to investigate the surface emulsification mechanism using chemical and topographical features to represent the retinal surface.

This dissertation consists of seven chapters:

Chapter 1 introduces the medical background of the thesis and the objectives of the study.

Chapter 2 provides a literature review of emulsion science and emulsification mechanisms, with further analysis into SiOil emulsification in eye studies. The methods and techniques reviewed are used in Chapters 3 to 6.

Chapter 3 describes the development of the spherical eye model with a tuneable saccadic sequence motion, and the experimental techniques used in the preparation and analysis of the oil-aqueous interface deformation, as well as the characterisation of the single-phase flow. Chapter 4 presents the results obtained in the experiments. The main factors affecting the stability of the oil-aqueous interface are investigated and comparison is made between the experimental data and numerical results

Chapter 5 describes the experimental set-up used to study the effect of surface and liquid properties on the moving TPCL. Chapter 6 presents the conditions under which the TPCL becomes unstable when moving across uncoated and coated substrates. The conditions giving rise to droplet formation are also investigated.

Finally, Chapter 7 concludes the thesis and makes recommendations to the clinicians on how to interpret the results and translate them into clinical procedures, as well as directions for future work.

Chapter 2 Review of literature on silicone oil emulsification

This chapter introduces the general principles underpinning emulsification, including the physical and chemical quantities involved in emulsification as well as the different instability mechanism leading to droplet formation. It then reviews the different SiOil emulsification mechanisms hypothesized for the eye, including *in-vitro* experiments, theoretical and numerical models published to date. This will give a quantitative and qualitative description of the state of understanding on eye emulsification, as well as the gaps in knowledge that require further investigation.

2.1 Emulsification

2.1.1 Emulsions

An emulsion is a dispersion of one liquid phase in a second, immiscible liquid as small spherical droplets. The droplets are labelled the dispersed phase and the surrounding liquid the continuous phase. Oils and water are generally immiscible: dispersions of oil in an aqueous phase are an oil-in-water emulsion, while the opposite case is a water-in-oil emulsion.

2.1.1.1 Interfacial tension

Emulsification involves the creation of new interfaces. The interfacial tension between two fluids, γ , (or surface tension when one of the fluid is a vapour) is defined as the force per unit length of a line in the interface, expressed in N/m. For simple liquids at a constant pressure and temperature and in strain equilibrium, the interfacial tension is physically equivalent to the interfacial free energy, usually expressed in J/m². The surface energy is the energy required to create unit area of the surface. The origin of the surface energy is the difference in the energy of interactions between molecules at the surface and those in the bulk. The latter have more interactions so work has to be done to generate the interface.

The Gibbs free energy change for emulsion formation (ΔG_f) can be expressed as (Chowdary *et al.*, 2017):

$$\Delta G_{\rm f} = \gamma \Delta A - T \Delta S^{\rm conf} \tag{2.1}$$

with ΔA the change in the interfacial area during the emulsification, *T* the absolute temperature, and ΔS^{conf} the change in configurational entropy due to formation of droplets. The sign of the free energy change will determine whether the emulsification is spontaneous. A net positive Gibbs free energy change means that emulsification is not a spontaneous process and requires external energy. Emulsion is also thermodynamically unstable owing to the increase in interfacial area. The interfacial tension tends to minimise the contact area between the two phases, leading to recombination of droplets and eventually phase separation.

Interfacial tensions or energies can be measured by several methods. One is the pendant drop method, where a droplet of the liquid is suspended at the tip of a needle in another fluid (see Figure 2.1). Analysis of the suspended drop shape with the Young-Laplace equation yields the interfacial tension:

$$\Delta P = \gamma \kappa = \gamma \left(\frac{1}{R_1} + \frac{1}{R_2} \right) \tag{2.2}$$

where ΔP is the Laplace pressure between the droplet and the surrounding fluid, κ the local curvature of the interface, R_1 and R_2 the principal radii of curvature of the pendant drop. Measurement of interfacial tension also depends on the temperature and the presence of other dissolved species such as salts. Gaonkar (1992) showed experimentally that the addition of salts to water decreased the interfacial tension of the soybean oil and water system, and the reduction is enhanced by a higher temperature. This is due to an increased solubility of any dissolved species in the liquid and increased concentration at the liquid-liquid interface which lowers the interfacial tension.



Figure 2.1: Schematic of a pendant drop with the principal radii of curvature, R_1 and R_2 . Labels L₁, L₂ and V indicate liquid 1, liquid 2 and air, respectively.

Emulsification involves two steps: (i) dispersion and (ii) stabilization of the droplets formed. The introduction of a chemical agent, called a surfactant, is necessary to promote the formation of a stable emulsion.

2.1.1.2 Surfactants

A surfactant is a substance that adsorbs at the interface between the dispersed and continuous phases, and prevents the droplets from coalescing. Surfactants are amphiphilic: their molecular structure has two parts of different affinity, a hydrophilic head and a hydrophobic tail. An ionic surfactant has a polar head group, and amphoteric surfactant has both cationic and anionic functional groups in the head part. A water soluble amphiphilic surfactant adsorbs at the oil-water interface, forms a cluster around the droplets (see Figure 2.2), and tends to stabilise an oil-in-water emulsion according to the Bancroft rule (Bancroft, 1912). The soluble surfactant molecules at the interface are in equilibrium with those in the bulk of the solution. Insoluble surfactants, such as surfactant with very long hydrocarbon chain, form a monolayer film at the interface and stay anchored at the surface.



Figure 2.2: Schematics of (a) an amphiphilic surfactant with a hydrophilic head and a hydrophobic tail, (b) surfactants at an interface between an oil drop (O) in an aqueous continuous phase (L)

The presence of surfactants can also introduce steric and entropic contributions which stabilise the dispersed phase. The Gibbs adsorption isotherm describes the effect of surfactant adsorbing at the surface on the interface tension:

$$\Gamma^{\infty} = -\frac{1}{\hat{R}T} \frac{d\gamma}{d\ln C}$$
(2.3)

with Γ^{∞} the surface excess concentration of surfactant, \hat{R} the gas constant, and C the concentration of the surfactant in the bulk liquid. A positive Γ^{∞} means γ decreases with increasing concentration. Γ^{∞} can also become negative when high concentration of salts are added to the aqueous phase. The surfactant is salted out of the aqueous phase and transferred to the oil phase, and the surface excess becomes negative (Ruckenstein and Beunen, 1984).

The change of interfacial tension with concentration can be measured using the pendant drop method. By introducing a soluble, amphiphilic surfactant in the liquid, its adsorption at the liquid interface decreases the interfacial tension. By increasing its concentration, the surfactant aggregates into micelles. There is a critical micelle concentration (CMC) where the further addition of surfactant do not decrease the interfacial tension, but only increases the number of micelles formed.

Proteins, such as milk and egg proteins, are commonly used as emulsifiers in the food industry. They stabilise emulsions by orienting their hydrophobic amino acids to the oil phase and hydrophilic amino acids to the aqueous phase (Lam and Nickerson, 2013). Insoluble proteins can give rise to the formation of a viscoelastic monolayer film at the

interface: this is an example of a non-simple interface (Hinderink *et al.*, 2021). The film formation leads to greater stability of the droplets and prevents coalescence.

2.1.1.3 Three-phase contact angle

The three-phase contact line (TPCL) in this application is the interface between two fluids and a solid. For a droplet of liquid placed on an ideal, rigid, smooth surface (Figure 2.3), the balance of forces acting at the TPCL is described by Young's equation:

$$\gamma_{\rm SV} = \gamma_{\rm SL_1} + \gamma_{\rm L_1V} \cos \theta_{\rm e} \tag{2.4}$$

with θ_e the static equilibrium three-phase contact angle (TPCA) defined in the denser phase, γ_{SV} the substrate/air interfacial tension, γ_{SL_1} the substrate/liquid interfacial tension, and γ_{L_1V} the liquid/air surface tension. The equation is still valid if the vapour phase (V) is replaced by a second liquid, L₂.



Figure 2.3: Schematic of a sessile drop of liquid. Labels L_1 , L_2 and V indicate liquid 1, liquid 2 and air, respectively.

When $\theta_e = 0$, the liquid is said to completely wet the solid surface, and when $\theta_e \neq 0$, the liquid is partially wetting the surface. When the liquid is water and θ_e is smaller than $\pi/2$, the surface is labelled hydrophilic, whereas surfaces with $\theta_e > \pi/2$ are hydrophobic.

Experimentally, the contact angle of a partially wetting liquid on an ideal solid substrate varies between two limits; the receding and advancing contact angles, θ_{rec} and θ_{adv} , respectively. The difference between the two values defines the contact angle hysteresis. The hysteresis has a thermodynamic origin and is caused by the existence of a frictional force that arises from creating a new surface behind the contact line

(Makkonen, 2017). In an experiment where liquid is added to a drop deposited on the surface, the contact line will be pinned while the contact angle increases until it reaches the advancing contact angle, beyond which the contact line moves. Similarly, when withdrawing liquid from a drop the contact angle will decrease until the receding contact angle is reached.

A real surface is rough and chemically heterogeneous. The local variation of surface roughness and heterogeneity intensifies the contact angle hysteresis via various mechanisms (Nadkarni and Garoff, 1992), such as the contact line being pinned by the local defects, liquid penetrating into the surface features, or different affinities of the liquid with the chemically heterogeneous surface. The wetting of real surfaces is characterised by the macroscopic apparent contact angle, θ_{app} .

Wenzel and Cassie developed models for the apparent contact angle to describe the wetting of rough and chemically heterogeneous surfaces, respectively. Wenzel studied the case of a rough and chemically homogeneous surface and assumed total impregnation of the liquid on the surface. The Wenzel equation describes the relationship between the apparent and the Young contact angles:

$$\cos\theta_{\rm app}^{\rm W} = \tilde{r}\cos\theta_{\rm e} \tag{2.5}$$

with the roughness ratio of the wetted area, $\tilde{r} \ge 1$. In the Wenzel model, the wetting affinities are amplified by roughness. Wenzel's model is not valid if air is trapped within the surface roughness.

The Cassie-Baxter model describes the wetting of flat chemically heterogeneous surfaces. Consider a flat substrate composed of *n* materials of different surface energies, distributed randomly over the surface at a fraction f_n of the total surface area. The Cassie-Baxter result is:

$$\cos\theta_{\rm app}^{\rm CB} = \sum_{n} f_i \cos\theta_i \tag{2.6}$$

with $\sum_{n} f_{i} = 1$.

Most real surfaces are both rough and chemically heterogeneous, and exhibit a mixed wetting state, between the pure Wenzel and Cassie wetting regimes. The apparent contact angle of a real surface has been derived and studied by Miwa *et al.* (2000)

and Marmur (2003). A droplet deposited on a real surface possesses multiple wetting states and gives different quasi-static apparent contact angles.

2.1.2 Fluid dynamics

When the emulsification process is not spontaneous, it requires the input of energy into the system to create interfaces between the two liquids. Understanding the flow regime and the forces generated in the fluids will help determine the mechanisms involved in droplet formation by interfacial break-up.

2.1.2.1 Boundary condition at the fluid-fluid interface

The motion of an incompressible fluid *i* of density ρ_i and viscosity μ_i is governed by the Navier-Stokes equations:

$$\rho_i \left(\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) = -\nabla P + \mathbf{F} + \mu_i \nabla^2 \mathbf{u}$$
(2.7)

$$\nabla \cdot \mathbf{u} = 0 \tag{2.8}$$

with **u** the velocity vector, *P* the pressure field, and **F** is any body force acting on a unit mass of fluid (for example, gravity force $\mathbf{F} = \rho_i \boldsymbol{g}$, \boldsymbol{g} the acceleration due to gravity). The equations are solved with the appropriate boundary conditions. Surface tension acts only at the interface and is taken into account through the boundary conditions. For the case of a fluid-fluid interface (shown in Figure 2.4), the normal and tangential stress boundary conditions are given by the stress balance equation:

$$\mathbf{n} \cdot \mathbf{\underline{T}} - \mathbf{n} \cdot \mathbf{\underline{\widehat{T}}} = \gamma \mathbf{n} (\nabla \cdot \mathbf{n}) - \nabla \gamma$$
(2.9)

With **n** the unit normal vector to the interface, $\underline{\mathbf{T}}$ the stress tensor, $\mathbf{n} \cdot \underline{\mathbf{T}}$ the stress exerted by fluid 1 on 2, $\mathbf{n} \cdot \hat{\underline{\mathbf{T}}}$ the stress exerted by 2 on 1, $\gamma \mathbf{n}(\nabla \cdot \mathbf{n})$ the normal curvature force per unit area associated with the local curvature of the interface $\nabla \cdot \mathbf{n}$, and $\nabla \gamma$ the tangential stress associated with gradients in surface tension.



Figure 2.4: Schematic representation of the interface between two fluids 1 and 2. $\underline{\mathbf{T}}$ is the stress tensor, \mathbf{n} the vector normal to the interface, \mathbf{t} the vector tangential to the interface, and the hat on the variable refers to quantities in fluid 2

The normal and tangential stress must balance at the interface. The normal stress balance is given by:

$$\mathbf{n} \cdot \mathbf{\underline{T}} \cdot \mathbf{n} - \mathbf{n} \cdot \mathbf{\underline{\widehat{T}}} \cdot \mathbf{n} = \gamma (\nabla \cdot \mathbf{n})$$
(2.10)

The normal stress balance shows that the curvature causes a pressure jump across the interface. The tangential stress balance is given by:

$$\mathbf{n} \cdot \underline{\mathbf{T}} \cdot \mathbf{t} - \mathbf{n} \cdot \underline{\mathbf{\hat{T}}} \cdot \mathbf{t} = \nabla \gamma \cdot \mathbf{t}$$
(2.11)

Gradients in interfacial tension may arise from gradients in temperature or chemical composition at the interface. The term $\mathbf{n} \cdot \mathbf{T} \cdot \mathbf{t}$ contains shear stresses, which give rise to velocity gradients in a fluid. Therefore, a non-zero $\nabla \gamma$ at a fluid interface will drive flow at the interface.

2.1.2.2 Dimensionless groups

For a flow characterised by a characteristic length \overline{L} and velocity \overline{U} , the fluid is determined by six physical variables ($\rho, \mu \equiv \rho v, \gamma, \overline{L}, \overline{U}, g$) expressed in three fundamental units: length, mass and time. Buckingham's Theorem indicates that the system is described by three dimensionless group:

$$Re = \frac{\overline{U}\overline{L}}{v} = \frac{\text{inertia}}{\text{viscosity}} \equiv \text{Reynolds Number}$$
 (2.12)

$$Fr = \frac{\bar{U}^2}{g\bar{L}} = \frac{\text{inertia}}{\text{gravity}} \equiv \text{Froude Number}$$
 (2.13)

$$Bo = \frac{\rho g \bar{L}^2}{\gamma} = \frac{\text{gravity}}{\text{curvature}} \equiv \text{Bond Number}$$
 (2.14)

The Reynolds number characterises the ratio of inertial to viscous forces and identifies the flow regime. Inertial forces result from the momentum of the fluid and the viscous forces arise from the frictional shearing between different layers in a flowing fluid. At low *Re*, the viscous forces are greater than the inertial forces, and the flow regime is laminar. The turbulent flow regime occurs when the inertial forces dominate.

The Froude number prescribes the relative magnitudes of inertial and gravity forces in the system. The Bond number quantifies the relative importance of forces induced by gravity and by surface tension. The two forces are comparable when Bo = 1 which gives a characteristic length scale, the capillary length scale, L_c :

$$L_{\rm c} = \sqrt{\frac{\gamma}{\Delta \rho g}} \tag{2.15}$$

with $\Delta \rho$ the difference in density between the two fluids.

Other dimensionless groups can be generated from these three groups by combination:

$$We = \frac{\rho \bar{U}^2 \bar{L}}{\gamma} = \frac{\text{inertia}}{\text{surface tension}} \equiv \text{Weber Number}$$
 (2.16)

$$Ca = \frac{\mu \overline{U}}{\gamma} = \frac{\text{viscous}}{\text{curvature}} \equiv \text{Capillary Number}$$
 (2.17)

The Weber number prescribes the relative magnitude of inertial and curvature forces within a fluid, and the capillary number those of viscous and curvature forces. At low Ca, often encountered in narrow spaces, flow is controlled by the capillary forces. At high Ca, the capillary forces are negligible compared to the viscous forces.

For oscillatory flows, the Womersley number is often used instead of Re, with Ω the angular velocity of the oscillations:

$$Wo = \sqrt{\frac{\rho \Omega \bar{L}^2}{\mu}} = \frac{\text{inertia}}{\text{viscous}} \equiv \text{Womersley Number}$$
 (2.18)

2.1.2.3 Moving contact line

The conventional equations for fluid motion no longer apply in the case of a moving TPCL. Huh and Scriven (1971) pointed out that the application of Navier-Stokes equations with the no-slip condition at the contact line leads to a divergent viscous energy dissipation there. This means that the contact line cannot move when applying continuum hydrodynamics with a no-slip boundary condition. The contact line singularity can be eliminated when a small length scale is introduced near the contact line to alleviate the conventional equations for fluid motion.

The definition of the contact angle in the moving contact line problem will then depend on the length scale, defined as the distance from the contact line. On the macroscopic scale, the contact angle is θ_{app} when the interface shape far from the contact line is quasistatic. On the hydrodynamic scale, Voinov defined the dynamic contact angle, θ_d , the local angle the interface makes with the substrate at a specified distance from the contact line (Voinov, 1976). On the molecular scale, Dussan introduced the microscopic or actual contact angle, θ_m , that is determined at the contact line (1979).

Cox (1986) analysed the dynamics of the moving contact line with three length scales (see Figure 2.5). The "outer region" considered the fluid flow in the macroscopic scale (such as capillary length of the system). The "intermediate" region referred to the contact line region of length scale approximated to $3Ca R/\theta_{app}$. The "inner" region focused on the nanometer-scale around the contact line, where microscopic features of the surface defined θ_{m} (Bonn *et al.*, 2009).



Figure 2.5: Definition of the contact angle at different length scales

Cox used this multiscale description to study the hydrodynamics involved in the movement of the contact line when one fluid (fluid A) displaces another (fluid B) from a solid surface. In the outer region, the interface shape is determined by the balance between gravity and surface tension and is characterised by L_c . In the intermediate region, the shape of the interface is determined by the viscous forces and the capillary forces, and is characterised by Ca. The inner region introduces a microscopic length scale, λ_m , to regularise the local flow at the contact line and to allow contact line motion. Cox used asymptotic matching between the three regions with appropriate boundary conditions and obtained an expression for the interface shape, $g(\theta, \lambda)$, as well as the critical capillary number that characterises a fluid entrainment transition:

$$g(\theta, \lambda) = \int_0^\theta \frac{d\theta}{f(\theta, \lambda)}$$
(2.19)

$$Ca_{\rm c} \approx \frac{{\rm g}(\pi,\lambda) - {\rm g}(\theta_{\rm e},\lambda)}{\ln(\epsilon^{-1})}$$
 (2.20)

with $\epsilon = \lambda_{\rm m}/L_{\rm c}$, $\lambda = \mu_{\rm B}/\mu_{\rm A}$,

$$f(\theta,\lambda) = \frac{2\sin\theta \left[\lambda^2(\theta^2 - \sin^2\theta) + 2\lambda\{\theta(\pi - \theta) + \sin^2\theta\} + \{(\pi - \theta)^2 - \sin^2\theta\}\right]}{\lambda(\theta^2 - \sin^2\theta)\{(\pi - \theta) + \sin\theta\cos\theta\} + \{(\pi - \theta)^2 - \sin^2\theta\}(\theta - \sin\theta\cos\theta)}$$
(2.21)

This asymptotic expression of the interface shape assumed small contact angles and small *Ca*. Snoeijer, Eggers, Chan and co-workers later developed equations to derive the full expression of the interfacial shape for any contact angle. Further detail is given in Chan *et al.* (2013) and Chan *et al.* (2020).

2.1.2.4 Dynamical wetting transition

The transition between one wetting state to another is called a wetting transition. Enforcing a large velocity at the TPCL can lead to the entrainment of liquid film or air bubbles, or breakup of liquid droplets.

Consider the example a liquid wetting a flat vertical wall with a contact angle $\theta_e < \pi/2$ (Figure 2.6). First, in the static meniscus case, the pressure varies according to $P(z) = P_0 + \rho g z$, with P_0 the ambient pressure. The normal stress balance requires that the static interface satisfies the Young-Laplace equation:



Figure 2.6: Schematic representation of a static meniscus, with fluid 2 being a liquid and fluid 1 being air.

The equilibrium shape of a meniscus results from the balance between the surface tension and gravity. The meniscus height rise, z_{eq} , is given by:

$$z_{\rm eq} = L_{\rm c} \sqrt{2(1 - \sin \theta_{\rm e})} \tag{2.23}$$

Consider now the vertical flat wall being withdrawing at constant speed, U, from the liquid bath. This is also referred to as the dip-coating experiment. For a plate speed lower than a critical value, the meniscus reaches a steady position after a transient time. The critical speed, U_c , corresponds to the speed of the plate beyond which the contact line cannot keep up with the plate and a film of the fluid is entrained. This critical speed defines the dynamic wetting transition of the liquid from partial wetting to complete wetting (liquid entrainment), where the viscous forces in the flow dominate over the capillary forces.

Landau, Levich and Derjaguin (1988; 1993) analysed the thin liquid film entrainment condition by considering two distinct regions described in Figure 2.7(b&c). The outer region is characterised by a quasistatic meniscus where gravity is balanced by the curvature pressure. The interface shape is defined by the macroscopic capillary length, L_c . The inner region of the entrained film is characterised by a balance between viscous forces and surface tension forces. The film is defined by a microscopic length

scale, the film thickness, *h*. They found an expression that links the microscale to the macroscale, the film thickness to the capillary length and the capillary number:

$$\frac{h}{L_c} \approx 0.94 C a^{2/3} \tag{2.24}$$

The presence of surfactant in the fluid will give rise to Marangoni stresses that increase fluid entrainment. Surfactant decreases the interfacial tension, increasing Ca and therefore the thickness of the film.



Figure 2.7: Wetting transition of a viscous liquid from partially wetting on a solid wall to liquid entrainment (fully wetting) when the velocity of the velocity of the is higher or equal to a critical speed U_c . Fluid 2 is a liquid and fluid 1 is air.

Blake and Ruschak investigated the dynamical wetting transitions experimentally with liquid 2 being a glycerol/water mixture with a viscosity of 0.1 Pa s. In the case where the substrate was withdrawn from liquid 2, the liquid was entrained on the substrate above a critical speed and the TPCL adopted a triangular configuration. They observed that liquid drops could be entrained at the vertex, the end part of the triangular TPCL (labelled A on Figure 2.8(a)). In the opposite case, where the plate was plunged into the liquid bath, the contact line adopted sawtooth patterns above a critical speed and air bubbles could break off at the vertexes (Figure 2.8(b)) (Blake and Ruschak, 1979). They reported that the air entrainment occurred at 19.4 cm/s and air bubbles were entrained from 25 cm/s, whereas the liquid entrainment started from 0.55 cm/s and liquid drops formed from 0.8 cm/s.



Figure 2.8: Schematic representation of the sawtooth contact line when the plate speed exceeds the critical speed (a) plate withdrawing from the liquid: liquid droplets are entrained on the plate at vertex A. (b) plate plunging into the liquid, giving rise to air bubbles

2.1.3 Droplet formation

2.1.3.1 Spontaneous emulsification

Emulsions can be formed without the input of external energy or very low energy input. Spontaneous emulsification happens when two immiscible liquids which are not at equilibrium are brought into contact. The gradients in chemical potential between the two phases may give rise to negative Gibbs free energy changes. Davies and Rideal (1961) identified three mechanisms for spontaneous emulsification. Firstly, the interface can break up due to interfacial turbulence created by the Marangoni effect. Local variation in interfacial tension drives convective flows, and diffusion of solute between the two phases will cause liquid to flow away from region of low interfacial tension, subsequently breaking up the interface and forming droplets.

The second mechanism is the transition to ultralow or negative interfacial tension causing the interface to increase spontaneously. The example to illustrate this mechanism is the spontaneous emulsification of mercury in water. Aoki *et al.* (2012) applied negative potentials to a drop of mercury in water: the mercury dispersed into droplets of 0.2-0.3 μ m when the dynamic interfacial tension approached transient negative values.

The third mechanism is a diffusion process. Ruschak and Miller studied a water, oil (toluene) and organic solvent (ethanol) system (1972; 1988). The alcohol was miscible in both the water and oil phases and was initially dissolved in the oil phase. The

alcohol-oil mixture diffused to the aqueous phase and gave rise to local saturation near the interface. The oil separated from the alcohol and led to spontaneous emulsification of oil droplets in the aqueous phase. Water droplets could also be formed in the oil phase when the alcohol diffused from the water phase to the oil phase.

2.1.3.2 Mechanical emulsification processes

Mechanical emulsification processes are more energy intensive. The main devices used in industry and academia are summarised in Table 2.1. Devices such as highpressure homogenisers and rotor-stator mixers with high energy input and large throughput are widely used in industrial applications. Microfluidic devices generate individual droplets and allow better control of droplet size as well as lower energy input.

Mechanical energy	High-energy				Low-energy
Devices	High pressure	Rotor-stator	Ultrasonic	Membranes	Microfluidics
System	Nozzle/valve disperser	Mixer	Sonotrode	Glass/ceramic membrane with pores	Micro-sized channels
Mechanism	Laminar extensional flow Cavitation	Shear-stress and/or inertia- stress in turbulent flow	Cavitation Turbulence	Pore diameter	Channel size
	Shear-stress and/or Inertia- tress in turbulent flow	Shear-stress in Iaminar flow			
Droplets	High throughput Uncontrolled size	Middle to high throughput Uncontrolled size	Low to middle throughput	Low throughput Controlled size	Low throughput Controlled size

Table 2.1: Mechanical emulsification devices, adapted from Urban et al. (2006)

2.1.3.2.1 High-energy mechanical processes

In a high-pressure homogeniser, liquid is forced through a valve/nozzle under the effect of pressure, with pressure drops usually ranging from 20 to 100 MPa, to achieve small sized droplets. When passing through the valve, the liquid undergoes laminar

elongational flow, then turbulent flow at the exit of the valve (Lee *et al.*, 2013). The elongated liquid thread becomes unstable via a Rayleigh-type instability, leading to drop formation. There are two types of Rayleigh-type instability in the laminar regime (Eggers, 1997):

- (a) The Rayleigh-Plateau instability develops when the elongated liquid thread length is 1.5 times longer than its radius. The pressure gradient in the liquid amplifies the instability and capillary effects drive the breakup of the liquid thread into segments of equal length. These segments then adopt a spherical shape in order to minimise surface energy.
- (b) The Rayleigh-Taylor instability develops when the two immiscible liquids have different densities and the less dense fluid is accelerated into the heavier liquid. The stream of liquid pushed into the denser phase can give rise to the formation of droplets of the less dense fluid. This instability is promoted by gravity and inhibited by surface tension and viscous forces. Similar to Rayleigh-Taylor, the Saffman-Taylor instability, also known as viscous fingering, occurs when a liquid is injected into a more viscous fluid (Saffman and Taylor, 1958). The pressure gradient in the fluid will amplify the perturbation whereas surface tension opposes the formation of fingers.

These liquid segments or drops can be further broken into smaller droplets by cavitation or by deformation in turbulent flow. Cavitation occurs when the absolute pressure in the liquid reaches its bubble point pressure (for a pure liquid, this is its saturated vapour pressure), and bubbles of vapour form. This can be explained using Bernoulli's equation (Jackson, Bondy and Sollner, 1935):

$$P + \frac{\rho u^2}{2} = \text{constant}$$
(2.25)

with u the average velocity. The velocity of the fluid increases as it passes through the homogeniser and results in a decrease of the hydrodynamic pressure. The energy released from the subsequent implosion of the vapour bubbles generates droplet formation (Taha *et al.*, 2020).

Hinze and Kolmogorov studied the deformation of a droplet in different flow regimes (Hinze, 1955; Frisch, 1995). Dynamic pressures and viscous stresses deform the droplets whereas interfacial tension opposes the deformation. The three forces

controlling the deformation and breakup of the droplet can be described by the generalized Weber group and Ohnesorge number (a viscosity group):

$$We_{\tau} = \frac{\tau D_{\rm drop}}{\gamma} \tag{2.26}$$

$$Oh = \frac{\mu_{\rm d}}{\sqrt{\rho_{\rm d} \gamma D_{\rm drop}}} \tag{2.27}$$

with τ a shearing force per unit surface area (could be either the dynamic pressure or viscous stress), the index d referring to the drop and D_{drop} the diameter of the drop. Large We_{τ} means that τ is greater than the surface forces, and the greater the deformation. There are three types of deformation: the drop can be elongated into a long thread leading to Rayleigh-Plateau instability then breakup; the drop can be flattened into an ellipsoid or torus shape and the stretch leads to breakup, and the droplet can undergo local deformation with parts of the droplet being pinched off.

Breakup occurs if the region of the flow pattern causing the deformation is sufficiently large to contain the deformed drop and if the flow pattern persists for sufficient time. There is a critical We_{τ} value at which breakup occurs when the flow pattern of the continuous phase persists for long enough. The main difference between the laminar and turbulent regimes is that there is a unique value for the critical Weber number in laminar flow, meaning that any drop larger than a critical size defined by the critical Weber number will breakup. In the turbulent regime, the droplet diameter will depend on the size of turbulent eddies.

Rotor-stator and mixer-blade systems are also widely used in industry to produce emulsions. These mixers move through the liquids at high speed and the stresses acting on the liquid lead to liquid deformation and droplet formation. Ultrasonic homogenisers or sonication are also used to disperse liquids into another using the sonic pressure surface waves to cause interfacial instability and the cavitation mechanism (Li and Fogler, 1978).

These conventional mixing and sonic emulsification methods produce large amount of droplets with poor control of the droplet size.

2.1.3.2.2 Microstructure emulsification devices

Compared to conventional emulsification devices, microstructure emulsification devices such as porous membranes or microfluidic systems generate droplets with lower energy input. Nakashima and co-workers introduced emulsification using microporous membranes in 2000 (Nakashima, Shimizu and Kukizaki, 2000) and Nisisako and co-workers introduced microfluidic emulsification systems in 2004 (Nisisako, Torii and Higuchi, 2004). These methods are also called "drop by drop" emulsification because they operate in the laminar regime and produce individual drops with controllable size.

These microstructure devices involve the injection a liquid into another continuous liquid phase through the pores of a membrane or a micro-channel outlet. Depending on the pressure pushing the dispersive phase and the flow rate of the continuous phase, the liquid breaks up in three main modes (Zhu et al., 2015). At low pressure and high flow rate, the dripping mode is observed, where the viscous shear force of the continuous phase breaks the liquid into droplets smaller than the pores or channel orifice. At medium pressure and high flow rate, the geometry-controlled mode will lead to the growth of a droplet larger than the pore size, and the interfacial forces will pinch the neck of the forming drop causing its detachment from the bulk phase. High pressure and high flow rate give rise to a jetting mode, where a long viscous thread is formed. The thread becomes unstable via the Rayleigh-Plateau mechanism due to surface tension seeking to minimize the interfacial area. The viscous forces oppose the thread deformation and the inertial forces favour a long thread. The balance between these forces dictates the droplet breakup condition and is characterised by the capillary number. At high Ca, emulsification is dominated by the viscosity forces, known as the jetting regime. At lower *Ca*, droplets are formed in the dripping regime.

The continuous phase flow also transports the newly formed droplets away from the pores which reduces the coalescence of droplets, and increases droplet stability. The droplet formation frequency through a microchannel (120 μ m width and 30 μ m deep) in Nisisako *et al.*'s study reached a maximum of 750 Hz for a continuous phase flow rate of 18 mL/h (2004). A higher frequency could be achieved if the continuous phase flow rate was increased, but this would give rise to polydisperse droplets.

2.1.3.3 Stability of moving contact lines

As mentioned above, a contact line moving over a smooth solid substrate can lead to droplet formation when the moving speed is greater than the critical velocity. Dipcoating experiments with liquid entrainment over topographical or chemical features have shown that droplets can be formed at lower speeds than the critical velocity.

Figure 2.9 gives a general example of the liquid pinning and pulling over a single feature, which has different topographical dimension or wetting properties than the rest of the substrate. The coated slide is plunged into a bath of liquid, then withdrawn at a constant speed. When moving across the feature, the contact line is pinned at the feature and the meniscus below becomes highly distorted. As the slide is pulled further out, the pinned liquid forms a long thread between the feature and the retracting meniscus. The liquid thread, also called a rivulet, narrows and develops a Rayleigh-type instability and breaks up into droplets (Young and Davis, 1987). A liquid film or primary drop is left pinned on the feature, and the satellite droplets could be either pinned to the solid surface or formed in air. Another mechanism that occurs at the tail of the primary droplet during the retraction period after the liquid thread has broken up is end-pinching or pearling (Ghigliotti, Zhou and Feng, 2013). In this, the curvature in the thread creates pressure gradient that leads to droplets pinch-off.



Figure 2.9: (a) A solid substrate (grey) with a single circular defect (red) of diameter w. (b-d) The solid substrate is pulled out of a liquid bath (blue) into air at a constant speed U, (c) The contact line is pinned at the feature, the liquid thread thins and (d) breaks up.

Van Gestel and co-workers experimentally studied hydrophilic solid substrates with hydrophobic features being withdrawn from a liquid bath of a water/glycerol mixture ($\mu = 220 \text{ mPa s}$; $\rho = 1250 \text{ kg/m}^3$; $\sigma = 61 \text{ mN/m}$; $L_c = 2.2 \text{ mm}$) (Van Gestel, He and

Darhuber, 2020). The apparent contact angle of the liquid varied from 71° to 100° on the hydrophobic feature and from 12° to 88° on the solid substrate. The critical speed of liquid entrainment (section 2.1.2.3) on the bare substrate was $U_c = 6.5 \text{ mm/s}$, corresponding to a critical capillary number, $Ca_c = 0.0235$. For $Ca \le Ca_c$, the hydrophobic feature entrained the liquid during the withdrawal and lead to a rivulet formation (similar to Figure 2.9(c)). Breakup of the rivulet lead to satellite droplets. They found a linear dependence between the size of the largest satellite drop and the feature dimension. For a circular chemical feature, increasing the feature diameter from 22 to 220 µm led to an increase in satellite drop diameter from 0.5 µm to 5 µm. There was also a non-linear dependence between the satellite drop size and the speed of withdrawal, varying from 1.5 to 7 µm for Ca changing from 10^{-5} to 10^{-4} .

Van Gestel and co-workers also simulated the effect of topographic features on the liquid entrainment. By varying the depth of rectangular scratches from 0.2 to 0.4 μ m, they found that only little liquid was entrained on the feature edge and the diameter of the largest satellite drop increased from 0.5 μ m to 2 μ m. Increasing the feature depth further, from 0.4 to 2 μ m, did not change the size of the largest satellite droplet but did entrain a liquid film all over the feature. In summary, they showed that the geometrical parameters of the features are the dominant factors in rivulet and droplet formation. Rivulet formation was governed by the height of the feature edge and the size of the droplets depended on the geometry of the feature, the contact angle hysteresis, and the dip-coating velocity.

2.1.3.4 Detachment of silicone oil droplets from a solid substrate

The formation of a primary drop or liquid film can also give rise to droplet formation in response to the shearing flow of the surrounding liquid. A number of workers have investigated the flow-induced motion of a sessile droplet on a solid substrate (Figure 2.10), from its deformation to partial or total detachment. The fluids are determined by eleven physical variables: ρ_{oil} , $\rho_{aqueous}$, μ_{oil} , $\mu_{aqueous}$, R, g, H, γ , θ , U_1 and v. Dimensionless analysis indicates that the system is described by eight dimensionless groups. Assuming R, U_1 and $\mu_{aqueous}$ as the basis parameters, the eight groups are summarized in Table 2.2.



 ρ_2, μ_2

- **Figure 2.10:** Schematic representation of an oil sessile droplet (liquid 2) on a solid subbrate subjected to a shearing flow of aqueous (liquid 1). Density ρ_i , viscosity μ_i , aqeuous flow velocity U_1 , lift velocity (detachment) v, contact angle θ , interfacial tension γ , droplet radius R, layer thickness H, gravity g.
- Table 2.2: Dimensionless groups characterising the oil sessile droplet on a solid susbtrate subjected to a shear flow of aqeuous.

Dimensionless Group		
$\Pi_1 = v/U_1$		
$\Pi_2 = H/R$		
$\Pi_3 = \theta$		
$\Pi_4 = \rho_{\rm aqueous} U_1 R / \mu_{\rm aqueous}$		
$\Pi_5 = \mu_{\rm oil} / \mu_{\rm aqueous}$		
$\Pi_6 = \rho_{\rm oil} / \rho_{\rm aqueous}$		
$\Pi_7 = U_1 / \sqrt{gR}$		
$\Pi_8 = \gamma/\mu_{\rm aqueous} U_1$		

Seevaratnam *et al.* (2010) presented experimental results for the deformation of silicone oil droplets subjected to a laminar shear flow of water in a rectangular channel. The droplet was deposited on a hydrophilic silica glass surface and immersed in water. Figure 2.11(a-c) shows a time sequence of a SiOil drop (0.92 Pa s) from rest to deformation under shearing flow. The droplet undergoes a "crawling deformation" where the droplet is elongated in the direction of the flow. Figure 2.11(d) represents the flow map of droplet behaviour ($\mu = 0.92$ Pa s) at different water flow rates (Q) and initial droplet radius (a_d): the experimental parameters are summarised in Table 2.3.

The flow map plots Ca versus a dimensionless number group G, defined as

$$G = \frac{Ca^2}{Re} = \frac{\mu_{\text{water}}{}^3 \overline{U}}{\gamma^2 \rho_{\text{water}} a_{\text{d}}}$$
(2.28)

with \overline{U} the average velocity in the rectangular channel. *G* is a parameter inversely proportional to the droplet radius. For the 0.92 Pa s oil, three distinctive regimes were observed: crawling and detaching (which corresponds to the images), sliding with no detachment, and oscillation alone. According to the flow map, a larger droplet subject to high shear flow rate undergoes a crawling deformation. The crawling deformation is usually followed by the partial detachment of the drop and entrainment of the mother drop in the water phase. The smaller daughter drop is left on the surface, undergoes further shearing flow and detaches completely from the substrate (Seevaratnam *et al.*, 2010).

Parameters	Values
Re (water)	50 - 700
Ca (water)	0.002 - 0.017
Q (water)	10 – 72 L/h
$\lambda = \frac{\mu_{\rm oil}}{\mu_{\rm water}}$	10 – 10 ⁴
γ	31 mN/m
$ heta_{ m e}$ (in oil)	140°
$ heta_{ ext{app}}$	90° – 140°

Table 2.3: Experimental parameters investigated by Seevaratnam et al. (2010)

The flow regime map depended on the oil viscosity. Figure 2.11(e) combines the flow maps for three different viscosity oils. For small viscosity ratios ($\lambda = 10 - 100$), only sliding and detachment was observed for large drops for a given flow rate. At high *Ca*, the inertial forces overcome the adhesion forces and lift the drop from the substrate. For the highest viscosity ratio tested ($\lambda = 10^4$), four regimes were observed, consisting of the three regimes seen with the 0.92 Pas oil case and an additional 'oscillation and sliding' region. At high λ , viscous and inertial forces lead to elongation of the droplet, followed by neck pinch-off and partial drop detachment, with the daughter droplets undergoing subsequent deformation.



Figure 2.11: (a-c) Oil droplet (2.6 μ m radius) deformation over time under a constant water flow rate with $\mu = 0.92$ Pa s, Ca = 0.0097 and $G = 6.1 * 10^{-7}$. (c) crawling droplet deformed into a 'mother' part (1) and a 'daughter' part (2). (d) Flow map of droplet behaviour (the circled data point corresponds to the experimental conditions in (ac)). Images from Figures 7 and 8 of Seevaratnam *et al.* (2010), with permission from *Chemical Engineering Science*. (e) Combined flow maps of three different viscosity oils. Dashed lines deliminate the different droplet behaviour regimes.

Lu and co-workers studied the effect of surface wettability on the deformation of sessile kerosene and SiOil drops under shearing flow of water in a similar experimental set-up as Seevaratnam and co-workers (Lu *et al.*, 2019). Their flow conditions are summarised in Table 2.4. They showed that under the same flow conditions as Seevaratnam *et al.* (2010), a higher wettability surface did not give rise to similar motion onset conditions.

Parameters	Values
Re (water)	0 – 2750
Ca (water)	10 ⁻³ - 10 ⁻²
Q (water)	0 – 80 L/h
$\lambda = rac{\mu_{ m oil}}{\mu_{ m water}}$	1 – 400
$\gamma_{ m SiOil-water}$	11 mN/m
$ heta_{ m e}$ (in oil)	45°, 75°, 85°, 118°

Table 2.4: Experimental parameters investigated by Lu et al. (2019)

By estimating the shear rate as the velocity of shear flow at the top of the drop over the height of the sessile drop, they found that a change in the static contact angle (defined in oil) from 75° to 45° required a larger shear rate (from 250 to 500 s⁻¹) to drive the motion of a 2 μ L droplet. An increase in drop viscosity from 60 to 401 mPa s only decreased the shear rate from 240 to 210 s⁻¹. By increasing the droplet volume, a lower critical shear rate was required to deform the drop. For the 45° contact angle case, the shear rate decreased from 250 to 100 s⁻¹ when the droplet volume increased from 2 to 10 μ L. The critical shear rate required to deform a droplet adhered to a solid substrate depended more on the wettability of the liquid over the surface and the size of the droplet, but less on the drop viscosity.

Dimitrakopoulos, Ding and Spelt investigated numerically the onset of motion of sessile droplets under viscous flows at low and moderate Re, especially the critical conditions of the transition between a stationary drop and continuously moving drop (Ding and Spelt, 2008; Ding, Gilani and Spelt, 2010). They found that by keeping the same continuous phase, droplets of different viscosity showed similar conditions for the onset of motion. For droplets with small or moderate initial contact angles ($\theta_e \leq$

110°), the upstream part of the drop started moving if $\theta_e < (\theta_{adv} + \theta_{rec})/2$, whereas the downstream part started moving when $\theta_e > (\theta_{adv} + \theta_{rec})/2$. Droplets with intermediate initial contact angles ($\theta_e \sim 70^\circ$) showed better stability than small or large contact angles, because they had the smallest values of contact angle hysteresis between upstream and downstream TPCA, leading to a stable drop shape in a shearing flow (Dimitrakopoulos, 2007).

2.1.4 Summary

Aside from spontaneous emulsification, emulsions are generally formed with the input of energy and stabilised by the presence of surfactants. The energy is required to deform the interface and create new interfaces. Droplet formation depends on the geometry of the emulsification device and the flow regime. Larger devices generally induce larger shear forces, creating smaller droplet size and larger numbers of droplets. Smaller devices have a smaller number of droplets but a better control of the droplet size distribution. Other liquid and interface properties also play an important role in emulsification, including the viscosity of the dispersed and continuous phases, the ratio of phase volumes and interfacial tension.

When droplets are formed at the three-phase interface (two fluids and one solid), the surface properties and the velocity of the solid substrate affect the stability of the three-phase contact line. Detachment of the droplets from the solid substrate depends on the continuous phase flow rate, the surface wettability and the pinning site dimensions.

In the next section, a review of the literature on SiOil emulsification in the eye is presented. These studies considered two interface locations where instabilities can arise: the bulk liquid-liquid interface or the three-phase contact line between the two liquids and the retinal surface.

2.2 Silicone oil emulsification mechanism

The eye chamber filled with a SiOil tamponade is modelled in Figure 1.6 and the fluids are determined by eleven physical variables: ρ_{oil} , $\rho_{aqueous}$, μ_{oil} , $\mu_{aqueous}$, R, g, Ω_{max} , γ , θ , volume fraction of oil (\emptyset) and length of the oil-aqueous interface, l, expressed in three fundamental units: length, mass and time. Dimensionless analysis indicates that the system is described by eight dimensionless groups. Assuming R as the characteristic length, Ω_{max}^{-1} as the characteristic time and ρ_{oil} as the characteristic mass, the eight groups are summarized in Table 2.5.

 Table 2.5: Dimensionless groups characterising the eye system filled with SiOil and aqeuous solution

Dimensionless Group		
$\Pi_1 = L/R$		
$\Pi_2 = \emptyset$		
$\Pi_3 = \theta$		
$\Pi_4 = \mu_{\rm oil} / \rho_{\rm oil} \Omega_{max} R^2$		
$\Pi_5 = \mu_{\rm aqueous}/\mu_{\rm oil}$		
$\Pi_6 = \rho_{\rm aqueous} / \rho_{\rm oil}$		
$\Pi_7 = g/R\Omega_{max}^2$		
$\Pi_8 = \gamma / \rho_{\rm oil} R^3 \Omega_{max}^2 (We)$		

In the eye, the main factors influencing oil emulsification are the hydrodynamics, interfacial science, and liquid properties. *Wo* characterises the eye saccadic motion and the relative importance between inertial and viscous forces. The flow regime depends on the geometry of the emulsification device, the flow rate and liquid viscosity ratio. *We* and *Ca* describe factors causing interface deformation. The values of characteristic groups for conditions representative of eye movements of aqueous and SiOil (Stocchino, Repetto and Siggers, 2010) are summarised in Table 2.6.

Laqua *et al.* (2013) recorded the eye movement of a human subject during a reading task. They calculated the acceleration work of the eye, and estimated the power of the movement and the energy delivered. For an eye radius of 11 mm, they found the power and energy generated by the eye to be $0.1 - 0.7 \mu$ W and $0.2 - 13 \mu$ J.

Dimensionless Group	Values
Wo	1 – 50
We	10 ⁻³ – 10 ⁻²
Са	10 ⁻³ – 10 ⁻²
$\lambda = rac{\mu_{ m oil}}{\mu_{ m water}}$	1000 - 5000

Table 2.6: Values of dimensionless groups associated with saccadic eye motion.

Prior work on silicone oil emulsification can be classified into three main categories. Initial studies used high energy input emulsification devices to generate droplets and focused on the effect of liquid properties on the emulsification rate and droplet size. Other workers focused on the dynamics of the fluids in the eye chamber during saccadic motion, and hypothesised that droplet formation resulted from the shearing flow at the oil-aqueous interface and the growth of surface instabilities leading to interface break-up. This hypothesis will be referred as the bulk emulsification mechanism, active at the bulk interface. A few recent studies have discussed a surface emulsification mechanism where the adhesion of the moving contact line on the retinal surface leads to droplet pinching off.

2.2.1 High energy input emulsification devices

Experimental papers before 2011 used *in vitro* models agitated under high mechanical power to study SiOil emulsification, and are summarised in Table 2.7. These studies investigated the effect of SiOil physico-chemical properties on the emulsification rate. They used cylindrical vials or glass cuvettes to model the eye chamber, and filled them with stratified layers of aqueous surfactant solution and SiOil. The former was water or saline containing different emulsifiers, such as proteins or extracted blood components. SiOils used were either pure PDMS, substituted PDMS, or blends of pure PMDS with higher molecular weight (HMW) polymers. Tests considered equal levels of fill or higher SiOil volumes.

Energy was provided by vortex and rotor stator homogenizers, shakers and sonication. Typical power inputs by these devices are much larger than the energy generated by the eye (Urban *et al.*, 2006; Laqua *et al.*, 2013). These tests produced oil emulsion after a short period of mixing (1 to 90 min). The emulsification mechanisms in these mechanical devices were described in section 2.1.3.2. The performance was guantified in terms of time onset of emulsification and the thickness of the emulsion layer. An oil was more prone to emulsification (also defined as less stable) when it took less time to emulsify and formed a thicker emulsion layer. Lower viscosity oils were found to be less stable and side group substitution on the PDMS chain destabilised the oil (Nakamura, Refojo and Crabtree, 1990; Heidenkummer, Kampik and Thierfelder, 1991). High molecular weight silicone oils and oil blends stabilised the interface, which is attributed to the increase in μ with molecular weights (Caramov et al., 2010, 2015; Williams et al., 2010). Partial filling of the vial (i.e. air was present in the vial) always led to emulsification whereas complete fill led to less or no emulsification. Some studies investigated the effect of proteins (Heidenkummer, Kampik and Thierfelder, 1991) and blood components in the eye (Savion, et al. 1977) and showed they enhanced SiOil emulsification. Reported oil droplet sizes ranged from 0.5 to 600 µm: the size variation depended on the power input and was also affected by the detection limit of the instrument used to detect droplets.

Dresp (2020) analysed different medical grade SiOils of 1 Pa s and 5 Pa s by gas chromatography coupled mass spectroscopy. The results showed that all the oils studied contained volatile oligosiloxane impurities (low molecular weight polymers) in the order of 1 - 500 ppm, and this concentration varied across the brands but also across the batches of the same brand. Dresp suggested that the allegedly more frequent emulsification with 1 Pa s oil compared to 5 Pa s oil might not be caused the lower dynamic viscosity, but perhaps by the lower-quality oils.

The key findings from these studies are the stabilising effect of viscous forces (oil viscosity) and the destabilising effect of surfactants at the interface. However, these studies employed energy input and eye chamber models that were not representative of the eye, so the droplet formation mechanism in these models cannot be directly applied to the emulsification phenomenon in the surgical case.
Table 2.7: Summary of studies on emulsification of silicone oi	il via high energy input i	in chronological order
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Source	Geometry / Energy source	Working fluids and volume fraction, ϕ_{oil}	Results
Nakamura, Refojo and Crabtree (1990)	Cylindrical vial (glass tube, 17 × 58 mm) Vortex (2,700 rp for 1 min)	SiOil & derivatives $(\mu_{oil} = [0.2 - 12.5] \text{ Pa s},$ $\emptyset_{oil} = 0.67)$ Aqueous solution of proteins and lipids	High viscosity oils (1 and 12.5 Pa s) did not emulsify Fluorosilicone oils (SiOil with fluorine side groups) emulsified more than PDMS of same viscosity. Partially filled vial lead to more emulsification
Heidenkummer, Kampik and Thierfelder (1991)	Cylindrical vial with flat base Water-bath shaker at a constant rate of 90 min ⁻¹ at 37°C	SiOil & derivatives ($\mu_{oil} = [1 - 10.8]$ Pa s; $\phi_{oil} = 0.5$) 0.1 wt.% of biological emulsifiers in water or saline	Droplet sizes ranged from 10 to 600 µm Lower viscosity oils formed more droplets Substituted oils were less stable than pure PDMSs. Emulsifiers (fibrinogen, fibrin, gamma globulins, serum) in saline accelerated the onset of emulsification
Savion, <i>et al.</i> (1977)	Cylindrical vial Sonication for 150 s, followed by centrifugation at 5000 g for 30 min Vortex for 60s	SiOil $(\mu_{oil} = 1 \text{ Pa s}; \phi_{oil} = 0.5)$ Human serum or blood with saline	Mean droplet size of $47\pm 28 \ \mu m$ (sonication) and $189\pm 168 \ \mu m$ (vortex) Increase in concentration of plasma and serum increased emulsification. No emulsification was observed without plasma or serum
De Silva, Lim and Schulenburg (2005)	Perspex sphere of 4 mL with or without a encircling band Horizontal rotating shaker at 100 Hz for 5 days at 37°C	SiOil & oil blends $(\mu_{oil} = 1 \text{ Pa s}; \phi_{oil} = 0.75 \text{ or } 0.9)$ Saline	The presence of the encircling band (mimicking a buckle indentation) reduced emulsification Higher volume fraction of oil reduced emulsification
Caramoy <i>et al.</i> (2011)	Glass cuvette (flat base) Sonication for 3 min, followed by centrifugation at 5000 g for 30 min	SiOil & oil blends ($\mu_{oil} = [1 - 5]$ Pa s; $\phi_{oil} = 0.5$) Plasma or serum	Serum lead to more emulsification than plasma Addition of HMW polymers to SiOil reduced emulsification.
Williams <i>et al.</i> (2010)	5 mL RBFs Mixer with orbital stirring at 2,000 rpm for 1 hour	SiOil & oil blends ($\mu_{oil} = [1-5]$ Pa s; $\phi_{oil} = 0.9$) Pluronic F68 or bovine serum albumin solution	Addition of HMW polymers increased the shear viscosity and extensional viscosity of SiOil. Droplets were formed but no trends observed in the results

Caramoy <i>et al.</i> (2015)	Glass cuvette with flat base, $4 \times 10 \times 40$ mm Sonication at 50 kHz for 3 min High-speed homogenizer at shear rate of 59,660 s ⁻¹ for 1 min.	SiOils and oil blends $(\mu_{oil} = [1 - 8] Pa s)$ Pluronic surfactant solution Sonication: $\phi_{oil} = 0.5$ Homogeniser: $\phi_{oil} =$ 0.001	Addition of HMW polymers increased the shear viscosity of the oil Sonication: Produced both oil-in-water and water-in-oil emulsions / Increase in oil viscosity decreases emulsification High speed homogeniser: No statistical difference between the different oils Contradictory results between sonication and homogeniser
Chan <i>et al.</i> (2017)	Glass syringes High pressure homogenizer Vortex mixing at highest speed for 3 hours Sonication for 1 min	SiOils & oil blends $(\mu_{oil} = [1 - 5] Pa s)$ 2 wt.% Pluronic F68 in saline Vortex/Sonication: $\phi_{oil} =$ 0.5 Homogeniser: $\phi_{oil} = 0.01$	Homogenizer yielded to more consistent results compared to the other two methods Laser light scattering measured most droplet size ranging from 0.5 to 1 µm

2.2.2 Bulk emulsification

The bulk emulsification hypothesis is that the shear stresses generated at the interface are large enough to overcome interfacial tension and generate oil droplets. Prior experimental, analytical and numerical studies are reviewed in this section to understand the fluid dynamics in eye chamber models. These investigations reproduced the real eye geometry and the eye saccadic motion more accurately.

2.2.2.1 Cylindrical eye chamber

In 2011, Chan and co-workers developed a mechanical platform with a stepper motor that delivered a saccadic motion. They used a cylindrical model of the eye chamber consisting of a transparent cylindrical container (internal diameter 20 mm, length 20 mm, volume 6.3 mL) mounted with its axis horizontal. The chamber was filled with a 4:1 oil/saline volume ratio. A stepper motor generated a saccadic motion with $A = 90^{\circ}$, $\Omega_{max} = 360^{\circ}/\text{s}$ and D = 250 ms, giving Wo = 1.6. They used this apparatus in three experimental studies, summarised in Table 2.8.

Study	Working fluids	Results
Chan et	SiOils & oil blends u = [0.005 - 125] Pas	Higher viscosity oil gave the highest angular
(2011)	$\phi_{oil} = 0.8$ Phosphate-buffered saline	The peak angular velocity of the oil attained between 310 and 340°/s for all oils
Chan, Cheung and Wong (2014)	SiOil $\mu_{oil} = [1 - 5] Pa s$ $\emptyset_{oil} = 0.48, 0.63, 0.8$ Phosphate-buffered saline	Addition of indents in the eye chamber reduced the peak velocity of the SiOil Increase in oil viscosity and volume fraction reduced the average relative velocity
Chan, Williams and Wong (2014)	Heavy SiOils $\mu_{oil} = [1.4 - 3.8]$ Pa s $\emptyset_{oil} = 0.8$ Phosphate-buffered saline	Addition of heavy additives (fluorinated olefin) to PDMS changed the flow behaviour: it took longer for the oil to come to rest after the chamber stopped moving

Table 2.8: Summary of experiments carried out by Chan and co-workers

These studies measured the maximum angular displacement of the oil during a saccade pulse by using the measurement method shown in Figure 2.12, and estimated the peak angular velocity of the oil phase. The peak velocity of the oil depended on factors such as the presence of an indent, oil viscosity and level of oil fill

with the latter factor being the least important. Under the saccadic condition employed by these studies, no droplets were formed in the eye chamber.



Figure 2.12: Peak angular velocity measurement method in a cylindrical eye chamber filled with SiOil (dark blue, $\phi_{oil} = 0.8$) and aqueous (light blue). The red mark is an indicator on the eye wall and the red arrows indicate the position of the TPCL. (a) eye chamber at rest, (b) the oil tamponade at its maximum angular displacement during saccadic motion. Image reproduced from Figure 1 of Chan *et al.* (2011) with permission from IOVS.

2.2.2.2 Spherical eye chamber

The motion of a single fluid phase in the eye cavity has been studied in experimental, analytical and numerical papers. These studies are summarised in Table 2.9, Table 2.10 and Table 2.11, respectively. They modelled the eye chamber as a rigid sphere with or without indentation. The fluid dynamics in a rigid sphere were described in spherical polar coordinates as defined in Figure 2.13(a).

These studies simulated the eye motion as a periodic sinusoidal oscillation or an eyelike saccadic motion as described by Becker *et al.* (1969). The oscillations of the chamber induced motion in the fluid due to the no-slip boundary condition, where the liquid on the wall moves at the same velocity as the wall. The chamber wall exerts shear forces on the fluid and the wall-driven drag results in a primary oscillatory motion of the fluid in the azimuthal direction. The motion is primarily located near the wall and penetrates into the core of the fluid. The velocity distribution depends on the dynamic viscosity of the fluid and the geometry of the chamber.



Figure 2.13: (a) Spherical polar coordinates defined in a solid sphere, with (r, ϑ, φ) the radial distance, polar angle and azimuthal angle, respectively. u_{φ} is the azimuthal velocity defined in the equatorial plane of the sphere (light blue). (b) Cross-section of a indented sphere, with the indent representing the eye lens of depth δ .

Repetto, Stocchino and Bonfiglio studied single-phase flow with $2 \le Wo \le 50$, the *Wo* values lying in the range associated with eye movements of vitreous humour and retinal tamponades (Stocchino, Repetto and Siggers, 2010). Repetto *et al.* (2005) showed that at larger *Wo* (associated with aqueous solutions, with lower viscosity), the boundary layer of moving fluid near the wall is shallow. Figure 2.14(a) shows an example of the azimuthal velocity profile in the equatorial plane with a periodic sinusoidal oscillation as input motion at the wall. The fluid motion is stronger near the wall with the maximum velocity located at the wall. For smaller *Wo* (associated with silicone oil tamponades), the velocity profile extends into the whole cavity and approaches solid body rotation (Figure 2.14(b)).

Bonfiglio *et al.* (2015) showed that a viscoelastic fluid could shift the location of maximum velocity away from the wall towards the centre of the sphere at certain resonant frequencies, changing the flow characteristics strongly. These findings have less relevance for tamponades as neither phase exhibits strong viscoelasticity. Stocchino *et al.* (2007) explored the effect of posterior chamber shape on the flow field. The presence of a lens indentation (Figure 2.13(b)) affected the flow field and introduced complex structure.

The calculated velocity profiles agreed with particle imaging velocimetry measurements reported by Bonfiglio *et al.* (2013). They also found that the primary (forcing) motion gave rise to a secondary, weaker, convection flow in the vertical plane.

The time-average secondary flow is referred to as the steady streaming. The intensity of the steady component was four times smaller than the oscillating flow. The steady streaming structure and streamline provided insights into mixing within the eye chamber, with applications for drug delivery in the normal eye.



Figure 2.14: Evolution of the dimensionless azimuthal velocity (u_{φ}) profile in the equatorial plane of the sphere over an entire period of the sinusoidal motion. (a) Wo = 30, (b) Wo = 1. Each curve is separated by $\pi/5$ s. Recalculated from Repetto *et al.* (2005).

Computational fluid dynamics (CFD) simulations of single phase Newtonian fluids in the eye chamber under sinusoidal and saccadic movements have also been reported (Abouali, Modareszadeh, Ghaffarieh, *et al.*, 2012; Modareszadeh *et al.*, 2013). Abouali *et al.* (2012) investigated water ($32.4 \le Wo \le 53.7$), glycerol ($1.5 \le Wo \le 2.4$) and SiOil ($1.0 \le Wo \le 1.7$) in a spherical and an indented sphere model (where the indent represented the lens). They showed a good agreement between their simulated results and the experimental ones from Repetto *et al.* (2005) and Bonfiglio *et al.* (2013), under the same periodic saccade motions.

These studies also determined the shear stresses generated within the fluid and at the wall. The maximum shear stress value, τ_{max} , was found at the equatorial plane on the wall of the sphere. With the indented sphere model, the largest τ_{max} was generated on the eye lens, with values approximately twice those on the retina wall. The maximum shear stress value also increased with saccade amplitude. In the case of an indented sphere filled with water, an increase in amplitude from 10° to 50° increased τ_{max} from 0.4 to 0.72 Pa. They reported that τ_{max} for water was always less than 1 Pa even for large amplitude motions. The shear stress depended on the viscosity and density of the fluid. Under the same saccade motion, SiOil and glycerol induced shear stresses with values of one to two orders of magnitude higher than the water case, but glycerol ($\nu = 5 \times 10^{-4} \text{ m}^2/\text{s}$, $\rho = 1260 \text{ kg/m}^3$, $\tau_{max} = 19.8 \text{ Pa}$) exerted a higher shear stress at the wall than a more viscous SiOil ($\nu = 10^{-3} \text{ m}^2/\text{s}$, $\rho = 970 \text{ kg/m}^3$, $\tau_{max} = 19 \text{ Pa}$) due to its higher density (Abouali, Modareszadeh, Ghaffariyeh, *et al.*, 2012).

Modareszadeh *et al.* (2011) estimated the effect of viscoelasticity on the behaviour of the vitreous humour using rheological data of porcine vitreous from Nickerson *et al.* (2008). The reported elastic and viscous components were 2.8 ± 0.9 Pa and 0.7 ± 0.4 Pa, respectively. They showed that the elastic component increased τ_{max} ten times over that with Newtonian saline: this was attributed to the additional polymer stress in the viscoelastic humour. Moreover, their simulations in both spherical and indented sphere models showed that the presence of the lens indent always increased τ_{max} and the indent accounted for 80% of the increase (Modarreszadeh and Abouali, 2014).

Table 2.9: Summary of	experimental stu	idies on fluid dyna	amics in a sphere	under eye-like motion
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Study	Geometry and working fluid	Motion	Results
Repetto, Stocchino and	Perspex sphere $R = 40 \text{ mm}$	Polynomial time law reproducing	Insight into the flow field: fluid motion was generated at the wall, spread towards the centre and then dissipated.
Cafferata (2005)	98% pure glycerol solution	eye saccades $Wo \sim 3.75 - 6.14$	$ au_{ m max}$ increased slightly with increasing A but strongly dependent on the viscosity of liquid.
		$A = 10 - 50^{\circ}$	Starting from rest, the motion is very close to periodic after only a few rotations of the domain.
Stocchino, Repetto and Cafferata (2007)	Perspex sphere with a lens indent, $R =$ 40.8 mm	Sinusoidal periodic rotations	Presence of lens generated a more complex flow field: generation of vortices structures that migrated at varying paths depending on Wo , which affected the distribution of characteristic and the leastion of $-$
		$\delta/R = 0.15, 0.2, 0.3$	$\tau_{\rm max}$ located on the lens for low <i>Wo</i> , but in the upper part of the lens at higher <i>Wo</i>
	70% & 98% glycerol solution	$Wo \sim 4.5 - 15$	$ au_{\max}$ increased linearly with <i>Wo</i> and <i>A</i> .
Bonfiglio <i>et al.</i> (2013)	Perspex sphere with a lens indent, <i>R</i> = 40.8 mm	Sinusoidal periodic rotations	3D flow field reconstructed using 2D PIV measurements in many horizontal and vertical planes.
		$Wo \sim 3.9 - 48.7$	Steady streaming component is obtained and gave insight in drug transport within the every estimated that drugs would take about 1 hour to disperse throughout the every
	Viscous fluid	$\delta/R = 0.3$	chamber
Bonfiglio <i>et al.</i> (2015)	Perspex sphere, $R = 12.5 \text{ mm}$ Sinusoidal periodic rotations		The artificial vitreous oscillated with larger amplitudes at some frequencies: the velocity at the core of the sphere had higher amplitude than at the wall.
	Viscoelastic artificial vitreous gel	<i>Wo</i> ~ 3.9 - 48.7	

Study	Geometry, working fluid, motion, assumptions	Results	
David <i>et al.</i>	Sphere	τ_{max} was proportional to eyeball radius, kinematic viscosity of vitreous and	
(1998)	Viscoelastic liquid	the frequency of sinusoid motion.	
	Periodic sinusoid rotation, $Wo \sim 5 - 20$	Maximum shear stress increased with increasing Wo .	
	Small Re	Shear stress at the wall grew more than linearly with the eye radius.	
	No secondary flow	Flow velocity in the inner core was out of phase with that at the wall and depended on the eye radius and ratio of the viscous to elastic components. A highly viscous fluid acted like a solid body, a highly elastic fluid had negligible phase lag.	
Repetto, Siggers and Stocchino (2008)	Sphere Newtonian fluid	Fluid flow had a leading-order oscillatory component and a steady-streaming component.	
	Periodic torsional oscillations, $Wo \sim 3 - 16$	Streaming flow had two counter-rotating toroidal vortices, one in each hemisphere (travelled from the centre towards the poles along the axis, then	
	Small-amplitude oscillations	towards the equator close to the wall before returning towards the centre).	
		Steady streaming intensity increased with amplitude, and with <i>Wo</i> . Steady streaming was weak for high-viscous fluid.	
Repetto,	Sphere with lens indentation, $\delta/R = 0.1 -$	Flow was governed by Wo , A and δ .	
Siggers and Stocchino	0.2	Shear stress amplitude was maximised at the centre of the indentation.	
(2010)	Newtonian fluid	Maximum velocity value increased with Wo.	
	Periodic torsional oscillations, $Wo \sim 1 - 15$	Steady streaming component had a larger effect on mixing than the	
	Small-amplitude oscillations	oscillatory component.	
Meskauskas,	Sphere	At small frequencies of oscillation, the velocity profiles are almost linear.	
Repetto and Siggers	Viscoelastic fluid	There were natural frequencies of oscillation in the range 10–25 rad s ⁻¹ that	
(2011)	Periodic torsional oscillations	could be resonantly excited by eye rotations. The maximum dimensionless velocity, which occurred near $r = 0.5$, was more than twice as large as the	

 Table 2.10:
 Summary of analytical studies on fluid dynamics in a sphere under eye-like motion

	Small-amplitude oscillations	maximum velocity of the boundary. The resonance generated larger wall shear stresses
Repetto,	Sphere	Maximum velocity of the steady streaming increased with Wo
Siggers and Meskauskas (2014)	Viscoelastic fluid	Complicated flow structures: five different regions in parameter space in
	Periodic torsional oscillations, $Wo \sim 1 - 20$	which the steady streaming flow assumed qualitatively different patterns
	Small-amplitude oscillations	Steady streaming intensity was larger for viscoelastic fluid than viscous fluid for small frequencies

Study	Geometry, working fluids	Motion	Parameters	Results
Abouali <i>et al.</i> (2012)	Abouali <i>et al.</i> Sphere with a lens Sinusoidal $A = 10 - 50^{\circ}$ (2012) indent, $R =$ periodic $L = 5D$ $12 \text{ or } 40.8 \text{ mm}$ oscillations $\delta/R = 0.1, 0.2, 0.3$ Water ($\nu = 10^{-6} \text{ m}^2/\text{s}$, Saccadic $wo \sim 1 - 53.7$ Glycerol ($\nu = 5 \times 10^{-4} - 2$ /	$A = 10 - 50^{\circ}$ L = 5D $\delta/R = 0.1, 0.2, 0.3$	$\tau_{\rm max}$ depended on liquid density, saccade amplitude, angular velocity, kinematic viscosity and radius of sphere. $\tau_{\rm max}$ increased with increasing viscosity up to 10^{-4} m ² /s, then plateaued from $10^{-4} - 2$ m ² /s.	
		Glycerol induced a higher $\tau_{\rm max}$ (19.8 Pa) than more viscous SiOil (19 Pa) due to its higher density. Flow field for SiOil and glycerol was like solid body rotation		
	$10^{-10} \text{ m} / 3, p = 1260 \text{ kg/m}^3$ SiOil ($u = 10^{-3} \text{ m}^2 / \text{s}$			Water: the velocity gradient normal to the wall was high near the wall
	$\rho = 970 \text{ kg/m}^3$			Secondary flow five times stronger for water than SiOil, the lens indent increased the secondary flow.
Modareszadeh <i>et al.</i> (2013)	Sphere with a lens indent, $R = 24 \text{ mm}$ Saline ($\nu = 10^{-6} \text{ m}^2/\text{s}$)	Saccade motion without and with latency time	$A = 10^{\circ}, 30^{\circ}, 50^{\circ}$ $\Omega_{max} = 328 - 547^{\circ}/s$ $L = 5D$	Flow patterns were symmetric in both equatorial and meridional planes: two main circulating regions in the equatorial plane, four vortices in the vertical plane. Vortices became stronger as amplitude increased. In- plane velocity components increased with amplitude.
			W0~57 - 74	Latency time weakened the convection mechanisms in both equatorial and meridional planes: intensity of vortices and in-plane velocity weakened.
Modarreszade h and Abouali (2014)	Sphere or sphere with a lens indent, $R =$ 24 mm A viscoelastic model of the vitreous fluid	Saccades	$A = 5 - 30^{\circ}$ $\Omega_{max} = 10 - 30 \text{ rad/s}$ $Wo \sim 31 - 61$	The viscoelasticity of the gel increased the τ_{max} (0.18 Pa) by 10 times compared to Newtonian saline. The lens indent accounted for 80% of the increase.

Table 2.11: Summary of numerical investigations on fluid dynamics in a sphere under eye-like motion

There is a lack of studies of two-phase flows in a solid sphere. Angunawela *et al.* (2011) and Yousefi *et al.* (2015) worked on an eye chamber filled with a gas tamponade, and their results are summarised in Table 2.12. They analysed the aqueous flow field for different gas levels of fill, ϕ_{gas} . The maximum shear stress was found near the equatorial plane on the eye wall, and increased from 0.2 to 2.5 Pa by increasing ϕ_{gas} from 0.2 to 0.8 under saccadic motion. They also simulated abrupt motions of the head, which generated higher shear stress at all gas levels of fill. The reported τ_{max} values for sudden head motions were between 10 – 15 Pa for ϕ_{gas} from 0.2 to 0.8. These τ_{max} values are all larger than the values reported for the liquid tamponade case, but there was no emulsification as there is no SiOil.

First author	Geometry, working fluids	Motion and parameters	Results
Angunawela et al. (2011)	Sphere $R = 12.5 \text{ mm}$	Vertical and horizontal	$\tau_{\rm max} = 0.2 - 2.5$ Pa for $\phi_{\rm gas} = 0.2 - 0.8$ under saccades.
	Gas tamponade / Water	/ Sudden τ Sudden 0 rectilinear representing H head motion τ $A = 30^{\circ}$ τ	$\tau_{\rm max} = 10 - 15$ Pa for $\phi_{\rm gas} = 0.2 - 0.8$ under head motions.
	$\phi_{\rm gas} = 0.2 - 0.8$		Horizontal saccades induced lower $\tau_{\rm max}$ than vertical saccades.
			$ au_{ m max}$ depended largely on the gas level of fill.
		$\Omega_{max} = 500^{\circ}/s$ $Re \sim 1000$ $W_0 \sim 37$	$\tau_{\rm max}$ located at the contact line and at the equator.
Yousefi et	Sphere or sphere	Horizontal	$\tau_{\rm max}$ occurred at the peak angular
al. (2015)	with a lens indent, R = 25 mm	saccades $4 - 20^{\circ}$	velocity, and located at the lens. $\tau = 0.2 - 0.7$ Pa for $\phi = 0.2 - 0.2$
	$\delta/R = 0.25$	A = 50 $Q = 500^{\circ}/s$	$v_{max} = 0.2 = 0.7$ ratio $\varphi_{gas} = 0.2 = 0.8$ under horizontal saccades.
	Gas tamponade / Water	$W_{max} = 300 \ / 3$ $Wo \sim 74$	
	$\phi_{\rm gas} = 0.2 - 0.8$		

2.2.2.3 Thin aqueous layer hypothesis

In the thin aqueous film hypothesis, the retinal tamponade does not make direct contact with the retina. The aqueous layer is present as a thin film between the oil and the wall, and it is hypothesised that the interface between oil-aqueous film may break down near the retinal wall under a shear flow instability generated by eye movements.

Isakova and Garcia-Gonzalez analysed the oil-aqueous film interface linear stability analytically, subject to a small perturbation (2014; 2017). They modelled the eye as a rigid sphere filled with the two liquids as concentric spherical volumes with an outer aqueous film of uniform thickness, d (see Figure 1.6(a)). By assuming that d is much smaller than the sphere radius, they neglected the curvature of the retinal surface and treated the system as flat layers (see Figure 2.15)



Figure 2.15: Sketch of the flat wall configuration with the two fluid layers.

In their studies, liquid 1 was a Newtonian fluid with $d = 30 \,\mu\text{m}$. Liquid 2 was immiscible and had different degrees of elasticity. The fluid dynamics were characterised by four dimensionless numbers: $Re_1 = \frac{\overline{U}d\rho_1}{\mu_1}$, $\lambda = \frac{\mu_2}{\mu_1}$, $We^{-1} = \frac{\gamma_{12}}{\rho d\overline{U}^2}$ and $\omega^* = \frac{\omega d}{\overline{U}}$. The groups had a value range representative of the eye saccadic rotation: $1 < Re_1 < 20$, $0 < We^{-1} < 1000$, $0 < \lambda < 200$ and $0 < \omega^* < 0.06$.

The interface was perturbed by small 2-D sinusoidal waves. A linear stability analysis calculated the amplitude of the perturbation and established whether it grew or decayed over time. Growth of the perturbation is indicated by the positive sign of the imaginary part of the complex solutions: a positive growth rate indicated the onset of interface instability.

For a given set of flow and liquid conditions, the flow became unstable at a minimum wavelength, L_{\min} . When both liquids were Newtonian, with a viscosity ratio of 10, the interface became unstable with a wavelength of $L_{\min} = 7.5$ mm. The flow became more stable as the viscosity of L2 (and λ) increased: L_{\min} increased to 16 mm for a viscosity ratio of 60. The viscosity ratio for medical SiOil tamponades and aqueous is between 1000 and 5000, which was much higher than the maximum value (200) studied in these simulations. For these values of λ , the L_{\min} is expected to be greater than the eye circumference, $2\pi R \approx 75$ mm. The flow was also more stable when the elastic component of L2 or We^{-1} were larger, Re_1 smaller, or the density ratio (ρ_2/ρ_1) closer to 1.

On the experimental side, Chan and co-workers introduced an eye-on-a-chip device in 2015 to study the thin film emulsification hypothesis (Chan *et al.*, 2015). They modelled the eye chamber as a thin disc cavity (diameter 25 mm, height 1 mm, volume 0.43 mL) with the side walls, top and bottoms faces coated with retinal ganglion cells (see Figure 2.16). The layer of cells on the disc walls acted as a hydrophilic coating that prevented the oil from adhering to the inner surface of the disc. Figure 2.16(b&c) give a simplified representation of the eye-on-a-chip for an easier visualisation of the configuration. There was an obvious oil-aqueous interface in the disc cavity with the aqueous layer thickness estimated roughly at 500 μ m. The SiOil wetted the top and bottom faces of the disc, forming a three-phase contact line on the top and bottom walls.

The disc cavity was filled with 0.4 mL SiOil and the rest with an aqueous cell culture medium. The device was mounted with the faces vertical on a mechanical platform that provided a saccadic motion, with $A = 10^{\circ}$, $\Omega_{max} = 390^{\circ}/\text{s}$, D = 50 ms and 0.3 < Wo < 20. The device was run continuously for four days. Using their experimental parameters, the values of the four dimensionless groups could be estimated as $\omega^* = 0.04$, Re = 2.5, $We^{-1} = 444$ and $1 < \lambda < 5000$.

Chan and co-workers observed oil droplets near the side walls from the first day of saccadic motion. The number of droplets formed increased with decreasing SiOil viscosity: the two lowest viscosity oils (5 and 100 cSt) gave 10 times more droplets than the other three more viscous oils (500, 1000 and 5000 cSt) tested. The number of droplets also increased with the number of days of motion: the increase was

significant in the two lowest viscous oils, giving 25 times more droplets on the fourth day compared to the first day. The droplet size increased with the SiOil viscosity and the median droplet size from the different oils converged after 4 days (the sizes were not reported). There were no statistical differences between the 1000 and 5000 cSt oils, both in terms of droplet number or size. Lu *et al.* (2018) used the same device in 2018 and reported droplet diameters ranging from 5 to 20 μ m, which was comparable with the size of the retinal cells.



Figure 2.16: (a) Top view of the eye-on-a-chip device filled with oil (transparent) and aqueous medium (light yellow). The lens indentation feature is present at the top (oval shape). The outer ring of yellow fluid is the cell maintenance flow arrangement. Image from Figure 2 of Chan *et al.* (2015). (b) Schematic representation of eye-on-a-chip: (i) top view, (ii) cross-section, yellow – oil phase, purple – aqueous, $d \sim 500 \,\mu\text{m}$.

Chan and co-authors attributed droplet formation primarily due to bulk interface emulsification mechanism at the interface between the oil and the thin aqueous layer. They attributed it to the relative motion between the two liquids creating a large enough shear stress at the oil-aqueous interface to cause the bulk SiOil to break up. They estimated the values of shear rate (6×10^4 to 14×10^4 s⁻¹) at the interface by assuming $d = 10 \,\mu\text{m}$ and using the peak angular velocity of the oil (Chan *et al.*, 2011).

According to the linear stability analysis of Isakova and Garcia-Gonzalez, a lower viscosity ratio interface can be perturbed by wavelengths shorter than the disc circumference. For a film layer thickness of 50 μ m and a viscosity ratio of 5 (5 cSt oil), a minimum wavelength of 6.5 mm is sufficient to give rise to interface instability. Although the film thickness is larger in the experimental eye-on-a-chip (500 μ m), the general trend can explain why the lowest viscosity oil in the disc gave rise to more oil droplets. A higher viscosity ratio will need longer wavelengths to perturb the interface, but the wavelength may become larger than the disc circumference. The convergence

of oil droplet size to a median value can be explained by the Hinze and Kolmogorov theory on the deformation of droplets in a continuous laminar shearing flow, the breakup of any drop of size larger than a critical size will occur when the flow pattern of the surrounding phase persists long enough.

This thin film emulsification hypothesis was not able to explain droplet formation in the high viscosity ratio cases. Lu and co-workers further investigated SiOil emulsification in the eye-on-a-chip device. They introduced the surface emulsification hypothesis, which consisted of the pinning and break-up of the moving three-phase contact line with the retinal cells acting as pinning sites for the oil droplets (Lu *et al.*, 2018). However, no video or images of the interface breakup or contact line adhesion in the eye-on-a-chip were reported. Instead, they developed a micro-channel device to study the surface emulsification mechanism, which is discussed in the next section.

2.2.3 Surface emulsification

The surface emulsification hypothesis suggests that surface features such as damaged retinal cells act as pinning sites for the adhesion of the SiOil-aqueous TPCL moving along the retinal surface, leading to formation of SiOil droplets on the surface which subsequently detach into the aqueous phase.

2.2.3.1 Retinal surface

The retinal surface could act as pinning sites if its surface contains topographical or chemical features. Figure 2.17 shows the retinal surface of rabbit eyes imaged with scanning electron microscopy with and without PVD. Without PVD, very dense vitreous fibres covers the retinal surface. After adding different concentrations of nakotinase (0.01, 0.1 and 1 fibrin-degradation unit [FU]), an enzyme that degrades fibrins, the vitreous fibres are increasingly degraded. The higher the enzyme concentration, the cleaner the retinal surface. With the vitreous fibres entirely removed, the retinal surface still appears rough. Although the roughness was not measured, the visual image indicates that the topographical features have dimensions about 10 to 100 μ m. If the vitreous fibres are not entirely removed from the surface, the fibres also represent large and dense topographical features on the retinal surface.



Figure 2.17: Scanning electron microscopy (SEM) images of the retinal surface 30 minutes after an intravitreal injection of physiologic saline (a) or 0.01 (b), 0.1 (c), or 1 (d) FU nattokinase. In the saline-injected eyes, SEM showed very dense vitreous fibres covering the retinal surface. (c,d) In contrast, the eyes treated with 0.1 or 1 FU nattokinase exhibited clear retinal surfaces, indicating the occurrence of posterior vitreous detachment. Scale bar = 50 μm. (Image and caption from Takano *et al.* (2006), with permission from IOVS)

Both water and SiOil were shown to fully wet animal retinas (pig, cow, sheep) in air by Rubowitz *et al.* (2020). Table 2.13 summarises the contact angles measured on retinal surfaces alongside with other substrates employed in studies in this field, under different fluid combinations. The different fluid combinations of the sessile drop measurement are shown in Figure 2.18. When the oil droplet is immersed in saline solution, it wets the retinal surface at a contact angle of 161.8°. Acrylic (polymethyl methacrylate, PMMA) coated with proteins gave similar results to the animal retina, and were commonly used in studies with eye chamber devices.

Table 2.13: Reported values of contat angles in Fawcett *et al.* (1994), (Sharma *et al.*, 2019) and Rubowitz *et al.* (2020). The definitions of the contact angle are sketched in Figure 2.18. OTS – octadecyltrichlorosilane, O – 1 Pa s SiOil, W – water (unless specified), and V – air.

Substrate	Glass slide	Protein coated acrylic	OTS coated glass slide	Animal retina
θ_{0}	7°	0°	7°	0°
$ heta_{ m W}$	5°	0°	110°	0°
$\theta_{\rm OW}$	129°	163.6° (saline)	0°	161.8° (saline)
$ heta_{ m WOV}$	36°	Not available	109°	30°



Figure 2.18: Schematic definition of contact angle with different system configurations: O – SiOil, W – water, and V – air, L1 and L2 indicates liquids 1 and 2.

2.2.3.2 Adhesion of silicone oil on the solid surface

Lu and co-workers developed a microchannel device to study the surface emulsification mechanism. The microchannel device consisted of a glass capillary with a square cross section of length 1 mm, and with all four inner surfaces coated with retinal ganglion cells (Lu *et al.*, 2018). Aqueous culture medium and SiOil (2000 cSt) were introduced into the channel, and a syringe pump was used to push the liquids in one direction (Lu *et al.*, 2019). Figure 2.19 shows a schematic representation of the device. By pushing the aqueous solution into the oil, the three–phase contact line moved across the cells and adhered to cells. The pinning points led to thread formation (~45 µm long, estimated from their figure) and subsequently break up due to end-pinching effects. This droplet formation mechanism is similar to that of Van Gestel *et al.* (2020), with the retinal cells being the topographical and chemical features on the surface.

Lu and co-workers only reported the formation of a primary drop (termed an "orphan drop") on the pinning site: no satellite droplets were reported. The primary drop diameter ranged from $5 - 10 \,\mu$ m (estimated from their figures), which was of the same order of magnitude as retinal cells size. However, they have not reported if the primary drop detached from the retinal surface.



Figure 2.19: Schematic of the oil-aqeuous system moving across a retinal cell-seeded surface, (b) the oil is pinned at a cell and the liquid is pulled into a thin thread, (c) break-up of the liquid thread leading to oil droplet formation.

2.2.4 Summary

Prior studies on SiOil emulsification investigated the bulk emulsification mechanism in *in-vitro* models not entirely representative of the real eye chamber geometry and movements. High agitation energy input from vortex mixers, homogenizers and sonication produced emulsions via cavitation, elongational deformation and Rayleigh-type instabilities. These studies showed that higher oil viscosity, higher molecular weight components, higher levels of oil fill and lower surfactant concentration stabilised the interface and inhibited emulsification. However, these procedures for preparing emulsions are not readily applicable to the processes in the eye.

The eye saccadic motion has been simulated in a few studies but only one or two saccadic motion sequences have been tried, and they did not cover the full range of parameters the eye motion can achieve. For the given set of saccadic motion and liquid conditions used in prior cylindrical eye models ($A = 90^{\circ}$, $\Omega_{max} = 360^{\circ}/s$, D = 250 ms, Wo = 1.6), the experimental studies did not support oil droplet formation by the bulk emulsification mechanism.

Single-phase fluid flow studies in spherical eye chambers showed that the chamber oscillations induced motion in the fluid, with SiOil having a larger velocity distribution than the aqueous solution. In an eye chamber filled with both SiOil and aqueous phases, the difference in velocity between the two fluids can induce surface instabilities. However, one oil-aqueous interface linear stability analysis showed that the viscosity ratio between medical SiOil tamponade and aqueous phases ($\lambda = 1000 - 5000$) promoted a stable interface for a thin aqueous film of thickness of 30 µm.

The recently proposed surface emulsification hypothesis has only been studied in a micro-channel device. It requires further investigation to understand the effect of surface properties and topographies on the pinning of the three-phase contact line, and determining the conditions of oil droplet detachment under a shearing flow.

This review has identified the following gaps in the literature on the understanding and study of silicone oil emulsification:

- (a) No experimental studies to date have proved the bulk emulsification hypothesis in 3D *in-vitro* eye models representative of the real eye chamber geometry and eye saccadic motions.
- (b) There is a lack of analytical and numerical studies that investigate one-phase and two-phase flow dynamics in the eye chamber under a range of saccadic motions.
- (c) The surface emulsification mechanism was recently introduced in the literature and has not yet been extensively studied. There are relatively few studies on characterising the surface topographies and properties of the retinal surface and how these local features could affect the stability of the three-phase contact line.
- (d) The thin aqueous layer hypothesis proposed by Isakova *et al.* (2014) and Garcia-Gonzalez *et al.* (2017) also lacks experimental and theoretical understanding in terms of how oil droplets are formed in the eye-on-a-chip device used by Chan *et al.* (2015) and Lu *et al.* (2018), and how liquid and interfacial properties influence the thin aqueous film stability.

Gaps (a) and (b) are investigated in depth in Chapters 3 and 4 on the bulk emulsification hypothesis, while Chapters 5 and 6 focus on developing a new experimental protocol to investigate three-phase contact-line motion across surface features (c). The thin aqueous film stability (d) is not investigated in this thesis, but a short critical review of the eye-on-chip-device has been performed in Chapter 6 to understand oil emulsification mechanisms and to translate the results into spherical geometries.

Chapter 3 Materials and methods to study bulk emulsification

In the next two chapters, a 3-D *in-vitro* model of the eye chamber was developed to investigate the bulk emulsification hypothesis. The eye saccadic motion was simulated using a mechanical platform. Different saccadic motions were used to investigate the stability of the oil-aqueous interface, and single-phase fluid dynamics were measured and compared to analytical calculations. Material in Chapters 3 and 4 has been published in Wang *et al.* (2020) and are accepted at the *Journal of Biomechanical Engineering*.

A description of the eye chamber model with the saccadic motion, and the experimental procedures to study the liquid-liquid interface stability are provided in Chapter 3.

3.1 Eye chamber model

3.1.1 Round bottom glass calibration

Bulk emulsification experiments were conducted using laboratory round-bottom glass flasks (RBFs) as a model of the eye chamber. The RBFs (borosilicate, Quickfit, neck joint 14/23) had volumes of 5, 10 or 25 mL, and radii of 5, 14 and 20 mm, respectively.

The flask shape was analysed to assess its sphericity. Each RBF was incrementally filled with a known volume of water. At each volume, lengths b and c were measured off the digital images and compared to the values expected for a sphere (see Figure 3.1(a)). The radius of the sphere was calculated from the final volume of water added to the RBF. The relationship between the radius b and the height of the spherical cap c for a sphere of radius R is:

$$b = \sqrt{c(2R - c)} \tag{3.1}$$

Figure 3.1(b&c) shows the base radius/height relationship for a spherical cap curve for 10 mL and 25 mL RBFs. The data show some discrepancies, indicating that the RBFs were not perfectly spherical. Similar deviations from a perfect sphere were observed with the 5 mL RBF.



Figure 3.1: (a) Schematic elevation of a solid sphere (centre C and radius R) filled with known volume of liquid. Blue line is the liquid/air interface, c the height of the spherical cap and b the interface radius. (b-c) Relationship between b and c: symbols - experimental data, solid line - geometrical model (equation (3.1)) for a sphere with radii (b) R = 14 mm and (b) R = 20 mm.

In surgical practice, the aim is fill the eye completely with the tamponade in order to obtain the greatest contact area between the tamponade and the retina wall and to reduce the optical side effects of an underfill of oil moving within the eye between saccades. The experiments in this thesis mainly focused on high levels of fill of tamponade ($\phi_{oil} \ge 90\%$). This allows closer representation of the clinical situation, but also avoids any effect of the neck of the flask and the non-perfect sphericity (since the deviation from a sphere is more significant near the neck area). The RBFs are assumed to be spherical in the following sections.

3.1.2 Saccadic motion simulation

To simulate the human eye saccadic motion, a mechanical platform was developed to drive the RBF with a programmable sequence. The mechanical platform consisted of a stepper motor (1.26 Nm Nema 23 Stepper Motor 2.8A 4-wires, 6.35 mm shaft) driven by a micro-controller (Single Axis TB6600 DC12-45V Two Phase Hybrid Stepper Motor Driver Controller, UK) which received commands from an open-source software Arduino. Each step of the stepper motor moved the shaft by 1.8° with a step accuracy of 5%. It took 200 steps for the motor to make one revolution. The rotation imposed by the stepper motor was thus not smooth. To run the motor as smoothly as possible, microstepping codes and a microstepper controller were introduced. The controller sent pulses to the motor in an ideal waveform for smoother rotation. The stepper motor

then could achieve precise positioning and smoother rotation via digital control and microstepping.

The motion sequence was coded in Arduino by Sebastien Cosfenoy (CEB, Cambridge). The parameters of the eye saccades: A, Ω , D, and L were adjustable inputs. Although the movement was not completely authentic, it provided a reasonable approximation to the eye motion and has been used in past work (Repetto, Siggers and Stocchino, 2010; Chan *et al.*, 2011; Abouali *et al.*, 2012). A bespoke shaft adapter connected the RBF to the shaft of the stepper motor. Tape was used to secure the chamber to the adaptor. Figure 3.2 shows a picture of the set-up.





To verify the motion driven by the motor, video recording and analysis were performed on a RBF completely filled with water and immersed in a bath of mineral oil. The mineral oil matched the refractive index of the glass flask; this feature was also exploited in particle imaging velocimetry studies. The angular displacement of the saccade in each frame was recorded by tracking a dot marked on the glass flask on videos taken with a digital camera at a speed of 60 frames per second. Internal calibration and verification of different motion sequences were performed to check the accurate positioning of the motor and the absence of slip between the adaptor, the motor and the eye chamber.

Figure 3.3 shows the calibration curve of the system for different saccade amplitudes with the same angular velocity ($\Omega_{max} = 200^{\circ}/s$) and latency time (L = 0.2 s). The

deviation from the line of equality at higher saccade amplitude is probably due to the refraction caused by the curved glass flask wall rather than motor slip. The motor specification was chosen as a high torque device, with sufficient power to drive the given load. Experiments with same saccade amplitude and different angular velocity gave similar results.



Figure 3.3: Calibration curve of the stepper motor/RBF system. A 25 mL RBF was filled with water and immersed in mineral oil. Dashed line is the line of equality

The stepper motor could also be inclined at an angle, up to 30° from the vertical. The angle was measured by a digital angle meter that provided the instantaneous inclination of the device.

3.1.3 Saccadic motion

The saccadic motion can be approximated as a series of periodic recurrent rectangle pulses, as shown in Figure 3.4. The period of the saccadic motion consists of two equal and opposite rectangular pulses separated by the latency time, giving $T_s = 2D + 2L$.



Figure 3.4: Schematic representation of a recurrent rectangular pulse.

A rectangular pulse with latency pauses can be expressed as a Fourier series. The Fourier coefficients of the angular velocity of the pulse were derived and the angular velocity was expressed as:

$$\Omega(t) = \sum_{i=1}^{\infty} -\frac{8\Omega_{\max}}{i\omega T_{s}} \left(\sin i\omega \frac{T_{s}}{4} \sin i\omega \frac{D}{2} \right) \sin(i\omega t) = \sum_{i=1}^{\infty} \Omega_{\max} B_{i} \sin(i\omega t)$$
(3.2)

with *i* an integer and ω the Fourier frequency.

The parameters of the saccadic motion used in the bulk emulsification experiments are summarised in Table 3.1. Three different values of *L* were considered to study the influence of this parameter on the dynamic response of the fluid in the eye chamber. L/D values of 0.5, 1 and 3 covered a range of possible behaviours. The parameter values are representative of a fairly wide range of medically relevant conditions (Becker and Fuchs, 1969).

Steps	Amplitude (°)	Maximum (°/s)	angular velocity (rad/s)
3	5.4	200	3.49
6	10.8	300	5.24
8	14.4	400	6.98
10	18	500	8.73
20	36	600	10.47
30	54	800	13.96

Table 3.1 Saccadic parameters used in the bulk emulsification experiments

3.1.4 Working fluids

Three chemical grade SiOils were used in this study to assess the effect of viscosity on the fluid motion and interfacial properties. All the SiOils were polydimethylsiloxane based, differing in molecular weight and thus viscosity. The oils were all less dense than water and their measured properties are summarized in Table 3.2. The measurements of the viscosity, density and surface tension are described in 3.2.

Name	Label	Supplier	μ (Pa s)	ho (kg/m³)	σ (mN/m)
Polydimethylsiloxane	PDMS A0.5	Sigma Aldrich	0.42	973	18
Brookfield™ Silicone Standard Oil	PDMS B1	Fisher Scientific	0.87	973	19
Brookfield™ Silicone Standard Oil	PDMS B5	Fisher Scientific	4.66	976	19

able 3.2: SiOils used in this thesis and the	ir measured properties at	room temperature
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Saline solutions were prepared according to the composition (see Table 3.3) given by Bausch & Laumb (Bausch + Lomb, 2018), a supplier of medical grade saline. Each batch of saline solution (1 L) was pH adjusted to 7.4 using analytical grade hydrochloric acid purchased from Fisher Scientific. In some experiments, the fluids were dyed to enhance the contrast and visibility. Oil was dyed with Oil Red EGN (1 wt%, Sigma) and aqueous solution with either Nile Blue A (1 wt.%, Sigma) or yellow sodium fluorescent salt dye (Sigma).

An amphoteric, non-ionic surfactant, Triton X-100 (TX-100, Fisher Scientific), was added to the aqueous solution to achieve different surface tensions. TX-100 was not soluble in the silicone oils studied. A blend of two components was used as an oilsoluble surfactant. consisting of а 1:1 (by mass) mixture of decamethylcyclopentasiloxane (97%, Sigma) and tetrakis(trimethylsilyloxy)silane (97%, Sigma). This mixture of a high molecular weight resin and a volatile low viscosity cyclopentasiloxane is labelled DTS.

All these agents were used as received without further purification.

Table 3.3: Saline composition.

Solute	Purity	Supplier	Molecular	Concentration	
	wt. %		g/mol	mmol/L	g/L
Calcium chloride, CaCl ₂	analytical grade	Fisher Scientific	110.98	3	0.333
Magnesium chloride, MgCl ₂	analytical grade	Fisher Scientific	95.211	1	0.095
Sodium acetate trihydrate, $C_2H_3NaO_2 \cdot 3H_2O$	99%-101%	Alfa Aesar	136.08	30	4.08
Sodium citrate tribasic dihydrate, C ₆ H ₅ O ₇ •2 H ₂ O •3Na	98.0%	Sigma Aldrich	294.1	15	4.41
Sodium chloride, NaCl	laboratory grade	Fisher Scientific	58.44	111	6.48
Potassium chloride, KCI	>99.0%	Sigma Aldrich	74.55	10	0.746

3.1.5 Sample preparation

The RBFs were washed in a dishwasher with acid wash, followed by sonication in deionised water at 50°C for 30 minutes, then dried overnight. In some tests the RBF was pre-wetted with an aqueous solution of surfactant for at least 30 minutes to imitate the hydrophilic nature of the retina (Fawcett, Williams and Wong, 1994). The solution was then discarded and the desired volume of aqueous solution delivered to the base of the RBF, followed by the SiOil, taking care to avoid any mixing or entrapment of air bubbles. The level of oil fill in the flask was always > 90 vol%. The flask was connected to the stepper motor and then lowered into a cubic bath of mineral oil which eliminated any parallax (see Figure 3.5)



Figure 3.5: Photographs of (a) 25 mL RBF with 3 mL TX-100 and dyed B1 oil ($\phi_{oil} = 0.91$). (b) RBF attached to the stepper motor (S) and immersed in a mineral oil bath (M), illuminated by light (F) and recorded by the camera (lens G).

In some experiments, the RBF were inclined, at angles from 10° to 30°. The angle of inclination, β , is defined between the vertical axis and the axis of rotation, as shown in Figure 3.6.



Figure 3.6: Schematic representation of a vertical RBF and (b) an inclined RBF with an angle of inclination β . Orange line indicates the interface between the liquid phases L1 and L2. Blue dashed line is the vertical axis and black dashed line the rotation axis.

3.2 Liquid properties

3.2.1 Rheology

The rheological properties of the working fluids were studied on an ARES controlled strain rheometer at room temperature and at 37°C. The silicone oils were tested for steady shear values and dynamic response. 50 mm roughened parallel plates or a Couette bath (cup diameter 34 mm, bob diameter 32 mm) were used. The shear rate

was increased from 0.1 s⁻¹ to 1000 s⁻¹ with the temperature controlled at either 25°C or 37° C.

The rheological investigations showed that the SiOils were all Newtonian over the range of shear rates studied. In a steady shear flow study, the fluid is sheared continuously in one direction over the duration of a test. Figure 3.7(a) shows an example for PDMS A1 at 25°C and 37°C for shear rates of 0.5 to 500 s⁻¹. Within the accuracy of the device, the viscosities are constant (the increase at a shear rate above 100 s⁻¹ is a machine artefact). Increasing the temperature reduced the viscosity, from 0.87 Pa s to 0.72 Pa s.

Oscillatory strain tests were also conducted, yielding the storage modulus, *G'*, and the loss modulus, *G''*. The former quantifies the elastic response and the latter the viscous response. The samples were exposed to increasing frequency (1 to 20 rad/s) at a constant strain amplitude of 1%. The loss modulus is about 100 times higher than the storage modulus for all frequencies, indicating that any elastic contribution is insignificant (Figure 3.7(b)). All the oils had a viscous behaviour, which was expected for a Newtonian fluid. Over the range of shear rates studied, the SiOils showed good shear stability and retained their original viscosity characteristics. Their rheological behaviour was not time-dependent.



Figure 3.7: (a) Effect of temperature on the viscosity of PDMS A1. (b) Shear modulusfrequency graphs of PDMS A1. Obtained on a ARES rheometer using roughened 50 mm diameter parallel plates and a gap of 1 mm at 25°C.

3.2.2 Density

A pycnometer (borosilicate glass, 25 mL, Brand Blaubrand) was used to measure the density of the liquids. Measurements were performed at room temperature and at 37°C using a water bath. Specific gravity was calculated by referencing all density values to the value measured for distilled water. The empty flask volume given by the manufacturer was 25.049 mL at 20°C and its mass 23.2442 g.

3.2.3 Surface/Interfacial tension

Interfacial properties were determined using a goniometer (DSA 100, Krüss, located in the BP Institute, Cambridge, UK) at room temperature. The instrument was connected to a computer running the proprietary Drop Shape Analysis 3 software. Surface and interfacial tensions were measured using the pendant drop method (see section 2.1.1.1). Before testing, syringes and needles (diameter 0.505 mm or 1.81 mm) were washed with an aqueous solution of Decon 90, followed by several rinses with ultrapure water, then dried in an oven at 60°C. Owing to the density of the oils used (less dense than water) and the difficulty in injecting them through the syringes, measurements of interfacial tension were made with aqueous droplets formed in the oil phase. A cuvette of optical glass 40×40×40 (mm) from Hellma Analytics was used to hold the oil. A drop of the aqueous solution (40 µL) was formed at the end of the needle and the interfacial tension (IFT) was measured over a period of 400 s. The IFT was calculated from the almost spherical shape of the droplet. The Bond number for the 40 µL droplet was about 0.008, which confirmed the drop was spherical. The value stabilised after 150 s and the steady state was recorded. The slope of the decrease was measured to be the same (~ -0.02 mN/m/s) for all the profiles. This decrease did not depend on the presence of surfactant or salts, and it was attributed to the kinetic energy/momentum of the drop being dissipated following the formation of the drop.

The effect of surfactant was investigated by varying the concentration of TX-100 in saline from 0.0001 to 1 wt.%. In oil soluble surfactant (DTS) testing, the concentration was varied from 0.01 to 1 wt.%.

3.2.4 Contact angle

The three-phase contact angle was calculated using the sessile drop method (see section 2.1.1.1). The solid substrate was first immersed in a bath of SiOil, then a drop of aqueous solution with volume 5 to 10 μ L was deposited on the solid substrate using the syringe. The drop was allowed to displace the oil and reach a static equilibrium state. Images of the sessile drops were recorded. The static equilibrium contact angle at the tamponade – aqueous – substrate interface was measured on the right and left sides of the drop and the average calculated. For the advancing contact measurements, the needle of the syringe was left in the drop and the drop volume was increased at a slow rate (10 μ L/min). The drop was filmed at a rate of 4 fps. As the drop volume increased, the three-phase contact line was observed to remain pinned to the substrate and the contact angle, measured in the aqueous phase, increased. The advancing contact angle was measured at the point of maximum increase of the contact line moved. This dynamic method proved more reproducible than static measurements.

3.3 Bulk emulsification set-up

3.3.1 Static interface shape

In order to study the static shape of the tamponade in the presence of the aqueous phase, the RBF was filled with an aqueous solution and sealed with a septum lid after ensuring that no bubbles of air were present. Two hypodermic needles were inserted through the septum, one connected to a syringe pump and the other to an open syringe acting as a waste container (see Figure 3.8(a)). A set volume of tamponade was injected using the syringe pump. When the tamponade was a silicone oil, the aqueous solution was also used to push the silicone oil into the flask. When the tamponade was injected, surplus aqueous phase in the flask was pushed out into the waste container. Owing to the affinity of SiOil for the surface of the needle, the tip of the needle was burnt with a flame to make it lipophobic before use. A camera was positioned in front of the flask and recorded the shape of the drop, illuminated from behind by a LED light source. PDMS was dyed with Oil Red O (Sigma Aldrich) for better visualisation. Aqueous solutions included water, saline and solutions of TX-100 in saline.

Selected lengths and angles were extracted from the digital images with the open source image analysis software ImageJ (National Institutes of Health, Bethesda, Maryland). Figure 3.8(b) shows an example with the geometrical parameters, angle of tamponade, α , three-phase contact angle, θ , and distances z_m and z_c marked. The flask was modelled as a sphere, shown by the yellow line. The blue lines define the angles subtended by the contact line. The red line defines the contact between the three phases (tamponade, aqueous solution and surface of flask). The contact line was also marked on the RBF during the experiment for easier detection on the image.

The shape of the tamponade interface and the contact angle were compared with a mathematical model (see Section 4.2) to check that the preparation protocol had been followed correctly.

A second set of experiments was performed by coating the surface of the RBF to mimic the hydrophilic nature of a retinal surface (Fawcett, Williams and Wong, 1994). The chamber was initially filled with 1 wt. % TX-100 solution in saline to coat the internal surface of the chamber for at least 30 minutes. SiOil was then injected as before, displacing the aqueous solution.



Figure 3.8: (a) Photograph of the glass flask/syringe pump set-up. (A) syringe filled with dyed PDMS, (B) RBF, (C) waste container, (D) syringe pump, (E) syringe filled with aqeuous solution. (b) Side image of a drop of silicone oil (1) injected from a hypodermic needle (3) within a RBF initially filled with water (2). Geometrical construction lines shown with angle of tamponade α , distances z_m and z_c marked.

3.3.2 Stepper motor experiments

After sample preparation, the RBF attached to the stepper motor was set into saccadic motion for a certain duration and filmed by digital cameras (Basler, acA640 – 750 μ m) fitted with long focal length lenses which allowed the interface shape and motion to be captured. The length of the interface perimeter at rest, l_0 , was extracted from images using ImageJ (NIH, Bethesda, Maryland) as well as the interface length during motion, l_m (see Figure 3.9). For each saccadic motion the interfacial strain was estimated using the dimensionless increase in length on the observation plane, Δl^* :

$$\Delta l^* = \frac{|l_m - l_0|}{l_0} \tag{3.3}$$

as the change in interfacial area was not readily calculable. The values are reported as percentages.



Figure 3.9: Photographs of the interface (solid white line) between B1 oil and saline with 1 wt.% TX-100 in a 25-mL RBF, $\phi_{oil} = 0.91$, (a) at rest, length l_0 , and during saccadic motion with (b) $A = 36^{\circ}$, $\omega_{max} = 600^{\circ}/s$ and L = 0.5D, length l_m marked, Wo = 2.2, We = 15.

3.3.3 Particle imaging velocimetry (PIV) analysis of one phase fluid

The aim of these experiments was to compare the results to the analytical and numerical predictions. A short description of the PIV principle and the details of the experimental set-up are provided in this section.

3.3.3.1 PIV principle

PIV is a flow visualization technique using optical cameras and laser light to capture the displacement of small neutrally buoyant seeding particles. In two-dimensional PIV, a light sheet illuminates a plane of the flow and the light scattering particles are captured and recorded on to consecutives frames of a digital camera. Each frame consists of multiple small interrogation windows where the local displacement of the particles is calculated using statistical correlation. The instantaneous velocity of the particles is deduced from the local displacement and the time difference between two consecutives frames. In Stereo-PIV, two cameras are used at different observation angles, and enables measurement of the third component of the flow velocity in the light sheet.

The seeding particles have a density close to the sample fluid in order to correctly capture the fluid flow and avoid sedimentation. An appropriate particle loading is required to obtain a homogeneous distribution of the particles over interrogation windows and to trace each particle individually. The time separation between consecutive frames is named pulse separation and the value employed depends on the fluid and the flow characteristics. The PIV recording consists of a combination of small interrogation windows that divides the observation plane into smaller rectangles. It is necessary to set a pulse separation value large enough for particles to undergo an appreciable displacement, but not so long that the particles leave the interrogation window. The spatial resolution of PIV results is limited by the size of the interrogation window.

In order to make PIV measurements, different components of the PIV system need to be time coordinated, for example, the recording camera, the laser lamp and the exposure time. The synchronizer controls the time sequence and manages all the timing events needed for doing PIV measurements. The success of PIV measurements depends crucially on the time correlation between laser pulse generation and camera recording achieved by the synchronizer unit. Single-frame PIV captures the illuminated flow on a single frame and uses statistical approaches to determine particle image shift. Double-frame PIV captures the flow onto two consecutives frames with the help of a fast camera: the particle positions in subsequent instants are registered on two successive frames.

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3.3.3.2 PIV experimental set-up

The 2D PIV setup used consisted of a digital camera connected to hardware and a pulsed Nd:YAG laser (Quantel Ultra). The laser pulse content, at 4 Hz, was: 15 mJ at 1574 nm, 75 mJ at 1064 nm, 45 mJ at 532 nm, 20 mJ at 355 nm, and 15 mJ at 266 nm. The laser pulse duration was 4 to 6 nanoseconds. The PIV measurements were carried at the observation plane parallel to the sphere axis, passing through the centre point. The laser light sheet had a thickness of about 1 mm and illuminated this vertical cross section of the flow.

The charge-coupled device (CCD) consisted of an array of 1280×1024 pixels (PCO SensiCam). A Nikon 50 mm manual lens was attached to the CCD camera for covering the field of interest. Both camera and laser were synchronized with a synchronizer. The frame field of view was 40 mm by 35 mm. The camera was calibrated and the data processing used a geometrical mask to filter out-of-plane and reflection noises. Velocity vectors were calculated from particle traces by the time-series cross-correlation method in DaVis software. The final interrogation size was 16×16 pixels starting from an initial size of 64×64 pixels. The pulse separation time was limited by the camera capturing frequency, at 4 Hz. The time-averaged velocity field was obtained by averaging a sequence of 200 velocity vector images. The validation of the PIV technique was carried out by comparing with theoretical and simulated data.

The sample fluid was either 1 wt.% TX-100 or A1 oil, seeded with glass particles at a loading of 0.04 mg/mL. The glass sphere particle sizes ranged from 9 to 13 μ m, and were purchased from Sigma Aldrich. The sample was set into motion by the stepper motor. The observation plane was the vertical meridional plane, corresponding to x = 0 in the Cartesian coordinates defined in Figure 2.12(a). Velocity vectors were recorded in the *y* – *z* plane. In the meridional plane, the radial coordinate (*r*) of the spherical polar coordinates and the *y*-axis coordinate of the Cartesian coordinates are equivalent.

Some initial studies with a two-fluid fill were conducted in the PIV system but these were not pursued further, since the bulk emulsification experiments did not give rise to droplet formation.

Chapter 4 Interfacial shape deformation

The bulk emulsification hypothesis postulates that SiOil droplets are formed from the breakup of the oil-aqueous interface under shear stresses. This chapters presents the validation of the RBF model and the sample preparation protocol, and then the stability of the oil-aqueous interface in the RBF under different saccadic motions.

First, the static interface shape between the two liquids was determined experimentally, then compared to analytical calculations. Factors affecting the interface shape, such as volume ratio, interfacial tension, contact angle and gravity, were studied. Secondly, the fluid dynamics in the RBF chamber were studied experimentally using the particle velocimetry imaging and compared to analytical model and numerical simulations. Finally, the stability of the interface was studied under a range of saccadic motions representing the physiological conditions of the eye. Numerical simulations were able to capture the interface deformation under certain saccadic conditions and gave estimates of the velocity fields and shear stresses in the observation planes that were not accessible via the experiments.

4.1 Static interface shape

4.1.1 Effect of surfactant addition

The chemical surfactant TX-100 was chosen to reproduce the potential presence of surface-active molecules in the vitreous humour after vitrectomy. The effect of the surfactant on the static interface shape was investigated.

4.1.1.1 Interfacial tension (IFT) decrease

TX-100 was a suitable surfactant candidate because of its solubility in saline and its transparency. The effect of TX-100 on the B1 SiOil/ saline interface was investigated over the concentration range of 0.0001 to 1 wt.%. Figure 4.1(a) shows that the IFT decreases with the addition of surfactant. The presence of salts only reduced the IFT of water by about 5 mN/m. Further increase of the concentration after 0.025 wt. % did not affect the IFT, which exhibited a plateau at 4.4 ± 0.5 mN m⁻¹ associated with micelle formation above a critical micelle concentration (CMC) of approximately 0.39 mM. Below the CMC, the data fitted the Szyszkowski equation well:

$$\gamma = \gamma_0 - \hat{R}T\Gamma^{\infty}\ln(1 + KC) \tag{4.1}$$

Equation (4.1) is for a non-ionic surfactant, with γ_0 the interfacial tension in the absence of surfactant, *K* the equilibrium constant for adsorption of the surfactant at the liquid/liquid interface, and *C* the bulk concentration of surfactant (Dharmawardana *et al.*, 1993). Fitting Eqn. (4.1) to the data yielded Γ^{∞} for TX-100 in saline of 2.2×10⁻⁶ mol m⁻². These values of CMC and Γ compared favourably with the values reported by Jañczuk *et al.* (1995) for TX-100 in water at 25°C, of 0.263 mol/L and a surface excess of 2.6×10⁻⁶ mol m⁻². The difference was attributed to the presence of salts in the saline and the difference in temperature. They also reported that the CMC decreased with increasing temperature and salt concentration, because the surfactant adsorbed less at the interface (Janczuk *et al.*, 1995).



Figure 4.1: Effect of TX-100 at 20°C on (a) B1 oil-saline interfacial tension at 20°C. Black locus shows the fit to the Szyszkowski equation [Eqn.(4.1), K = 97.9 L/mol]. Dotted and dashed horizontal lines indicate the IFT values for surfactant-free saline and water, respectively. *C* is the concentration of TX-100 in saline. (b) B1 oil-saline with DTS in the oil

The effect of DTS in SiOil was also analysed over the concentration range of 0.01 to 1.0 wt. %. These low molecular weight siloxane molecules represented manufacturing impurities that could be present in the silicone oil (Nakamura, Refojo and Crabtree, 1990; Williams *et al.*, 2010; Dresp, 2020). Figure 4.1(b) shows that the presence of

the oil soluble surfactant does not have effect on the IFT in the concentration range tested. Adding DTS to the oil at the 0.01, 0.1 and 1 wt.% levels modified the IFT between saline and oil from 27 to 26.6, 27.1 and 27.5 (\pm 0.5) mN m⁻¹, respectively, which was considered small. This finding was consistent with the measurements by Lu *et al.* (2019) made with DTS concentrations in 100 cSt oil in the range 0 – 0.5 wt.%. They reported that the addition of the surfactant to 100 cSt oil did not change the IFT but did increase the number of oil droplets formed in the eye-on-a-chip system. They also reported the presence of water-in-oil droplets in their experiment, highlighting that water droplets had not been reported in clinical instances before (Lu *et al.*, 2020).

These results indicated that although the impurities did not affect the interfacial tension, they can still increase the number of droplets formed and the type of emulsion. The emulsification mechanism in an eye-on-a-chip is, however, different to a real eye system, so the transposition of those results to eyes needs careful consideration.

4.1.1.2 Three-phase contact angle

The three-phase contact angle (TPCA) between SiOil, aqueous and solid substrate was measured using the sessile drop set-up described in 3.2.4. Unless specified, all the TPCAs were measured in the (denser) aqueous phase. Using a glass microscope slide as substrate and the B1 oil, the addition of surfactant to saline decreased the TPCA from 50° to 17° (see Figure 4.2). The contact angle reached a constant value when surfactant concentration was 0.12 mM ($\ln C = -9.1$), which was below the CMC (0.39 mM). The complementary contact angle in the oil phase increased from 130° to 163°. These values were consistent with the literature: Sharma *et al.* (2019) reported a TPCA of 129° (measured in the oil phase) for a 1 Pa s SiOil on a hydrophilic glass slide immersed in water. Fawcett, Williams and Wong (1994) reported a TPCA of 161.8° (measured in the oil phase) for a SiOil (1000 cSt) on a retinal surface, in a phosphate buffered saline environment. When measured in air, both oil and aqueous wetted the glass substrate fully, which is similar to the behaviour of the two liquids on a retinal surface in air. Rubowitz *et al.* (2020) reported 0° contact angle for both oil and aqueous on the retinal surface of animal eyes (cow, sheep and pig).

By considering Young's equation (eqn. (2.4)) defined for oil (O) and aqueous (L) on a glass substrate (S), a change in the TPCA involves a change in γ_{SL} and/or γ_{LO} , but not

 γ_{SO} , since the latter quantity is a characteristic of the oil and the substrate alone. Addition of surfactant decreases γ_{LO} as discussed above. The value $\cos \theta_{WO}$ thus increased with the addition of surfactant. The large decrease in the IFT from $\ln C = -11.1$ to -7.9 (Figure 4.2) indicates that γ_{SL} has also increased, which is likely due to surfactant adsorption on the substrate with increasing surfactant concentration. Further increase of surfactant after 0.12 mM ($\ln C = -9.1$) did not affect the contact angle, which is likely due to the saturation of interfaces with the surfactant.

TX-100 makes the glass substrate a suitable model of the retina surface, achieving a comparable TPCA of 163° when measured in oil. The majority of tests in the thesis were conducted with a TX-100 concentration of 1 wt.%, above its CMC, to ensure a hydrophilic surface and a low IFT scenario to favour emulsification. Operating above the CMC also meant that there was a supply of surfactant available to adsorb on any freshly created interface. Any droplets formed in the system would be expected to be stabilised by the surfactant. Tests were also conducted with no surfactant present in the saline phase to gauge its impact.



Figure 4.2: Effect of TX-100 on B1 oil/saline TPCA (black) and IFT (orange) on glass at 20°C. Insets show the picture of a 0.025 wt.% TX-100 in saline drop on the glass substrate immersed in B1 oil ($\ln C = -7.9$).

4.1.2 Analytical model

A model for the shape of liquid-liquid interface between a tamponade and the aqueous solution at a given volume ratio was developed by Eames *et al.* (2012). By assuming an axisymmetric interface around the vertical axis, the static balance analysis on the liquid interface (equation (2.10)) between the interfacial forces and the buoyancy forces gives:

$$\gamma(\nabla \cdot \mathbf{n}) = \Delta \rho g(z - z_m) \tag{4.2}$$

with z_m the minimum height of the interface, defined in Figure 3.8(b).

In cylindrical polar coordinates, the unit normal vector of the interface is defined as (Eames *et al.*, 2010):

$$\mathbf{n} = \mathbf{r} - \frac{\frac{\partial r}{\partial z}}{\left(1 + \left[\frac{\partial r}{\partial z}\right]^2\right)^{1/2}} \mathbf{z}$$
(4.3)

By combining the two equations, the interface shape is described by:

$$-\frac{\frac{\partial^2 r}{\partial z^2}}{\left(1 + \left[\frac{\partial r}{\partial z}\right]^2\right)^{3/2}} + \frac{1}{r\left(1 + \left[\frac{\partial r}{\partial z}\right]^2\right)^{1/2}} = \frac{\Delta \rho g(z - z_m)}{\gamma}$$
(4.4)

This equation was integrated numerically from the position of the three-phase contact line, z_c , to z_m using MATLAB (R2017b, Mathworks), and the final solution satisfied the boundary conditions:

$$r = 0, z = z_m \tag{4.5}$$

$$\frac{\partial r}{\partial z} = \frac{z_c / \sqrt{R^2 - z_c^2} - \tan \theta}{1 + \tan \theta \, z_c / \sqrt{R^2 - z_c^2}} \tag{4.6}$$

and the conservation statement:

$$V_{\text{tamponade}} = \int_{-R}^{R} 2\pi r^2 dz \tag{4.7}$$

Finally, the tamponade angle is defined at the contact line:

$$\alpha = 2\cos^{-1}\left(\frac{z_c}{R}\right) \tag{4.8}$$

4.1.3 Angle of tamponade

The shape of the tamponade – aqueous interface depended on the volume ratio, the interfacial tension, contact angle and gravity. The angle of tamponade is plotted against the volume fraction of the tamponade in Figure 4.3 for a series of cases. The angle of tamponade increased with the volume fraction of the tamponade. It is known from the literature that the greater the tamponade angle, the greater the surface contact between the tamponade and the retina, and hence, the greater the effectiveness of the tamponade (Fawcett, Williams and Wong, 1994). This is consistent with the surgical protocol of filling the vitreous chamber with the maximum amount of tamponade.



Figure 4.3: Evolution of the angle of tamponade with the tamponade volume fraction in a spherical chamber model for different aqueous/tamponade systems. Solid lines represent the mathematical model described in section 4.1.2

For the water/air system, the experimental data followed a spherical cap model with h defined in Figure 3.1(a):

$$\alpha = 2\cos\left(1 - \frac{h}{R}\right) \tag{4.9}$$

The result is consistent with the findings by Fawcett *et al.* (1994). The water/air system has $L_c \sim 3 \text{ mm}$ owing to a large difference in density (~ 1000 kg/m³): the gravity term dominates surface tension and promotes a flatter interfacial shape.

The oil/aqueous system gave different tamponade shapes depending on the treatment of the glass wall (via θ) and the presence of surfactant in the aqueous phase (via γ and L_c). Aqueous and oil had a high *Bo* (~ 100), indicating the effect of gravity was important. Figure 4.3 shows that the decrease in IFT from 0.03 to 0.004 mN/m shifted the curve upwards, whereas reducing the TPCA shifted the curves downwards. The experimental data showed good agreement with the model predictions, and the RBF pre-coated with TX-100 solution gave comparable contact angle and angle of tamponade results to the literature on eyes (Eames *et al.*, 2010).

4.1.4 Interfacial shape

In addition to predicting the effect of $\emptyset_{tamponade}$ on the angle of tamponade, the mathematical model gave the interfacial shape (eqn. (4.4)). Figure 4.4 presents the predicted tamponade interface shapes for TPCAs of 15°, 20° and 50°. Figure 4.4(a) features the same contact point and different contact angles. The liquid wetting the surface with a higher contact angle requires a smaller level of fill of oil to achieve the same retinal coverage than the liquid with a smaller contact angle. Figure 4.4(b) shows the shape of the interface when the volume ratio is kept the same. A smaller contact area between the tamponade and the retinal wall.



Figure 4.4: Theoritical calculation of the tamponade interfacial shape for three different threephase contact angles (a) at the same contact point, $\emptyset_{tamponade} = 0.44, 0.59$ and 0.61 for TPCAs 50°, 20° and 15°, respectively. (b) at the same level of fill, $\emptyset_{tamponade} = 0.9$.

Figure 4.5 compares photographs of a RBF sample filled with aqueous and SiOil liquids, and the calculated shape of the oil/aqueous interface. The theoretical shape was obtained using the experimental values of the contact angle, interfacial tension and volume ratio in equation (4.4). The experimental and the predicted tamponade shapes show good agreement.

The agreement in the angle of tamponade and the interfacial shape supports the spherical model of the eye chamber. The approximation of the eye chamber by a round bottom flask is therefore validated.



Figure 4.5: Comparison between calculated shape of the interface and photographs of the experimental 25-mL RBF sample filled with oil and aqueous, $\phi_{oil} = 0.91$, (a) B1 oil:saline (b) B1 oil:saline with 1wt.% TX-100.

4.2 Fluid dynamics in a sphere

This section investigates the fluid dynamics in a spherical chamber under saccadic motion. Results have been obtained with a single-phase liquid in the chamber and numerical simulations of the flow undertaken by Dr. Jheng-Han Tsai are presented here for comparison.

4.2.1 Analytical model of a single phase

Consider a solid sphere filled with a Newtonian fluid, undergoing a periodic saccadic motion about the rotation axis passing through the centre of the sphere. The governing equations are the dimensionless Navier-Stokes and continuity equations (introduced in section 2.1.2.1):

$$Wo^2 \frac{\partial \mathbf{u}}{\partial t} + Wo^2 \mathbf{u} \cdot \nabla \mathbf{u} = -\nabla P + \nabla^2 \mathbf{u}$$
 (4.10)

$$\nabla \cdot \mathbf{u} = \mathbf{0} \tag{4.11}$$

with $\mathbf{u} = (u_r, u_\vartheta, u_\varphi)$ the velocity expressed in spherical polar coordinates (r, ϑ, φ) and scaled by $R\Omega_{max}$, the azimuthal velocity of the wall at the equatorial plane. All length quantities are scaled by the sphere radius R, and time quantities by the maximum angular velocity, Ω_{max} . A no-slip boundary condition is imposed at the wall, so the velocity of the fluid adjacent to the retina wall has the same velocity and is given by the azimuthal velocity condition:

$$u_r = u_{\vartheta} = 0, \qquad u_{\varphi(r=1)} = A \sin \vartheta \ \Omega(t) / \Omega_{\max}$$
(4.12)

with $\Omega(t)$ defined by eqn. (3.2) and A is the amplitude of the saccade.

By assuming a small amplitude motion, the velocity and the pressure terms were linearised and only the leading-order terms were used in the calculations:

$$\mathbf{u} = A\mathbf{u}_1 + O(A^2), \qquad P = AP_1 + O(A^2)$$
 (4.13)

In the first-order solution, the radial and zenithal components are null, and the azimuthal component satisfies:

$$\frac{\partial u_{\varphi_1}}{\partial t} = \frac{1}{Wo^2} \left[\frac{1}{r^2} \frac{\partial}{\partial r} \left(r^2 \frac{\partial u_{\varphi_1}}{\partial r} \right) + \frac{1}{r^2 \sin(\vartheta)} \frac{\partial}{\partial \vartheta} \left(\sin(\vartheta) \frac{\partial u_{\varphi_1}}{\partial \vartheta} \right) - \frac{u_{\varphi_1}}{r^2 \sin^2 \vartheta} \right]$$
(4.14)

$$u_{\varphi 1 (r=1)} = \sin(\vartheta) \,\Omega(t) / \Omega_{\max} \tag{4.15}$$

By using the Fourier series developed for $\Omega(t)$ and by applying the principle of superposition for the square wave, the dimensionless azimuthal velocity component was derived and reported here:

$$u_{\varphi 1} = \sin(\vartheta) \sum_{n=1}^{\infty} B_n \left[-\frac{i}{2r^2} \left(\frac{\sin kr - kr \cos kr}{\sin k - k \cos k} \right) e^{int} + \frac{i}{2r^2} \left(\frac{\sin pr - pr \cos pr}{\sin p - p \cos p} \right) e^{-int} \right]$$
(4.16)
$$k = Wo \ e^{-\frac{i\pi}{4}}, \ p = Wo \ e^{\frac{i\pi}{4}}$$
(4.17)

The azimuthal velocity developed for small amplitude is valid for all Womersley numbers:

$$u_{\varphi} = A u_{\varphi 1} \tag{4.18}$$

By assuming the velocity in the azimuthal direction only depends on the radial coordinate, applying Newton's law of viscosity in spherical coordinates gives the dimensionless shear stress expression (eqn. (4.19)). By inputting the velocity $Au_{\varphi 1}$ into equation (4.19), the shear stress in the azimuthal direction was calculated:

$$\tau_{r\varphi} = -\left(\frac{\partial u_{\varphi}}{\partial r} - \frac{u_{\varphi}}{r}\right) \tag{4.19}$$

$$\tau_{r\varphi} = -A\sin(\vartheta) \sum_{n=1}^{\infty} B_n \left[-\frac{i}{2r^2} \left(\frac{(k^2 r^2 - 2)\sin kr + 2kr\cos kr}{\sin k - k\cos k} \right) e^{int} + c.c. \right]$$
(4.20)

with *c*.*c*. denoting the complex conjugate. The dimensional shear stress, $\tau_{r\varphi}^*$, is equal to $\mu\Omega_{\max}\tau_{r\varphi}$, with μ the dynamic viscosity of the Newtonian fluid.

4.2.2 Single phase fluid flow

4.2.2.1 Analytical azimuthal velocity profile

Using Matlab and the equations developed in the previous section, the azimuthal velocity profiles of a single-phase fluid in the equatorial plane were calculated for different saccade conditions and at different times of the saccade period. Figure 4.6 shows a typical saccade velocity over time plot with two successive saccade pulses

in antiphase. The circled numbers (0 to 7) indicates the times taken to calculate the plotted azimuthal velocity profiles.



Figure 4.6: Solid sphere wall velocity ($\Omega_{\max} u_{\varphi}$ for r = 1). Saccade parameters: $\Omega_{\max} = 200^{\circ}/s$, $A = 5.4^{\circ}$. Circled numbers (0 to 7) indicate the times: 0, $L/2 - \Delta s$, $L/2 + \Delta s$, L/2 + D/2, $L/2 + D - \Delta s$, $L/2 + D + \Delta s$, L + D and $2L/2 + D + \Delta s$ secondes, with $\Delta s = 0.001 \text{ s}$.

Figure 4.7 shows the azimuthal velocity profile for a Newtonian fluid with Wo = 1 at the eight different times labelled 0 to 7 on Figure 4.6. When the wall is at rest at times 0 and 1, the fluid is also immobile. At time 2, where the wall just starts its saccade pulse, the fluid is dragged along by the wall, reaching its maximum velocity at the wall (r = 1). The moving layer penetrates to about r = 0.6 after 101 ms. By times 3 to 4, the velocity distribution has developed fully and extends to the inner core of the fluid via viscous drag. The wall comes back to the initial position at times 5 and 6, and the fluid's velocity profile decays back to close to rest position at the middle of the latency period, at time 6. Flow reversal between the pulses results in the maximum in velocity around $r \sim 0.75$ in profile 5.

Figure 4.8 studies the effect of Wo on the velocity profile. High Wo values correspond to a sphere filled with a single aqueous phase, whereas low Wo cases correspond to high viscosity liquid, such as SiOil. For Wo = 40, only the fluid near the wall is moving and the core fluid is static. This moving layer of fluid near the wall is called the oscillatory boundary layer and has a thickness of the order of the Stokes boundary layer thickness. A higher Wo arises with lower viscosity fluid or larger sphere radius or wall velocity. Isakova *et al.* (2014) interpreted the Womersley number as the ratio between the sphere radius and the boundary layer thickness: a larger *Wo* leads to a thinner oscillatory boundary layer. These calculations indicate that with the SiOil, the wall motion is transmitted through the oil phase but for water, it is limited to a narrow band near the wall.



Figure 4.7: Azimuthal velocity profile in the equatorial plane of the solid sphere at different times of the saccade period, defined in Figure 4.6. Saccade parameters: $\Omega_{\text{max}} = 200^{\circ}/\text{s}, A = 5.4^{\circ}, Wo = 1$ (low viscosity fluid case).



Figure 4.8: Azimuthal velocity profile in the equatorial plane for (a) Wo = 20, (b) Wo = 40. Saccade parameters: $\Omega_{max} = 200 \text{ °/s}$, $A = 5.4^{\circ}$, L = 0.2 s. Profiles plotted from r = 0.5 for better visualisation of the different curves. Labels indicate times in Figure 4.6.

The following velocity profiles are all calculated for Wo = 1 to allow the impact on boundary layers to be seen clearly. Figure 4.9 illustrates the effect of saccade angular velocity. To keep Wo constant, the saccade duration was modified in tandem with the angular velocity. The most obvious difference in increasing the angular velocity occurs in the curves at times 3 and 4. At lower angular velocity, the two curves are almost coincident, indicating that the maximum velocity envelope was attained by half way through the saccade duration. For higher angular velocities, the difference in velocity between the fluids near the wall and at the centre is greater, which results in longer time being needed for the fluid in the core to reach its maximum velocity.



Figure 4.9: Azimuthal velocity profile in the equatorial plane at different Ω_{max} . Saccade parameters L = 0.2s, $A = 5.4^{\circ}$, Wo = 1.

The influence of the latency time and the saccade amplitude is shown in Figure 4.10. The curves were plotted at the same instant in a saccade period, immediately before a subsequent pulse starts (equivalent to time 1 in Figure 4.6). The difference is noticeable near the wall, where higher latency time or lower amplitude motion leads to fluid almost slowing down to rest. A longer latency time gives the fluid enough time to come at rest before being subjected to another saccadic pulse. A higher amplitude led to larger fluid displacement, resulting in greater motion in the fluid at the end of a half period.



Figure 4.10: Azimuthal velocity profile in the equatorial plane at time 1 on Figure 4.6. Saccade parameters: $\Omega_{max} = 200^{\circ}/s$, Wo = 1 (a) $A = 5.4^{\circ}$, and (b) L = 0.2 s.

4.2.2.2 PIV results

The 2D flow fields of the meridional plane (vertical, x = 0) was measured with the PIV system for a single fluid in the round bottom flask. Figure 4.11 shows the steady streaming velocity fields obtained for the B1 SiOil. The flow is symmetric and comprises of two counter-rotating vortex-like structures in both hemispheres. The flow is first dragged from the wall towards the equatorial plane, then sent radially inwards and finally travels from the centre towards the poles along the axis of rotation. This is a flow pattern common to all the analysed velocity fields, and is similar to that observed in a perfect sphere by Repetto *et al.* (2008).

Figure 4.12 compares the steady streaming fields of the single SiOil phase (Wo = 2.1) to the single saline phase (Wo = 44). The velocity magnitude is higher near the rotation axis in the lower Wo case, but near the wall for higher Wo. This can be

explained by the oscillatory boundary layer being located near the wall for the water phase, and the lack of acceleration within the interior of the fluid. It should be noted that these velocities are all small compared to the maximum forcing velocity at the wall, which on the equator reached 0.21 m/s.



Figure 4.11: 2D steady streaming velocity on the meridional plane x = 0 and Wo = 2.1 (B1 oil). The origin of the axes is not coincident with the centre of the sphere.



Figure 4.12: PIV measurements of steady streaming fields and contour plot of the averaged steady streaming velocity \overline{V} on the meridional plane x = 0 and (a) B1 oil, Wo = 2.1, (b) Saline, Wo = 44

4.2.2.3 Comparison between experimental, numerical and analytical results

Figure 4.13 compares the PIV measurements of 2D velocity fields with the numerical results generated by Dr. Jheng-Han Tsai using OpenFOAM. The PIV flow measurements give the averaged steady streaming flow scaled by $R\Omega_{max}$, V^* , the radial outward component $\overline{V_y}$. and the vertical velocity component $\overline{V_z}$. The highest steady streaming flow was located near the vertical axis of rotation and the equatorial plane was a plane of symmetry. The experimental values are in general smaller (by a factor of 2 to 3), which was attributed to the limitations in the camera acquisition rate (maximum value of 4 Hz) and a misalignment of the laser light sheet. The time elapsed between two consecutives frames is higher than the saccade period, so the velocity is averaged over a longer period of time, and this is thought to explain the lower values in experimental results. The CFD simulations did, nevertheless, give reasonable semi-quantitative predictions of the velocity fields measured in the experimental RBF.



Figure 4.13: Comparison of (a) PIV and (b) simulation results for (i) flow pattern in meridional plane (x = 0), with contour colours showing velocity magnitude and arrows direction, (ii) y-velocity, (iii) z-velocity. Test conditions: B1 oil, $\Omega_{max} = 600$ °/s, $A = 18^{\circ}$, L = D = 30 ms, Wo = 2.1.

Only the PIV and simulation results in the meridional planes were compared because the PIV setup was only able to capture the vertical planes. The CFD simulations were able to capture the velocity fields on different planes, such as the azimuthal velocity profiles in the equatorial plane. Figure 4.15 shows the simulated azimuthal velocity profiles along the radial direction in the equatorial plane, at selected times in Figure 4.14. There is reasonably good agreement between the analytical solution and the simulation results. The main difference is that the analytical profiles show the motion coming to rest by the end of the latency period (circled time 3), whereas the motion in the simulation does not. This discrepancy was attributed to the difference in chamber geometries: the analytical solution assumed spherical symmetry, while the simulation geometry had cylindrical symmetry with a neck at the top of the flask. The numerical model nevertheless captured the key features of the motion.



Figure 4.14: Angular velocity profile over one cycle of saccade period *T*_s : Circled numbers 1, 2, 3, 4, I, II, III, IV are sample times in analytical and numerical simulations.



Figure 4.15: Comparison of azimuthal velocity profiles $(u_{\varphi}^* = R\Omega_{\max}Au_{\varphi 1})$ on the equatorial plane predicted by (a) analytical approach, and (b) CFD simulation, at key times during the saccadic cycle marked on Figure 4.14: (i) start (1,3) and end (2,4) of pulse stages: (ii) evolution of velocity profile during one forcing stage (3, I-IV, 4). Test conditions: B1 oil, $\Omega_{\max} = 600^{\circ}/s$, $A = 18^{\circ}$, R = 20 mm and L = D.

Figure 4.16 shows the calculated and simulated shear stress profiles at times defined on Figure 4.14 for a single phase oil or aqueous solution. The wall was subjected to both positive and negative $\tau_{r\varphi}^*$ with the maximum $\tau_{r\varphi}^*$ value located on the wall. At times 2, $\tau_{r\varphi}^*$ was about 20 Pa for the oil case and 1 Pa for the aqueous case (in absolute value). The 2 order of magnitude difference was in agreement with the findings of Abouali *et al.* (2012).

The simulated results in the y - z plane shows that $\tau_{r\varphi}^*$ is the smallest at the centre of the sphere and increased with the radius (Figure 4.16(ii)). In the aqueous case, the shear stress was null in almost the whole fluid and was only important near the wall,

in agreement with the calculated profile on the equatorial plane. The $\tau_{r\varphi}^*$ value range in oil (-20 to 10 Pa) was comparable to those (-10 to 20 Pa) found by Repetto, Stocchino and Cafferata (2005) in the case of a glycerol solution (*Wo* = 6.14) set under a saccadic motion of $A = 10^\circ$ and $\Omega_{max} = 328^\circ/s$.



Figure 4.16: (i) Analytical calculation and (ii) numerical simulation of shear stress on the equatorial plane at key times during the saccadic cycle marked on Figure 4.14: Test conditions: $\Omega_{max} = 600$ °/s, $A = 18^{\circ}$, R = 20 mm and L = D. (a) B1 oil, (b) 1 wt.% TX-100 in saline

The agreement between the results for the single one-phase case was reasonable, providing confidence to support the use of the same numerical methods for a two-phase fluid flow in a round-bottom flask geometry. The two-phase flow simulation allowed the more complex flow fields of the experimental eye chamber model to be captured and provided quantitative estimates of quantities such as local shear stresses on planes that are not readily accessed experimentally.

4.2.3 Numerical simulation of two-phase liquids flow

The CFD simulation was run for an oil-aqueous system consisting the B1 oil and the 1 wt.% TX-100 in saline in a 91:9 ratio. Experimentally, the oil-aqueous interface was deformed after one or two saccade periods and reached a steady state shape, as shown in Figure 4.17. The simulation calculated a spin-up time about 0.2 s to reach a qualitatively similar shape (Figure 4.18), which is comparable to one saccade period $(T_s = 0.24 \text{ s})$.



Figure 4.17: Experimental pictures of the two-fluid case, B1 oil:saline with 1 wt.% TX-100, $\phi_{oil} = 0.91$. Saccade parameters: $\Omega_{max} = 600$ °/s, $A = 36^{\circ}$, L = D and R = 20 mm.



Figure 4.18: Simulated images of the two-fluid case, B1 oil (grey)/saline with 1 wt.% TX-100 (black), $\phi_{oil} = 0.91$. Saccade parameters: $\Omega_{max} = 600$ °/s, A = 36°, L = D, R = 20 mm.

The contour profiles of the *z*-component of the velocity and the shear stress are plotted on the meridional plane for two different saccade cases in Figure 4.19. The largest velocity values were located on the rotation axis and near the fluid-fluid interface. The values were 3 to 4-fold higher in the higher amplitude case (approximatively 5X greater). The higher amplitude gave rise to a larger velocity near the wall which, when distributed within the two fluids, created a higher velocity difference near the interface. This was in agreement with the azimuthal velocity profiles. This resulted in greater deformation of the interface shape, forming a dome on the axis which is observed on the picture (Figure 4.19(b,i)).

The shear stress profiles showed that for the low amplitude case, the shear stress was largest within the oil phase, and decreased with distance from the wall (Figure 4.19(b,ii)). This is consistent with the velocity decreasing as $r \rightarrow 0$. The shear stress

at the interface had value range of 0 - 2 Pa. In the higher amplitude case, the shear stress changed strongly near the fluid-fluid interface, varying from 1 to 10 Pa. The higher shear stress values near the interface were consistent with the larger deformation of the interface shape. Angunawela *et al.* (2011) reported a maximum shear stress at the wall around the same order of magnitude for a gas-aqueous system in the eye, but their value was achieved under a combination of saccadic motions and head motions.

The shear stress profile along the radial direction was also calculated for a singlephase fluid in a sphere using eqn. (4.20). Figure 4.20 and Figure 4.21 show the evolution of the shear stress profiles for a single-phase B1 oil or 1 wt.% TX-100 when subject to the same saccadic motions used in the CFD simulations. The shear stress was higher near the wall with the maximum value located at the wall during a saccade pulse or in the range r = [0.8 - 1] during the deceleration phase (latency time). The maximum shear stress value on the equatorial plane for the oil case was about 14 Pa for a saccade amplitude of $A = 5.4^{\circ}$, and 38 Pa for $A = 36^{\circ}$. The latter value was higher than the maximum value of 20 Pa found in literature (Abouali *et al.*, 2012), this could be explained by the fact that the analytical approach was only valid for small amplitude.

The difference in the maximum $\tau_{r\varphi}^*$ values between the oil and aqueous case was about 1 to 10-fold for the lower amplitude case, and 1 to 18-fold for the higher amplitude case. These values were higher than the simulation result (Figure 4.19(b,i), but they were calculated on the equatorial plane whereas the oil-aqueous interface was below the equatorial plane.

Figure 4.20 and Figure 4.21 also shows the variation of the shear stress profile with the observation plane defined by the polar angle, ϑ . The shear stress values were the highest on the equatorial plane and decreased in the parallel planes with decreasing ϑ . At high saccade amplitude, the difference in $\tau_{r\varphi}^*$ values between the oil and aqueous case on the planes $\vartheta = \pi/4$ and $\vartheta = \pi/6$ were of order 5 to 15-fold at the wall, and 3 to 10-fold at r = 0.8. These were of the same order of magnitude as the values at the oil-aqueous interface in Figure 4.19(b,ii).



Figure 4.19: Simulation results for two-fluid case, B1 oil:saline with 1 wt.% TX-100, $\phi_{oil} = 0.91$, $\Omega_{max} = 600$ °/s, L = D, R = 20 mm, calculated at circled time 4 on Figure 4.14, showing (i) *z*-axis velocity and (ii) shear stress τ_{yx}^* (equivalent to $\tau_{r\phi}^*$ defined in eqn. 4.19). Black dashed locus indicates the interface between oil and saline.



Figure 4.20: Evolution of the shear stress profile over an entire period of a saccadic cycle in the (i) equatorial plane, $\vartheta = \pi/2$, (ii) $\vartheta = \pi/4$ and (iii) $\vartheta = \pi/6$. Each curve is separated by $T_s/20$ s. Test conditions: $\Omega_{max} = 600$ °/s, A = 5.4 and L = D.



Figure 4.21: Evolution of the shear stress profile over an entire period of a saccadic cycle in the (i) equatorial plane, $\vartheta = \pi/2$, (ii) $\vartheta = \pi/4$ and (iii) $\vartheta = \pi/6$. Each curve is separated by $T_s/20$ s. Test conditions: $\Omega_{max} = 600$ °/s, $A = 36^{\circ}$ and L = D.

4.2.4 Summary

The PIV and CFD studies were performed in order to:

- (i) Validate the eye chamber model and the saccadic motion driven by the stepper motor set-up. Comparison with prior analytical and experimental studies showed that the RBF flasks combined with the tuneable saccadic motion sequence achieved similar single-phase flow behaviours.
- (ii) The validation of the eye model and the single-phase CFD simulations allowed calculation of the two-phase flow which was representative of the eye model filled with oil and aqueous phase. The simulations were able to predict the time required to deform an interface under a saccadic motion, and provided quantitative estimates of velocity magnitudes and shear stresses within the fluids and at the wall. These allowed a better understanding of the fluid dynamics in an eye chamber under saccadic motion.

4.3 Interface deformation

This section summarises the experimental results obtained with the stepper motor setup and RBFs. The stability of the bulk oil-aqueous interface is studied under different saccadic motions and liquids properties. The extent of interface deformation is quantified by the dimensionless change in interface length, Δl^* , defined in eqn. (3.3). The liquid flow behaviour was described by *We* calculated with the density of the oil. The effect of liquid and interfacial properties, flask geometry and level of fill is presented and discussed. The data also include tests with very large amplitude and with the eye chamber inclined, to simulate larger eye and head motions.

4.3.1 Influence of viscosity

The above section on fluid dynamics in a sphere showed that the motion of the wall is transferred to the fluid by viscous drag. The difference in dynamic viscosity between the silicone oil and aqueous phases resulted in differences in local velocity profiles near the interface, causing the interface shape to deform. Figure 4.22(a) shows that the oil viscosity has a significant effect on Δl^* , when the motion is characterized in terms of *We* (the length scale used to calculate *We* was the RBF radius, *R*). The

deformation was highest at high inertia, with the B5 oil achieving deformation 3-fold higher than the two lower viscosities. A higher viscosity induced a greater difference in velocity between the oil and aqueous phases, which led to higher shear forces that deform the interface. For all three oils, the results show that the deformation becomes significant ($\Delta l^* > 1$) when We > 1: $We \sim 1$, corresponding to similar capillary (surface tension) and viscous stresses, appears to be a critical value for large interface deformation. Figure 4.22(b) shows the same values with the motion characterized by Wo, for comparison. Under the same inertial force, the higher viscosity oil has a larger deformation. The critical Wo value for large interface deformation increased with decreasing oil viscosity.



Figure 4.22: Effect of SiOil viscosity on the interface extension, with the motion characterised by (a) *We* and (b) *Wo*. A 25-mL RBF, $A = 14.4^{\circ}$, $\phi_{oil} = 0.91$, B1 oil/aqueous phase saline with 1 wt% TX-100.

4.3.2 Influence of interfacial tension

Figure 4.23 shows the effect of surfactant on the interfacial length ratio under different saccadic conditions. The largest value of Δl^* is for a higher We, corresponding to a smaller surface tension. The data between the cases with or without surfactant followed the same trend, showing that the flow behaviour was indeed characterised by We, describing the relative importance between inertia and interfacial forces. TX-100 reduces the interfacial tension between the oil and saline phases by a factor of 6 and thus increases the effect of inertia, quantified in We, 6-fold. The silicone oil-water interface was therefore less stable in the presence of surfactants. This agreed with

prior studies investigating the effect of proteins on the oil emulsification (Heidenummer, 1991 & Savion, 1996).



Figure 4.23: Effect of surfactant on the interface extension. 25mL RBF, $\phi_{oil} = 0.91$, B5 oil/saline. Red dashed triangle show the gradient for y = x.

4.3.3 Influence of the saccadic motion

Figure 4.24 summarises the influence of the saccadic motion characteristics on the interfacial length ratio for a 25mL RBF filled with B5 oil and 1 wt.% TX-100 in saline. Larger D/T ratios led to larger Δl^* , particularly when We > 1. Shorter latency times meant that the fluid motion did not decay completely before the next forcing stage started, and this was expected to cause stronger convection currents and interfacial deformation. The experiments were also performed with other oil viscosity and level of fill, and the same behaviour was observed (data not presented)



Figure 4.24: Effect of saccade characteristics on interfacial extension. 25mL RBF, $\phi_{oil} = 0.91$, B5 oil/saline with 1 wt.% TX-100

4.3.4 Influence of level of fill and flask volume

The level of oil fill had a stabilising effect on the interface: Figure 4.25 shows that a higher ϕ_{oil} resulted in lower interfacial deformation. A larger oil level of fill meant a thinner aqueous layer, which would be closer to the two "concentric spheres" configuration in the eye model. Prior work by Isakova and Garcia-Gonzalez showed that the thin aqueous layer hypothesis promoted a more stable interface at higher viscosity ratio ($\lambda > 200$). The viscosity ratio for the studied SiOils and the saline solution was between 500 and 5000, which was much higher than the 200. The experimental results with oil level of fill were consistent with the oil-aqueous thin film linear stability studies (Isakova *et al.*, 2014; Garcia-Gonzalez and Fernandez-Feria, 2017).

Figure 4.26 shows that the volume of the RBF had no effect on the interfacial length ratio. The size of the eye chamber did not affect the stability of the aqueous-oil interface. It is noteworthy that the range of RBF sizes is much larger than the variation in eye dimensions. These results indicate that macroscale phenomena (scaled by R) are not significant in the dynamics.

The results for the other oils and saline (without surfactant) were not plotted here, but similar behaviours were observed.



Figure 4.25: Effect of oil level of fill on interfacial deformation, B1 oil: saline with 1 wt.% TX-100.



Figure 4.26: Effect of flask volume on interface extension, B1 oil: saline with 1 wt.% TX-100, $\phi_{oil} = 0.91$.

4.3.5 Influence of eye shape

10mL and 25mL RBFs were modified by Cambridge Glassblowing Company to add either a lens indentation or a buckle indentation. The lens indent was created on the equatorial plane of the RBF and the depth was $\delta = 7 \text{ mm}$. The buckle was located on the equatorial plane of one half of the flask with the same depth as the lens. Figure 4.27 shows photographs of the modified RBFs.



Figure 4.27: Photograph of a 10 mL RBF modified with (a) a lens indentation and (b) inclined at 30°, or modified with (b) a buckle indentation inclined at 30°. Scale bar = 1 cm.

The presence of the indent affected the value of the deformation ratio, the extent depending on the observation plane of the camera. Figure 4.27 shows side views of the indented RBFs. A front view of the RBF corresponds to the indentation directly facing the camera (not shown here). A comparison between the side and front view results for the indented RBFs is shown in Figure 4.28. As with spherical chambers, there is an overall trend change around We = 1. Below We = 1, the interface was deformed to a small extent. Above We = 1, the deformation ratio increased almost proportionally with We. The side view Δl^* values for both indented flasks were higher than the front view values, which was consistent with the presence of the indentation in the plane of observation. The indentation was known to induce a more complex flow near the lens and a larger shear stress near the wall (Stocchino, Repetto and Cafferata, 2007). In the side view, the lens indentation gave rise to higher Δl^* than the buckle indentation for the same saccade motion. This could be due to the shape and extent of the indentation, which affected the fluid motion differently.



Figure 4.28: Comparison between two camera views on the same sample under same saccadic conditions. Black data are experimental results in a buckled RBF and red data for lens RBF. 10mL modified RBF, B1 oil/saline, $\phi_{oil} = 0.91$. Dashed triangle show the gradient for y = x.

Figure 4.29(a) compares the indented and non-indented flasks in the side view format. The lens indent gave rise to three times higher deformation than non-indented flask and the scleral buckle doubled the values. The presence of indentation created more complex local velocity distributions, which was reported in the single-phase fluid simulations of Bonfiglio et *al.* (2013). The higher values obtained with the lens indent could be attributed to the increase in shear stress at the indent (see 2.2.2.2).

Adding surfactant gave similar trends to the case without indentation. The addition of TX-100 in saline destabilised the interface further (see Figure 4.29(b)).



Figure 4.29: Effect of (a) identation and (b) surfactant on interface extension (lens indentation). Test conditions: 10mL RBF, B1 oil/saline , $\phi_{oil} = 0.91$, side view.

4.3.6 Influence of gravity

By inclining the RBF, the effect of gravity on the interface stability can be studied. No significant impact of inclination was observed for the range of β values considered (see Figure 4.30(a)). The addition of surfactant on an inclined and buckled RBF also showed a destabilizing effect on the interface stability (see Figure 4.30(b)).



Figure 4.30: Effect of (a) inclination, β , and (b) surfactant on interface extension ($\beta = 30^{\circ}$). Test conditions: 10mL buckled RBF, B1 oil/saline , $\phi_{oil} = 0.91$, side view.
4.4 Summary

Figure 4.31 summarizes the bulk emulsification experiments for all cases considered using saline with 1 wt% TX-100 as the aqueous phase in spherical RBFs, including different flask diameters, levels of fill, and silicone oil viscosity (0.5, 1.0 and 5.0 Pa s). A clear trend is evident, of low Δl^* for We < 1 and Δl^* increasing linearly with We for We > 1. The transition at We = 1 corresponds to a characteristic velocity of about 0.045 m/s.

Atmakidis and Kenig (2010) showed that the critical velocity difference to give rise to interface deformation between two stratified immiscible fluids in a cylinder was given by:

$$\Delta u_c^2 = 2 \frac{\rho_{\rm oil} + \rho_{\rm aq}}{\rho_{\rm oil} \,\rho_{\rm aq}} \sqrt{\gamma g(\rho_{\rm oil} - \rho_{\rm aq})} \tag{4.21}$$

The difference in dynamic viscosity between the silicone oil and saline solution resulted in differences in local velocities causing the interface shape to change. This deformation is known as the Kelvin-Helmholtz instability. Δu_c for B1 oil and 1 wt.% TX-100 in saline was calculated as 0.07 m/s, which is slightly higher than the characteristic velocity calculated above. The difference could come from the geometry of the container. The observation of significant interface deformation from We = 1 was consistent with increasing characteristic velocity leading to larger velocity difference between the oil and aqueous phases.

For high *We*, the flows were governed by inertia, which is generated by viscous drag. The interface was more deformed at high amplitude and velocity saccade motions, and shorter latency times. Shorter decay time between saccade pulses caused stronger convective flows and interfacial deformation. The addition of surfactant, increase in viscosity and the presence of lens indent were the most significant factors in increasing interfacial deformation.

Droplet formation caused by interfacial break-up was not observed in any of these experiments, which spanned the expected intensity of saccadic motion, ratio of liquid viscosities, and weakest interfacial tensions expected to arise in normal physiological conditions. Although the bulk emulsification mechanism at the liquid-liquid interface has been the main hypothesis of previous work on SiOil emulsification, the

experiments conducted here indicated that the bulk emulsification was not the leading mechanism of the SiOil droplet formation.

Simulations of the two-phase flow were not conducted since the experimental results did not lead to emulsification and the computational effort would be very large (several days to weeks). However, other physical mechanisms such as sloshing of the interface due to large head motion were not included in the study. This will require further studies to include these more complex movements of the eye.



Figure 4.31: Effect of inertia in interfacial extension for different oils, volume ratios, the aqeuous phase being saline with 1 wt.% TX-100

The RBF model has limitations. The presence of the neck was not representative of the almost spherical eye chamber, and the thin aqueous layer configuration in the upper part of the chamber was ignored. However, the experiments with inclined RBFs (Figure 4.27(b,c)) was able to recreate the thin aqueous layer in the upper part of the chamber since inclined RBF is almost spherical at the top. No droplets were observed in the upper part (or at the bulk interface) in the stepper motor experiments.

The RBF model does not include topographical features of the retina, but since this chapter's primary focus was on fluid behavior for the bulk emulsification hypothesis, the topology could be ignored. A further shortcoming of these bulk emulsification experiments was the resolution of the camera: it was only able to detect droplets larger than 10 µm. Any droplet smaller than this might have been missed by the observer.

The average test duration of the stepper motor experiments was 3 minutes. Longer experimental times (up to 3 - 4 days) were considered for a limited set of saccadic conditions. In human eyes, oil emulsion becomes visible after several months, which is an extensive period and is difficult to reliably test. However, test times between 3 minutes and 3 days involved a sufficient number of saccadic cycles such that any fluid-induced instability (should these occur) would be expected to appear. Fluid phenomena or changes in fluid properties involving a longer timescale are likely to be related to diffusion or physiological changes in the solid-liquid interface. However, the impact of diffusion of, say, a surfactant molecule is not expected to be significant, as the stepper motor tests featured concentrations above the CMC. The tests with surfactants, involving low IFT, did not exhibit bulk emulsification.

It is noteworthy that the rotation of the inclined RBF involved motion of the three-phase contact line. Experiments with the inclined RBFs with or without indentation gave rise to oil droplets forming on the flask wall near the three-phase contact line in a few experiments. This directed the work towards investigating the surface emulsification hypothesis. Due to the difficulty in analyzing droplet formation on a curved wall, the surface emulsification investigation was carried in a simpler model of the eye chamber, which is described in Chapters 5 and 6.

Chapter 5 Materials and methods for the moving contact line experiments

The purpose of the next two chapters is to describe the motion and stability of the oilaqueous three-phase contact line (TPCL) when moving across bare and featureprinted substrates. The 3-D model of the eye is replaced by a 2-D geometry - a vertical flat plate – as the interest is on features at the length scale of the contact line where the retinal surface can be considered to be locally flat (albeit rough owing to the presence of the vitreous membranes, cell walls, underlying blood vessels and other physiological features). The tested liquids were the SiOils and aqueous solutions considered in Chapter 3.

Different motions of interest were studied to assess the surface emulsification hypothesis shown in Figure 5.1 and Figure 5.2:

- (i) The TPCL is dragged by the substrate and moves at the same speed (Figure 5.1(c)). The dragging motion can entrain one liquid as a film on the substrate if the substrate reaches a critical speed, which characterises the dynamic wetting transition described in section 2.1.2.4. If the substrate is smooth and homogeneous, the liquid film may adopt a triangular configuration at high substrate speed (Figure 5.1(d)), giving rise to trailing vertexes that can break into liquid droplets. This higher speed condition was not investigated here due to the limitation of the size of the experimental setup.
- (ii) The substrate is immobile and the TPCL moves towards the equilibrium position.
 If the substrate contains features (Figure 5.2(a)), the motion of the TPCL across the feature can give rise to liquid pinning and rivulet formation (Figure 5.2(b)).
 The rivulet can become unstable and break into oil film and/or drops formation (Figure 5.2(d)).
- (iii) The TPCL moves relative to the substrate (Figure 5.1(b)). This depends on the speed and the surface properties of the substrate. During the relative motion, if the TPCL moves across a surface that presents different surface energies, such as silane-coated substrates, it will give rise to different wetting behaviours since the oil prefers to wet the silane coating more than the aqueous (Figure 5.2(c)). The silane features can pin the TPCL and the dewetting of the TPCL over the feature can give rise to oil film and/or drops formation (Figure 5.2(d)).

(iv) The pinned oil on surface features submerged in the aqueous phase is moved with the substrate. Is the flow moving past the pinned oil fast enough to cause it to move/deform/detach from the substrate?



Figure 5.1: Schematic representation of the TPCL motion and stability over bare substrates. Yellow – Oil, blue – Aqueous, grey – substrate, red line – TPCL, red features – oil drops, I – level of liquid-liquid fill in the chamber away from the plate, U – substrate velocity, U_c – critical velocity, z_{eq} – equilibrium position of the TPCL, z_{SS} – steady state position of the TPCL. (a) substrate at rest, (b) the TPCL has a relative motion to the substrate, (c&d) the TPCL moves with the substrate.



Figure 5.2: Schematic representation of the TPCL motion and stability over feature coated substrates. Yellow – Oil, blue – Aqueous, grey – substrate, black square – feature, red line – TPCL, U – substrate velocity, U_c – critical velocity, z_{eq} – equilibrium position of the TPCL, red features – oil drops, P – primary drop or oil film, S – satellite drop. (a) substrate at rest, (b,i) the TPCL moves with the substrate (forcing stage), (b,ii) then restores to z_{eq} (restoration stage), (c,i) the TPCL has a relative motion to the substrate, (b,iii) & (c,ii) formation of liquid rivulet, (d) breakup of the rivulet into liquid droplets on substrate.

Experimental techniques used for surface patterning and studying the wetting transition of the TPCL are described in this chapter.

5.1 Substrate characterisation

5.1.1 Solid substrates

Two solid substrates were used as the vertical flat plate: borosilicate glass microscope slides (dimension $75 \times 25 \times 1$ mm, Fisher Scientific) and cast acrylic (polymethyl methacrylate, PMMA) slides ($75 \times 25 \times 1$ mm, Engineering & Design Plastics Ltd, UK). Glass and acrylic are regularly employed to imitate retinal surfaces in this field of study (see Tables 2.7 and 2.13). Glass slides were used as received without further cleaning.

5.1.2 Plasma cleaning

Acrylic slides were plasma cleaned for one minute on each side, rendering the surface more hydrophilic (Plasma Surface Technology, Diener Electronic). Contact angle measurements of sessile drops of water were recorded on different spots of the substrate and at different times.

The non-treated acrylic slide had a contact angle with water in air of $88 \pm 2^{\circ}$. After plasma treatment, the contact angle value decreased to 49°, then stabilized around 57 \pm 3° after about 20 minutes (see Figure 5.3). The initial drop in contact angle was of the same order of magnitude as that recorded by Darain *et al.* (2012), who reported the water contact angle on acrylic slides decreasing from 70.5° to 21.6° after 40 s of plasma treatment.

The stabilised contact angle value proved to be stable for at least 5 days, which was considered to be suitable for the moving contact line experiments. Plasma treated acrylic slides are labelled plasma acrylic in subsequent sections.



Figure 5.3: Effect of plasma treatement and time on advancing contact angle of water on acrylic slides in air at room temperature. Sessile drop of water (5 μ L).

5.1.3 Silane coating

A solution of 1% vol/vol trichloro(1H,1H,2H,2H-perfluorooctyl)silane (97%, Aldrich) was prepared in isopropanol (ACS reagent, \geq 99.5%, Sigma Aldrich). A glass coverslip (dimension 24 x 50 mm, Thomas Scientific) was placed on a spin-coater (WS-650MZ-23NPP, Laurell Technologies Corporation) and 200 µL of the silane solution was dispensed on to its centre. The solution was then spun at 2000 rpm for 30 s, and dried in the oven at 50°C for 30 min.

The same solution was also used for printing features on substrates, described in 5.2.2.

5.1.4 Substrate surface energies

The surface free energy of solids can be calculated using contact angle measurements. In the Owen and Wendt method, the surface free energy is expressed in terms of dispersive and polar components:

$$\gamma_{\rm SL} = \gamma_{\rm SV} + \gamma_{\rm LV} - 2(\gamma_{\rm SV}^{\rm d} \gamma_{\rm LV}^{\rm d})^{0.5} - 2(\gamma_{\rm SV}^{\rm p} \gamma_{\rm LV}^{\rm p})^{0.5}$$
(5.1)

with γ_i^d and γ_i^p the respective dispersive and polar components of the surface free energy.

Pure liquids of known surface tension were used for sessile drop measurements: deionised water, toluene (Fisher Chemical), glycerol (\geq 99.5%, Merck), ethylene glycol (Reagentplus, \geq 99%, Sigma-Aldrich), dodecane (anhydrous, \geq 99%, Merck) and dimethyl sulfoxide (anhydrous 99.9%, Aldrich). Their dispersive and polar components are summarised in Table 5.1.

Fluid	Dispersive component $\gamma^{\rm d}_{ m LV}$ (mN/m)	Polar component $\gamma^p_{\rm LV}$ (mN/m)	Total $\gamma_{\rm LV}$ (mN/m)
Dodecane	24.9	0	24.9
Toluene	26.1	2.3	28.4
Dimethyl sulfoxide	36.0	8.0	44.0
Ethylene glycol	31.5	16.7	48.2
Glycerol	33.6	29.7	63.3
Water	21.8	51.0	72.8

Table 5.1: Surface free energy components at 20°C, L – Liquid and V – Air. (Janczuk, Wojcik and Zdziennicka, 1993; Gurau *et al.*, 2006).

The contact angle measurements for the different liquids on each substrate are presented in the form suggested by Eqn. (5.2) in Figure 5.4. There is a reasonably linear fit in each case:

$$\frac{\gamma_{\rm LV}(1+\cos\theta)}{2\sqrt{\gamma_{\rm LV}^{\rm d}}} = \sqrt{\gamma_{\rm SV}^{\rm p}} \left(\frac{\sqrt{\gamma_{\rm LV}^{\rm p}}}{\sqrt{\gamma_{\rm LV}^{\rm d}}}\right) + \sqrt{\gamma_{\rm SV}^{\rm d}}$$
(5.2)

Linear regression gave the dispersive and polar components of the solid surface energy reported in Table 5.2.



- **Figure 5.4:** Owens & Wendt plot for the substrate used in this work. *R*² indicate the goodness of fit.
- **Table 5.2:** Measured dispersive and polar components of solid surface energy, at room temperature. S Solid and V Air. Values in square brackets are reproduced from Mader-Arndt *et al.* (2014) and Yu *et al.* (2015)

Substrate	$\gamma^{\rm p}_{\rm SV}$ (±5 mN/m)	$\gamma^{\rm d}_{\rm SV}$ (±3 mN/m)	γ_{SV} (±6 mN/m)
Glass	42 [35]	21 [29]	63 [64]
Silane coated glass	8 [1]	17[21]	25 [22]
Acrylic	20 [16]	12 [18]	41 [34]
Plasma acrylic	37 [50]	15 [13]	52 [63]

Overall, the measured dispersive and polar components of solid surface energy agreed reasonably well with values reported in the literature. The glass substrate has a relatively high surface energy of 63 ± 6 mN/m, which agrees with the value (64 mN/m) reported by Mader-Arndt *et al.* (2014). The difference in the polar component between experimental and literature values may come from the use of the glass slide without further purification steps. A cleaning step could increase the hydrophilicity of the glass.

The substrates differed primarily in the polar term. The dispersive term is linked to the material density. Surfaces that contained hydroxyl groups can be silanized via the formation of a covalent -Si - O - Si- bond between the hydroxyl groups and the alkoxy group of the silane. Silanization is known to make the glass surface more hydrophobic (Van Gestel, He and Darhuber, 2020), which is seen from the decrease of the glass polar surface energy term from 42 to 8 mN/m. Plasma treatment is commonly used to clean surfaces and increase surface energy: plasma acrylics showed an increase in the polar component of the surface energy from 20 to 37 mN/m. Darain, Wahab and Tjin (2012) attributed the increase of surface hydrophilicity to the increase in oxygen-containing groups on the acrylic surface after plasma treatment.

The difference in surface energy between the silane coating and glass or plasma acrylic is about 38 and 27 mN/m, respectively. This is expected to result in different wettability behaviour when the oil-aqueous TPCL moves across a silane-coated substrate.

5.1.5 Static apparent contact angles

Static contact angle measurements of the working fluids on the four different substrates were performed using the methodology reported in 3.2.4. The notations of the contact angles were introduced in Chapter 2 (Figure 2.18). The average apparent contact angles are summarised in Table 5.3.

Oil and water both had high affinity with the glass, with their contact angle being less than 10°. The contact angle values of water drops on the four substrates agreed with those in the literature. The silane coated substrate was oleophilic and hydrophobic: oil had a higher affinity than water, with its contact angle on silane being 69°. No directly comparable values were found in the literature, but Sharma *et al.* (2019) reported a contact of angle of 7° for a drop of SiOil on octadecyltrichlorosilane coating. This value is lower than the one obtained with trichloro(1H,1H,2H,2H-perfluorooctyl)silane coating, which could be due to the fluorinated groups showing higher lipophobicity than silane with only hydrocarbons groups (Dalvi and Rossky, 2010). The wettability of the oil on both glass and plasma acrylic slides was comparable, but water preferred to wet the glass over plasma acrylic. This was consistent with the glass slides having a higher polar component than plasma acrylic.

Table 5.3: Measured contact angles (±3°) of aqueous drops on different solid substrates in (i) air or (ii) immersed in B1 oil. O – B1 oil, W – deionised water, L – Saline, T – 1wt.% TX-100 in saline. Values in square brackets are reported by Fawcett, Williams and Wong, (1994), Mader-Arndt *et al.* (2014); Yu *et al.* (2015), Sharma *et al.* (2019) and Rubowitz *et al.* (2020). Notation explained in Figure 2.18.

Substrate	θ ₀ (°)	$oldsymbol{ heta}_{\mathrm{W}}$ (°)	$\boldsymbol{ heta}_{\mathrm{L}}\left(^{\circ} ight)$	$\boldsymbol{ heta}_{\mathrm{T}}\left(^{\circ} ight)$	θ _{W0} (°)	$ heta_{L0}$ (°)	θ _{T0} (°)
Glass slide	9.3 [7]	4.1 [5]	4	5	48 [51]	51	17°
Silane coated glass	69	105 [107]	109	52	141	145	70
Acrylic	12	68 [75]	71	22	119	117	69
Plasma acrylic	12	38 [40]	40	8.7	71	77	8.2 [6.4]

5.2 Contact printing of silane feature on substrate

The addition of features with controlled dimensions to the solid substrate was investigated to assess the effect of chemical and topographical heterogeneities on TPCL motion.

5.2.1 Polydimethylsiloxane stamp preparation

The fabrication of polymethylsiloxane (PDMS) stamps consists of creating a master and casting the PDMS polymer solution on the master to produce a negative replica of the master. The master was fabricated by laser machining dots and lines on a polycarbonate block ($400 \times 10 \times 5$ mm) by Laser Micromachining Limited, UK. Photographs of a line and dots features on the polycarbonate block are shown in Figure 5.5(a,i)&(b,i). The polydimethylsiloxane polymer solution (Sylgard 184, Dow Corning, US) was prepared by mixing 1:10 weight ratio of curing agent to silicone elastomer base, followed by casting onto the polycarbonate master and curing for 6 hours at 50°C. The removal of the PDMS structure from the master gives the PDMS stamp with the associated feature. Figure 5.5(b,ii) shows a schematic representation of the PDMS stamp with dot features.



Figure 5.5: Optical microscope images (plan view) of features on the polycarbonate master (a,i) Line B and (b,i) Dot 7. Schematic representations of (a,ii) a line feature on a polycarbonate block, (b,ii) a cured PDMS stamp with dot features with the blue arrow indicating the orientation. Fabrication sequence: (c,i) silane solution pipetted onto the features of the PDMS stamp, (c,ii) contact printing of silane features using a PDMS stamp, (c,iii) silane coated substrate left to dry. (d) Plan schematics of solid substrate prior and after contact printing.

5.2.2 Contact printing and characterisation

Prior to printing features on the solid surface, the substrate slides were dusted using nitrogen gas, and 4 μ L of 1% v/v trichloro(1H,1H,2H,2H-perfluorooctyl)silane in isopropanol was spread across the feature on the PDMS stamp using a micropipette.

The silane solution was left to dry on the stamp for at least 5 min. The inked stamp was then brought into contact with the substrate for 10 s (Figure 5.5(c)). The contact printed slide must be handled carefully to avoid distortion of the features. The slides were left to dry for at least 10 min before being used in an experiment. Figure 5.5(d) shows a schematic representation of the substrate prior and after contact printing.

The feature dimensions are summarised in Table 5.4. Scanning electron microscopy images obtained by Takano *et al.* (2006) showed topographical features on the retina with estimated widths of 10 microns and lengths ranging from 10 to 100 microns (see Figure 2.17). The line and dot feature dimensions were selected to reflect these retinal topographical features.

Labels	Length mm	Width mm	Depth mm	Dot-Dot distance mm
Line A	30	0.018	0.013	-
Line B	30	0.03	0.026	-
Line C	30	0.05	0.053	-
Line D	30	0.1	0.1	-
Dot 3	-	0.027	0.027	0.5
Dot 4	-	0.027	0.027	1
Dot 5	-	0.05	0.054	0.5
Dot 6	-	0.05	0.054	1
Dot 7	-	0.1	0.1	0.5
Dot 8	-	0.1	0.1	1

Table 5.4: Line and dot feature dimensions

To assess the quality of the contact printing, the silane solution was mixed with 5 mg/mL fluorescein sodium salt (Sigma-Aldrich, peak excitation at 494 nm and peak emission at 512 nm) and the feature-printed slides were observed under a fluorescence microscope (Leika, UK). Figure 5.6 shows that the patterns were successfully printed on the solid substrate with the correct size.



Figure 5.6: Fluorescent microscopic images of (a) Dot 5 and (b) Line D

5.3 Three-phase contact line motion

The experiments described in this section investigated the motion of the TPCL on two different solid substrates, glass and plasma acrylic. Some experiments used silane-printed substrates as an approximation to the topographical features present on the retinal surface. All the tests were conducted at room temperature.

5.3.1 Static meniscus as starting position

The solid substrate was clamped onto the Texture Analyser, a programmable forcedisplacement probe (TA.XTplusC, UK) and slowly lowered into a rectangular Perspex box (dimension 78 × 54 × 75 mm) pre-filled with the SiOil and saline solutions. Figure 5.7 shows a photograph and schematic of the Texture Analyser set-up. The substrate was held motionless in the centre of the box to establish a static meniscus as shown in Figure 5.8(a). The box was tilted slightly so that the liquid interface did not form a meniscus on the wall through which the camera monitored the substrate (Figure 5.7(c)). When using silane-printed slides, the features were located at a distance $z_{\rm f}$ above the equilibrium TPCL (Figure 5.8(b&c)). The static meniscus was always established first before subsequent motion sequences. Figure 5.9 shows a close-up view of the TPCL and the meniscus.



Figure 5.7: (a) Photograph and (b) schematic representation of the Texture Analyser set-up.
(c) Schematic of the tilted box so that the wall meniscus is flat at A and raised at A'. L1 – SiOil, L2 – Aqueous solution, U – substrate velocity.



Figure 5.8: (a) Photograph and (b) schematic representation of the static meniscus. A vertical solid slide is positioned through the interface between the oil and aqueous solutions. The orange line indicates the silane feature on the substrate. (c) Side view of the meniscus with z_{eq} the height rise, θ_e the static equilibrium contact angle, and z_f the initial position of the printed features (represented in orange).



Figure 5.9: (a) Front and (b) side view of the static meniscus between B1 oil and saline on glass

The rise of the static meniscus, z_{eq} , depended on L_c and θ_e , the static equilibrium contact angle defined in the aqueous phase (see Eqn. 2.23). The values of these parameters for the B1 oil-aqueous system on glass and plasma substrates are summarised in Table 5.5. The calculated meniscus rise was in the range of 2 to 6 mm and the values agreed with the experimental observation.

Once the static meniscus was established, the slide was moved the desired distance in the vertical direction at the required speed, set on the Texture Analyser software. The maximum speed of the device was 40 mm/s. This value is lower than the average wall speed achievable in the RBF (130 mm/s, for R = 12 mm and $\Omega_{\text{max}} = 600^{\circ}/\text{s}$). The Texture Analyser was thus only able to achieve a third of the speed that can be encountered in the eye.

For all the tests in this section, the starting position of the substrate was similar, and a fresh new slide (printed or unprinted) was employed for each experiment.

		Glass		Plasma Acrylic	
Solution	L _c (mm)	θ _e (°)	z _{eq} (mm)	θ _e (°)	z _{eq} (mm)
Saline	9.1	50	6	77	2
1 wt.% TX-100 in saline	3.5	17	4	10	4

Table 5.5: Measured θ_e and calculated L_c and z_{eq} for the B1 oil/aqueous system on two different substrates

5.3.2 Fluid entrainment on bare substrate

As described in section 2.1.2.4, the liquid entrainment transition corresponds to the change of a liquid from partially wetting to fully wetting on a substrate. To characterise the dynamic wetting transition for the oil - aqueous solution on a bare substrate, the experiment consists of finding the critical speed of the slide, U_c , at which the TPCL stays attached at its initial position on the slide when the slide is moving down, and a film of oil is entrained (Figure 5.1(c)). The substrate was lowered into the bath of oil and aqueous solutions at a constant speed, ranging from 0.01 to 15 mm/s, until the bottom of the slide reached the base of the bath. The position of the TPCL was recorded at 10 fps during this plunging stage. The displacement of the contact line

was extracted from the video using ImageJ and the instantaneous speed calculated. This speed was compared to the slide speed, and if the two speeds were the same, then the oil is entrained and the value was recorded as U_c and compared to the prediction of the Cox model (section 2.1.2.3, eqn 2.20).

5.3.3 Restoration stage

From the static meniscus position, the substrate was moved 5 or 10 mm downwards into the bath at a constant velocity of 1, 5, 10 or 40 mm/s. The position of the TPCL was recorded from images taken with a Basler camera at 10 fps during the motion of the substrate and after the substrate stopped moving. Figure 5.10 gives an example of the position of the TPCL over time: (i) in the first stage, the TPCL moves downwards at steady speed – in this case, at the speed of the slide; (ii) in the restoration stage, the TPCL rises, the speed changing with time (and *z*, dependence on *z* discussed later); (iii) in the final stage, the TPCL stabilises at z_{eq} . In the plot, the distance is scaled by z_{eq} for the system.



Figure 5.10: Example of contact line displacement during forcing and restoration stages. Inset shows the displacement of the TPCL during the first stage of the slide descending. Blue dotted line shows the behaviour expected at the slide speed, 40 mm/s. Label C_i indicates where the slide has travelled i mm. Conditions: glass slide, B1 oil/saline system, $z_{eg} = 6$ mm

The velocity of the TPCL, U_{TPCL} , was estimated from the gradient of the displacementtime curve by differentiation. The variation of U_{TPCL} with z is discussed in Chapter 6.

5.3.4 Cyclic motion

The Texture Analyser was also programmed to run cycles of controlled vertical displacement at selected speed and latency time. The periodic cyclic motion is represented in Figure 5.11. The latency time was set at the average for a saccade latency: $L_s = 0.2 \text{ s}$. In some experiments, the cyclic motion was preceded by a downward motion step, of a set distance, at 40 mm/s. This allowed the TPCL position to start from a non-equilibrium position, *i.e.* $0 < z(t = 0) < z_{eq}$. The cyclic motion of the vertical substrate provided a first approximation to the saccadic motion of the eye wall. A digital camera recorded the position of the TPCL at 10 fps during the cyclic motion.



Figure 5.11: Schematic representation of a displacement motion set by the Texture Analyser. Zone A is a downward displacement step and zone B the periodic cycle.

Figure 5.12 shows the TPCL motion observed for two different initial positions. In Figure 5.12(a), starting from the static meniscus position ($z = z_{eq}$), the substrate was moved at 5 mm/s. The liquid was dragged by the substrate, the TPCL moved in phase with the slide, and the highest point of the TPCL did not change between cycles. Similar results were observed for higher speeds 10 and 40 mm/s (not plotted here). If the eye saccadic motion was always the same speed, the TPCL would move with the substrate at the average wall speed achievable in the eye. The saccadic motion varied in amplitude, angular velocity and latency time, which would give rise to different starting position of the liquid meniscus.

In Figure 5.12(b), starting from a non-equilibrium position ($z < z_{eq}$), the TPCL moved relative to the plate and reached the equilibrium position after five cycles. This was attributed to the upwards hydrostatic force (buoyancy) exerted by the aqueous phase on the interface. The downward velocity of the TPCL in each cycle was – 5 mm/s in both plots. Likewise, the upward velocity was + 5 mm/s. This indicated that the relative motion of the TPCL occurred during the latency period. Over 5 cycles, there were approximately 10 latency periods, or 2s of motion. This suggested that the TPCL travelled 0.35 z_{eq} in 2s, at an average velocity of 1.9 mm/s.

Increasing the substrate velocity did not change the dynamics of the restoration stage (see Figure 5.13). In both 10 mm/s and 40 mm/s tests, the TPCL reached its equilibrium height after about 5 cycles. Restoration occurred continuously and the timescale depended mainly on the initial position of the TPCL.

The eye saccadic motion is not entirely periodic: the displacement can change from one saccadic pulse to another, all of which could lead to different starting positions of the TPCL. The non-equilibrium starting position was investigated to approximate the eye conditions and to study the motion of TPCL when moving across a feature at some natural frequency – in this case where U is driven by buoyancy.



Figure 5.12: Examples of TPCL position (blue circles) over 5 cycles. Test conditions: U = 5 mm/s, 10 mm displacement, B1 oil – saline, glass, initial TPCL position at (a) $z = z_{eq} = 6 \text{ mm}$) and (b) $z = 0.65 z_{eq}$. Red dashed lines idicate the trajectory of a point at the substrate wall. Blue dashed lines link the peaks and troughs of each cycle. Grey shaded bands show latency periods.



Figure 5.13: Effect of substrate velocity *U* on TPCL position over several cycles. Test conditions: 10 mm displacement, B1 oil – saline, glass, initial TPCL position $z = 0.65 z_{eq}$ (a) 10 mm/s and (b) 40 mm/s. Blue dashed lines link the peaks and troughs of each cycle.

5.3.5 Oil droplet formation

The feature width, w, the oil viscosity and the substrate properties were varied to investigate liquid entrainment over an individual feature. The substrate was either dipped once at constant speed U or moved in a cyclic motion described in the previous section. The motion of the TPCL across the feature was recorded. All experiments were repeated three times.

Figure 5.14 shows an example where the TPCL moved across a line of dots; as it retreated it was pinned to the dots, then forming rivulet, subsequently leaving oil droplets on the pinning sites. Droplet diameters and spacing were extracted from the video using ImageJ, and the average values calculated for all the droplets formed were compared to the feature width.



Figure 5.14: Photographs showing (a) pinning of the TPCL (TX-100/B1 oil) over dot features printed on a glass slide (Dot 8, indicated by the yellow dotted lines); (b) formation of rivulets, then droplets at pinning sites (droplets are indicated by yellow arrows). Substrate motion: single dip and buoyant rise, U = 5 mm/s, $z_f = 4 \text{ mm}$. Scale bar = 1 mm.

In experiments with feature-printed plasma acrylic, the silane film detached from the plasma acrylic when plunged into a layer of TX-100 solution. This indicated that the bonding between the plasma acrylic and the silane was not strong enough and the affinity between TX-100 solution and the substrate was higher than that between the silane and substrate. As a result, only the experiments with feature-printed plasma acrylic plunged in a bath of saline were analysed.

5.3.6 Droplets under shearing flow

Two different experiments were conducted to investigate the conditions giving rise to oil droplet detachment.

First, using the Texture Analyser setup, the feature-printed slides were held in the liquid bath after formation of oil droplets on the silane features. The slides were then moved in the vertical plane with a cyclic motion sequence (with the first displacement downwards) at U = 40 mm/s, 10 mm displacement, and L = 0.2 s. The maximum

speed (40 mm/s) allowed by the Texture Analyser was higher than the critical speed of liquid entrainment, U_c .

The second test consisted of investigating the behaviour of oil droplets on printed features under saccadic motion generated by the stepper motor device described in Chapter 3. Figure 5.15 shows a schematic representation of the experiment where a laboratory test tube coated with vertical line feature was used as the solid substrate. The stepper motor allowed higher substrate speeds to be studied than Texture Analyser. When the test tube was vertical, the shear flow induced in the aqueous phase by the stepper motor motion was orthogonal to the vertical line feature. Inclination of the tube at an angle β (see Figure 5.15(c)) allowed the shear flow to be oriented differently towards the line feature.

Test tubes (13 mm diameter) were pre-washed in a dishwasher with acid wash, followed by sonication in deionised water at 50°C for 30 minutes, then dried overnight. A vertical line of silane features was contact printed on the external surface of the test tube using the same procedure and stamps as in section 5.2. The test tube was filled with mineral oil to match the refractive index of the glass tube, and then lowered slowly into a stratified bath of oil and aqueous. Once all the silane features had entered the aqueous phase and oil droplets formed, the tube was rotated following a saccadic motion sequence with the features always submerged in the aqueous phase. The experiments were recorded with a Basler camera at 50 fps. The saccade parameters were varied with 5° $\leq A \leq 30^{\circ}$, 200 $\leq \Omega_{max} \leq 800^{\circ}/s$, and L = 0.2 s, corresponding to linear speeds ranging from 2.3 to 91 mm/s (with R = 6.5 mm).



Figure 5.15: Schematic representation of (a) a glass test tube coated with a vertical line feature, (b) the test tube introduced in a oil/aqueous bath, with the line feature completely immersed in the aqueous phase, with droplets generated by the immersion step, (c) the test tube inclined at angle β , where $\beta \leq 15^{\circ}$.

Chapter 6 Contact line instabilities

The surface emulsification hypothesis postulates:

- (i) the retinal surface contains topographical or chemical features that act as pinning sites for the adhesion of the SiOil-aqueous TPCL;
- (ii) when moving across the features, the TPCL could either form a liquid film on the feature or a rivulet originating from the feature acting as a pinning point. The instability of the rivulet gives rise to oil strands or primary droplets on the features and surrounding substrate, and possible satellite droplets in the aqueous phase (Figure 5.2);
- (iii) the pinned oil may subsequently be subjected to a shearing flow from the aqueous phase, leading to deformation followed by partial or complete detachment from the surface. This is similar to the mechanism described in previous studies on the flow-induced motion of silicone oil droplets from a solid substrate (Seevaratna*m et al.*, 2010; Lu *et al.*, 2019).

This chapter presents the experimental results obtained with the moving contact line experiments on two solid substrates differing in their wetting affinity (glass and plasma acrylic). The stability of the TPCL was investigated when moving across a smooth and homogeneous surface or being dragged by silane features printed on a smooth surface. The stability of the four-phase contact line (arising at the interface between oil, aqueous, substrate and silane) was assessed under different motion sequences in order to investigate the conditions for the onset of motion of a pinned oil droplet. The effect of different feature widths, surface properties, substrate velocity and liquid properties on the stability of the contact line are discussed.

6.1 Contact line velocity

6.1.1 Entrainment speed on bare substrate

The contact line motion was first characterised on bare solid substrates. The critical speed for liquid film entrainment was characterised using a vertical slide moving in a stratified bath of SiOil and aqueous. Figure 6.1 shows a representation of the entrainment of an oil film in the aqueous phase on the solid substrate. The critical speed of oil entrainment U_c corresponds to the speed of the plate at and above which

the oil completely wets the substrate and forms a film on the surface. The film entrainment is characterised by a dimensionless group, the critical capillary number, defined:

$$Ca_{\rm c}({\rm oil}) = \frac{\mu_{\rm aqueous}U_{\rm c}}{\gamma}$$
 (6.1)

with γ the interfacial tension between the oil and aqueous phases.



Figure 6.1: Schematic representation of (a) a static meniscus with fluid 1 the SiOil and fluid 2 the aqueous solution, (b) vertical plate plunging at a speed $U \ge U_c$, leading to oil film entrainment.

Assuming the vertical plate is smooth and homogeneous, the Cox model (section 2.1.2.3) can be applied to calculate the critical capillary number for different viscosity ratios and contact angles. Figure 6.2(a) shows the dependence of $Ca_c(\text{oil})$ on the viscosity ratio, $\lambda = \mu_{\text{oil}}/\mu_{\text{aqueous}}$, and the contact angle, θ_e , calculated from equation (2.19). By increasing λ , Ca_c decreases: the higher the viscosity ratio, the lower the substrate velocity required to entrain a film of the more viscous liquid in the less viscous one. Medical SiOils and eye saline solutions feature viscosity ratios ranging from 1000 to 5000. The retina is hydrophilic (Rubowitz *et al.*, 2020): θ_e , defined in the aqueous phase, is expected to be smaller than $\pi/2$. Considering the case where $\theta_e = 0.87$ (corresponding to the SiOil-saline system in the eye chamber), the difference in Ca_c values between the two limiting λ values was of order of 5 (1.8×10^{-4} and 3.6×10^{-5}).

Figure 6.2(b) plots Ca_c against λ for three values of θ_e . The contact angles $\theta_e = 0.3$ and $\theta_e = 0.83$ correspond to the values measured on the glass substrate with the B1 oil/1 wt.% TX-100 in saline and the B1 oil/saline systems, respectively. $\theta_e = 3$ is chosen to describe the case of a hybrophobic but oleophilic substrate. Ca_c decreases for a given θ_e when λ increases. Adding surfactant reduces the contact angle, increasing Ca_c for a given value of λ . In terms of surgical procedure, this suggests that the presence of natural surfactants makes the TPCL more stable.

The critical speed was calculated using equation (6.1) and the results are plotted in Figure 6.3 for the oil and aqueous entrainment cases at different viscosity ratios. Increasing the oil viscosity decreased U_c . The values for aqueous entrainment were of the same order of magnitude as the oils, the main differences being that the slide was moving upwards and there is a wide range of contact angles (about 0 - 2 rad) where U_c varies little. The liquid entrainment experiments were only conducted for the case of an oil film being entrained in the aqueous phase, since only oil droplets were observed in clinical studies. The data points were plotted on Figure 6.3 and show reasonable agreement with the theoretical values.



Figure 6.2: Critical capillary number for oil (O) entrainment in the aqueous phase (W) at (a) different viscosity ratios, λ , (b) contact angle θ_e (in rad), evaluated using Eqn. (2.19). Parameter $\epsilon = 10^{-3}$. Insets in (a) show the interface shape and contact angle between oil and aqueous on the solid substrate.



Figure 6.3: Predicted critical liquid entrainment speed of (a-c) oil by the aqeuous solution, (d-f) aqueous by the oil. Solid line represents the theoretical values from the Cox model (eqn 2.19). Data points are obtained with the liquids and substrates used in this Chapter.

The liquid entrainment experiments were not conducted on silane-coated substrates, but the critical speed was calculated using the Cox model (Eqn. (6.1)) for two contact angles, $\theta_e = 1.22$ and $\theta_e = 2.53$, corresponding to the values measured on the silane-coated glass with the B1 oil/1wt.% TX-100 in saline and the B1 oil/saline systems,

respectively. The values are summarized in Table 6.1 and show that lower speeds are required to entrain oil in aqueous on a silane surface, about 10 to 100 times lower than on plasma acrylic and glass substrates.

	U _c (n	nm/s)
	$\lambda = 1000$	$\lambda = 5000$
$\theta_e = 1.22$	0.073	0.073
$\theta_{\rm e} = 2.53$	0.083	0.017

Table 6.1: Predicted critical liquid entrainment speed on silane-coated glass for two different viscosity ratios and contact angles.

The plate plunging experiments were difficult to perform at displacement distances larger than the height of the liquid bath in the Texture Analyser set-up. In the range of accessible distances (0 - 30 mm) and speeds (0 – 40 mm/s), the TPCL did not adopt a triangular configuration or sawtooth patterns (Figure 2.8, reported by Blake and Ruschak, 1979). Neither instability of the TPCL nor direct droplet formation was observed in tests with bare (uniform) substrates.

The typical wall velocity of the retina wall (R = 12 mm) under saccadic motion ($\Omega_{max} = 600^{\circ}/s$) is of the order of 0.14 m/s, which is larger than U_c for the 1 Pa s and 5 Pa s cases. The eye saccade amplitude ranges from 1° - 50°. If the eye wall displacement was assumed to be similar to the arc length of the eye sphere: *i.e.* RA = 0.2 - 10.5 mm, these distances are accessible by the Texture Analyser, but not the speeds. The set-up needs to be changed in order to investigate higher speeds: one possible arrangement would be to use a lever mechanism on a strain frame to drive the motion, and the pivot position can then set the gain. This could be worth investigating as the thin film at higher speeds could give rise to rivulets and possibly droplets.

Blake and Ruschak (1979) investigated the liquid entrainment of a glycerol/water mixture (viscosity 0.1 Pa s) in air using a dip-coating system, and reported a liquid entrainment speed of 55 mm/s, with liquid drops starting to be entrained in the air at a speed of 80 mm/s. They also noted a higher speed being required for air bubble entrainment (250 mm/s) than air entrainment (194 mm/s) in the glycerol/water mixture. This indicated that it would be worth investigating silicone oil entrainment in aqueous

at higher speeds. The dragging of the smooth substrate at speeds much higher than U_c was not investigated here. The other naturally occurring motion is that of the restoration stage (equivalent to the latency period of a saccade), where buoyancy drives the motion of the TPCL.

6.1.2 Contact line speed during the restoration stage

In the restoration stage of the plate plunging experiment (Figure 5.10), the TPCL returned to the equilibrium position after the solid substrate stopped moving. The restoration stage gave some insight into how fast buoyancy forces can cause the TPCL to move following a rapid displacement, e.g. a saccadic pulse.

Figure 6.5 shows an example of the velocity of the TPCL, U_{TPCL} , plotted against its relative position, $z_{\text{eq}} - z$, during the restoration stage following a plunge of 5 mm displacement at 10 mm/s. In region II, where $(z_{\text{eq}} - z) > 1 \text{ mm}$, U_{TPCL} is linearly dependent on the displacement (and net buoyancy force).



Figure 6.4: Effect of displacement from equilibrium position on the instantaneous velocity of the TPCL, U_{TPCL} , during the restoration stage. Test condition: substrate speed 10 mm/s, displacement 5 mm, B1 oil/saline, glass substrate. Construction line in region II shows the fit to the data to obtain gradient *m*.

Similar experiments were performed for a second displacement distance (10 mm) and four different values of the plunge velocity U (1, 5, 10 and 40 mm/s). The results for bare glass slides and plasma acrylics are presented in Figure 6.5. All the results show

a linear relationship between the displacement and U_{TPCL} for $(z_{\text{eq}} - z) > 1 \text{ mm}$: the velocity of the contact line increased with the buoyancy driving force.



Figure 6.5: Effect of displacement from equilibrium position on the instantaneous velocity of the TPCL, U_{TPCL}, during the restoration stage: (a) bare glass slides, (b) bare plasma acrylics. Open symbols: oil-saline system / Solid symbols: oil-surfactant system (1 wt.% TX-100 in saline). Construction line shows fit of 0.01 Pas oil/TX-100 data to obtain gradient *m*.

The contact line motion is driven by buoyancy forces per unit length of contact line, $F_{\rm B}$, and capillary forces per unit length of contact line, $F_{\rm C}$, and resisted by the drag force arising from viscous dissipation in the liquid, $F_{\rm D}$. Assuming that dissipation only occurs near the contact line, a force balance per unit length at the contact line gives:

$$F_{\rm D} = F_{\rm B} + F_{\rm C} \tag{6.2}$$

The capillary force is given by $F_{\rm C} = \gamma(\cos \theta_{\rm eq} - \cos \theta)$, and depends on the difference between equilibrium and instantaneous contact angles. The viscous dissipation term, $F_{\rm D} = 3\mu_{\rm oil}U_{\rm TPCL}L^*/\theta$, is derived from the motion of a simple wedge advancing on a surface (Huh and Scriven, 1971; De Gennes, 1985; Thampi *et al.*, 2016). Here $L^* = L_{\rm c}/\lambda_{\rm m}$, where $\lambda_{\rm m}$ is a microscopic length defined in section 2.1.2.3. The buoyancy force is related to the density difference and displacement, given by $\Delta \rho g(z - z_{\rm eq})$. This will act on an area per unit length which is not known readily but is expected to be related to $L_{\rm c}$. For the purpose of this analysis, let this area per unit length be $c_1L_{\rm c}$, where c_1 is a dimensionless function which is expected to depend on θ (related to the shape of the meniscus). Equation (6.2) can then be written as:

$$\frac{3\mu_{\rm oil}U_{\rm TPCL}L^*}{\theta} = \Delta\rho g c_1 L_{\rm c} (z - z_{\rm eq}) + \gamma (\cos\theta_{\rm eq} - \cos\theta)$$
(6.3)

$$U_{\rm TPCL} = \frac{\gamma \theta c_1}{3\mu_{\rm oil}L^*} \left[\frac{(z - z_{\rm eq})}{L_{\rm c}} + \frac{(\cos \theta_{\rm eq} - \cos \theta)}{c_1} \right]$$
(6.4)

Figure 6.5 shows that the velocity is dominated by buoyancy at large displacement values, and this is reflected in eqn. (6.4), where the second term on the right-hand side $(\cos \theta_{eq} - \cos \theta)$ lies between -1 and 1, and the first term becomes important at large values of *z*.

Figure 6.6 plots the values of *m*, obtained from Figure 6.5, against viscosity ratio, λ . The gradient of the linear dependency increases with decreasing oil viscosity. The low viscosity oil also restored faster than the higher viscosity oils, for both substrates. Equation (6.4) indicates that *m* is inversely to μ_{oil} , thus inversely proportional to λ : this agrees reasonably with Figure 6.6. The presence of surfactant reduced *m* by a factor of about 2 in the low viscosity oils, and only a little for the high viscosity oils (Figure 6.5). The gradient of each plot in Figure 6.6 was measured and the results indicated that *m* was proportional to $\gamma^{0.5}$. The restoration speed was also affected by the substrate material in the least viscous oil (0.01 Pa s): *m* is lower than 1 on plasma acrylics, as shown in Figure 6.6. Oil and aqueous wets plasma acrylic than glass (Table 5.3). The relationship of U_{TPCL} with TPCA is not linear in eqn. (6.4) and requires further investigation, such as finding the expression c_1 .



Figure 6.6: Measured gradient, *m*, against viscosity ratio $\lambda = \mu_{oil}/\mu_{aqueous}$ for data sets in Figure 6.5. G – glass, P – plasma acrylic

6.2 Droplet formation

In all the tests performed with bare substrates in the Texture Analyser set-up, no droplets were formed on the solid surface. It was noted above that there is a need to investigate higher velocities to explore the stability of the entrained thin liquid film.

This section focuses on the TPCL pinning and moving across silane features printed on solid substrates, investigating the effect of surface energies, feature dimensions and orientation on the behaviour of moving contact line. The silane features are either lines of dots or continuous lines. There are two motions of interest:

- (i) The TPCL has a relative motion to the substrate when the substrate is moving at a speed $U < U_c$ (Figure 6.7)
- (ii) After a forcing stage, the TPCL restores to the equilibrium position when the substrate is immobile (Figure 6.8).



Figure 6.7: Schematic representations of TPCL motion across silane features (black vertical line) printed on the substrate (grey rectangle). Yellow – SiOil, blue – aqueous solution, red line – TPCL, red segments – SiOil strands. (a) z_{eq} is the meniscus height rise; (b) the TPCL moves relative to the substrate and reaches a steady state position, z_{ss} . The TPCL is dragged by the line feature and formed oil strands on the feature; (c)The TPCL is dragged by the substrate at velocity *U* higher than U_c , the critical velocity. The TPCL restores after the substrate stopped moving. The dewetting over the feature give rise to oil strand formation.

In Figure 6.7, the feature is a vertical, continuous line. At substrate speed $U < U_c$, the TPCL moves relative to the substrate and has different affinity with the bare substrate and the silane feature. The oil wets the feature more slowly and the TPCL is dragged downwards, forming an oil thread at the pinning point: the liquid thread then subsequently breaks into shorter oil strands (Figure 6.7(b)). At substrate speed $U \ge U_c$, the TPCL moves with the substrate downwards, and when the slide stops moving, the TPCL restores to its equilibrium position. During the restoration stage, the TPCL dewets the bare substrate and the line feature at different speeds, leaving oil threads on the feature that can break into shorter oil strands (Figure 6.7(c)).


Figure 6.8: Schematic representations of TPCL motion across silane features (black horizontal line) printed on the substrate (grey rectangle). Yellow – SiOil, blue – aqueous solution, red line – TPCL, red segments/circles – SiOil strands/drops. (a) z_{eq} is the meniscus height rise; (b) the TPCL moves relative to the substrate and reaches a steady state position, z_{ss} . The TPCL is dragged by the line feature and formed oil strands on the feature; (c)The TPCL is dragged by the substrate at velocity U higher than U_c , the critical velocity. The TPCL restores after the substrate stopped moving. The dewetting over the feature gives rise to oil strands, primary and secondary drop formation.

In Figure 6.8, the feature is a horizontal, continuous line. Whether the TPCL dewets the feature at the forcing speed of the substrate (Figure 6.8(b)) or at natural restoration speed (Figure 6.8(c)), the TPCL is first stopped at the horizontal line and then dewets from the line ends, leaving oil strands on the feature. Before the TPCL fully detaches from the feature, it forms a liquid bridge between the horizontal line and the bulk liquid (Figure 6.8 (b,ii)&(c,ii)). The bridge can break up into a primary drop on the feature and satellite drops on the substrate (Figure 6.8 (b,iii-iv)&(c,iii-iv)). Details of the mechanisms will be developed in this section.

This section investigates the conditions under which TPCL pins onto the features and leaves oil strands, and if these pinned oils detach from the surface during the wall motion. The effect of different feature dimensions, substrate velocities, oil viscosities and interfacial tensions were investigated.

6.2.1 Dot features

The motion of the TPCL (one step plunge) across the dotted features gave rise to rivulets followed by primary oil drop formation on each dot feature (Figure 5.2(d) & Figure 5.14). In all the experiments with 1 Pa s oil, the rivulet did not generate satellite drops.

Figure 6.9 shows the diameter of the oil droplets on the dot feature as a function of the dot feature width w. An increase in w resulted in larger oil droplets. A wider feature led to higher surface contact area between the TPCL and the silane coating, with more liquid being potentially pinned to the surface. The D_{oil}/w ratio was constant and equal to 1 for the B1 oil-saline systems. This was expected from the TPCA (35°) of an oil droplet on silane immersed in saline as shown in Figure 6.10(b).



Figure 6.9: Effect of dot width on oil droplet diameter. Test conditions: U = 1 mm/s, 10 mm displacement, $z_{eq} = 5 \text{ mm}$, glass substrate, $U_c(\text{oil}) = 1.5 \pm 0.3 \text{ mm/s}$. Liquids were B1 oil and aqueous (Aq): (a) saline, (b) 1 wt.% TX-100 in saline. Error bars show the standard deviations.

Figure 6.9(b) shows the case with 1 wt.% TX-100, where the D_{oil}/w ratio was again constant, at 1.37. This agreed with the ratio calculated with eqn. (6.5). All the oil droplets which were generated on the silane dots did not detach over time.



Figure 6.10: Schematic representation of (a) an oil droplet pinned to a silane feature of width, *w*, at different contact angles: (b) 35° and (c) 110°.

$$D_{oil} = w(1 + \tan \zeta) \tag{6.5}$$

6.2.2 Line features

6.2.2.1 Effect of line width

The moving contact line experiments with the vertical line feature gave rise to oil thread formation followed by its break-up into shorter oil strands. Figure 6.11 shows an example of the oil strands pinned on the vertical line feature. The width of the pinned oil strands, D_{oil} , increased with the line width in similar fashion to the dotted features (not shown in here). However, the increase in feature width did not affect the oil strand spacing, l_{ss} , (see Figure 6.12).



Figure 6.11: Schematic representation of (a) a solid substrate with a printed vertical line feature (Line D), (b) plunged into a bath of SiOil and saline at U = 3 mm/s, leading to formation of (c) oil strands immersed in saline. (d) Photograph of the experimental results with the oil in white and the substrate in black. Scale bar = 1 mm. D_{oil} is the width of the pinned oil, l_{ss} the spacing between two pinned oil strands and l_{s} the length of the oil strand.



Figure 6.12: Oil segment spacing, l_{SS} , against silane vertical line width. Test condition: U = 3 mm/s, $z_{eq} = 1 \text{ mm}$, glass substrate, B1 oil and saline.

The shape and length of the oil strands depended on the TPCA, IFT, and the substrate speed.

6.2.2.2 Effect of surfactant

The shape of the pinned oil depended on the presence of surfactant. Figure 6.13 shows the pinned oil shapes formed with saline and 1 wt.% TX-100 in saline.



Figure 6.13: (a) Photograph and (b) schematic representation of spherical caps formed on a vertical line feature. Scale bar = 1 mm. D_{oil} is the width of the pinned oil, l_{dd} the spacing between two pinned oil droplets and *w* the line width. Test condition: Line D, glass substrate, U = 3 mm/s, B1 oil and 1 wt.% TX-100 in saline

The presence of surfactant caused the oil threads to break up into spherical caps on the silane feature, almost evenly spaced across the length of the feature (Figure 6.13). In the absence of surfactant, the thread broke into shorter strands (but longer than spherical caps) as shown in Figure 6.11. Adding 1wt.% TX-100 in saline increased the TPCA defined in oil from 35° to 110°, causing the oil diameter to increase from *w* to

1.37w (Figure 6.10(c)). The surfactant also caused the oil strands to minimize their area in contact with the silane feature, leading to the configuration of oil spherical caps instead of short oil strands.

Using the measured solid surface energies and contact angles (section 5.1), the interfacial energies between liquids and substrate can be calculated from Young's equation (2.4). When replacing saline by 1 wt.% TX-100 in saline, the interfacial energy between the aqueous phase and the glass substrate increased from 0.5 to 26.4 mN/m and the interfacial tension between aqueous and oil decreased from 27 to 4.4 mN/m. Both trends increased the contact angle in the oil phase, which is consistent with the TX-100/oil case adopting a more spherical oil shape on the silane feature (Figure 6.10(c)).

6.2.2.3 Effect of substrate speed

The pinned oil strand length, l_s , depended on the speed of the substrate. The slides printed with a vertical line feature were plunged into the oil-aqueous bath at different substrate speeds, and the pinned oil strands were analyzed from images taken from the videos. Experimental results for the B1 oil – saline system are described first.

At substrate speed $U < U_c$, the TPCL moves relative to the substrate as shown in Figure 6.7(b). Due to higher affinity between the oil and the silane, the TPCL was dragged by the line feature. The oil formed a liquid thread on the feature and broke into shorter oil strands pinned on the feature. Figure 6.14 shows some images of the oil strands formed on the vertical feature line. In this example, the strand length, l_s , had an average value of 1.1 \pm 0.9 mm.



Figure 6.14: (a) Image sequences and (b) sketch of oil strands (white segments) forming on a vertical line feature whose start (S) and end (E) points are indicated by the blue dashed lines. Yellow line indicates the location of the TPCL, the white arrow indicates the motion direction of the substrate. Test conditions: substrate speed U = 1 mm/s, $z_{eq} = 1 \text{ mm}$, glass substrate, Line D feature, B1 oil-saline, $U_c = 6 \pm 0.3 \text{ mm/s}$. Scale bar = 1 mm.

Figure 6.15 shows some photographs of the oil strands formed on a vertical line feature at different substrate plunging speed. For speeds lower than U_c , the strand length, l_s , increased with U. Figure 6.16(a) plots l_s against Ca(oil). Above Ca_c , the oil formed a long thread on the line feature: the thread was almost continuous in the frame length (16 mm) of the video. This shows that at lower speed, capillary forces are important, and the surface tension minimises the interfacial area by breaking the oil thread into shorter strands. At higher speed, the inertial forces favour a longer thread/film and oppose the thread deformation (Zhu *et al.*, 2015). The spacing between oil strands, l_{SS} , was also measured and is presented in Figure 6.16(b). The values did not vary noticeably with the substrate speed.



Figure 6.15: Photographs of oil strands/threads formed on silane line feature C at different substrate speeds. White lines are the oil segments. Test conditions: B1 oil-saline, glass slide, $U_c(oil) = 6 \pm 0.3$ mm/s. Scale bar = 1 mm



Figure 6.16: Effect of *Ca*(oil) on oil segment (a) length, (b) spacing. Test conditions: vertical line C, B1 oil-saline, glass slides. The vertical red dashed line indicates $Ca_c(\text{oil}) = (2.7 \pm 0.1) \times 10^{-4}$, the critical condition for liquid entrainement for $\theta_e = 0.83$ rad. l_s and l_{ss} were defined in Figure 6.11

Similar experiments were conducted with B1 oil and 1 wt.% TX-100 in saline. In the presence of surfactant, the pinned rivulet broke into spherical droplets rather than strands at all speeds. No significant change was observed in the droplet size or spacing at different substrate speeds (Figure 6.17). The aqueous phase was saturated with the surfactant (above CMC), so this was unlikely to be due to the surfactant concentration. The surfactant was readily present at the newly formed interfaces and could have controlled the droplet shape and kept the shape at the lower energy configuration.



Figure 6.17: Effect of substrate speed on oil droplet diameter and spacing. Test conditions: vertical line C, B1 oil/1wt. % TX-100, glass slides. The red vertical dashed line indicates $Ca_c = (4.5 \pm 0.9) \times 10^{-4}$, the critical condition for liquid entrainement

6.2.2.4 Effect of substrate material

When using plasma acrylic instead of glass slides, the surface energy of the solid substrate was decreased from 63 to 41 mN/m. Low surface energy materials are less attractive to liquid molecules and more difficult to bond to than higher surface energy ones (Packham, 2003): the use of plasma acrylics allowed the investigation of a lower surface energy material than glass but still presenting a difference in energy from the silane coating (25 mN/m). Pinned oil formation was only analyzed in the oil/saline system because the silane patches detached from the substrate when using TX-100 solution. This indicated that the TX-100 adhered strongly to the silane feature and the acrylic surfaces.

The critical speed of entrainment of B1 oil by saline on acrylic slides was 1.5 ± 0.3 mm/s (Figure 6.3). The experiments were conducted with vertical line-printed plasma acrylics using substrate speeds lower than U_c . At 0.01 mm/s, oil did not attach to the silane feature. For $0.05 \text{ mm/s} < U < U_c$ ($2.2 \times 10^{-6} < Ca < Ca_c$), the oil strand lengths were similar in size to the feature width (Figure 6.18). Around U_c , the strand length was about 0.07 ± 0.02 mm. The strand spacing, l_{SS} , was of the same magnitude as the values on the glass substrate (Figure 6.16(b)), but the strand lengths, l_s , were smaller than the values on the glass substrate in the same *Ca* range (Figure 6.16(a)). This could be attributed to the smaller difference in surface energies between

silane and acrylics than silane and glass. There was no preferential affinity of the oil towards silane, as in the glass case, the TPCL was dragged downwards by the silane but did not form a long thread that subsequently broke into shorter strands: instead it formed shorter strands directly.



Figure 6.18: Average oil strand length, l_s , and spacing, l_{ss} , against Ca(oil). Test conditions: vertical line C, B1 oil-saline, plasma acrylic slides. The vertical red dashed line indicates $Ca_c = (6.2 \pm 1.3) \times 10^{-5}$. l_s and l_{ss} were defined in Figure 6.11

6.2.2.5 Horizontal line features

The orientation of the line feature also affected the TPCL dewetting process. The horizontal line was printed across the whole width of the substrate slide, as shown in Figure 6.8(a). For substrate speeds higher than U_c , the TPCL moved with the substrate in phase (Figure 6.8(c)). When the substrate stopped moving, the TPCL restored to its equilibrium position. The TPCL stopped at the line feature (Figure 6.19(a)), then started to detach from the ends of the line, and moved inwards (Figure 6.19(b)). The dewetting process left an oil thread on the feature. The liquid thread subsequently broke into smaller strands due to capillary effects minimizing the contact area between the oil and silane submerged in the aqueous phase (Figure 6.19(c&f)). The pinned oil strand lengths and spacing on the horizontal line feature followed similar trends and values as the vertical line features, on both substrates.

Before the TPCL completely detached from the line feature, it formed a liquid bridge between the line and the bulk liquid (Figure 6.19(c&d)). This rivulet eventually broke up into a primary drop on the feature and satellite droplets on the substrate vertically above the feature (Figure 6.19(e)). This result is consistent with Van Gestal and coworkers' work on liquid rivulet behaviour on patterned surfaces, with rivulets detaching from the edges of the pattern and forming primary and satellite droplets (Van Gestel, He and Darhuber, 2020).



Figure 6.19: Photographs of TPCL pinning and dewetting from a vertical line D feature (yellow dashed line). White arrows indicate the direction of the dewetting, yellow arrows indicate primary (P) and satellite (S) oil droplets. Test conditions: U = 10 mm/s, 10 mm displacement, $z_{eq} = 2 \text{ mm}$, glass substrate, B1 oil-saline.

In all the experiments with the 1 Pa s oil, the primary and satellite droplets all remained pinned to the substrate surface and did not detach from the surface over time.

6.2.2.6 Effect of oil viscosity

Experiments were also conducted with lower and higher viscosity oils (A0.5 and B5 oils, respectively). The latter did not give reliable and reproducible results due to the TPCL not moving as a uniform front on the feature-printed substrates. The TPCL was pinned to some surface areas away from the feature zone, leading to a change in shape and speed of the TPCL. Despite much effort, these unwanted effects could not

be eliminated. Future experiments should include cleaning and purification of the substrate after feature printing. Thus, only results with A0.5 oils are reported here.

Figure 6.20 shows some photographs of the oil strands formed on the vertical line C feature in the A0.5 oil/saline/glass system. For $U < U_c$, increasing the substrate plunge speed led to longer oil strand lengths (Figure 6.21(a)), which was similar to the B1 oil case. No trend was evident in the segment spacing, l_{SS} , as shown in Figure 6.21(b), but the average value of l_{SS}/w (2.7 ± 1.5 mm) was smaller than the B1 oil case (3.7 ± 1.0 mm). For speeds near and above U_c , the oil rivulet broke into alternate sequences of small droplets and oval-shaped segments (Figure 6.20 (b)). Figure 6.20 shows a photograph of an example of this for U = 20 mm/s: the smaller drops had a diameter smaller than the line width, and the segment was wider. The oval-shaped segments had an average length of $0.13 \pm 0.04 \text{ mm}$ and the droplets a diameter of $0.02 \pm 0.01 \text{ mm}$.



Figure 6.20: (a) Photographs of oil strands (white lines) formed on vertical line feature C at different substrate speeds. (b) Schematic representation of alternate sequences of oil droplet and oval-shaped segment. Test conditions: Line C, glass slide, A0.5 oil-saline, $U_c = 9 \pm 0.3 \text{ mm/s}$.



Figure 6.21: Effect of substrate speed on oil strand length and spacing. Test conditions: vertical line C, A0.5 oil-saline, glass slides. The vertical red dashed line indicates $Ca_c(\text{oil}) = (4.0 \pm 0.9) \times 10^{-4}$

Experiments with surfactant led to the formation of spherical droplets on the vertical line feature. Figure 6.22 shows that the droplet diameters were proportional to the feature width. The $D_{\rm oil}/w$ values lay around 1.37, as calculated earlier for a SiOil/TX-100 system (eqn (6.5), section 6.2.1). The droplet spacing did not vary significantly, with an average value of 0.21 ± 0.05 mm



Figure 6.22: Effect of feature width on oil droplet diameter. Test conditions: A0.5 oil/1wt. % TX-100, glass slides, U = 0.5 mm/s, $Ca_c = (8.9 \pm 1.1) \times 10^{-5}$. Dashed line indicates $D_{\text{oil}}/w = 1.37$ (Figure 6.10(c)).

Experiments were also conducted with the horizontal line feature and SiOil/TX-100/glass system. The main differences between the A0.5 and B1 oil lay in the formation of rivulets and the behaviour of the satellite droplets. With the lower viscosity oil, the liquid film split at different points across the line feature (Figure 6.23(c)): the

liquid bridges narrowed in width and became a series of regular strands that detached from the line, forming primary droplets on the feature and satellite droplets that rose in the aqueous phase due to the density difference (Figure 6.23(d&e)).



Figure 6.23: (a-d) Image sequences of the TPCL dewetting from a horizontal line feature (indicated by the yellow dashed line), forming pinned oil drops on the feature and rivulets. The rivulet breaks into primary (P) and satellite (S) oil drops. (e) Satellite drops (showed by yellow arrows) detach and rise in the aqueous phase. Test conditions: 10 mm downward step at 10 mm/s, $z_f = 1$ mm, glass substrate, Line D feature, A0.5 oil/TX-100, Scale bar = 2 mm.

This was the first observation of formed oil droplets not adhered to the surface following the breakup of a rivulet. The experimental condition of a downward step motion followed by the restoration stage (10 mm downward step at 10 mm/s, $z_f = 1 \text{ mm}$) was repeated on the same feature width and other feature widths. Detached secondary droplets were observed in all these experiments.

This droplet formation mechanism needs further investigation in order to validate the surface emulsification hypothesis. Potential future work could investigate the effect of feature dimensions (width and length), the effect of substrate motion and the effect of surface energies on the formation of detached satellite droplets. It would be also worth studying the generalization of the results with A0.5 oil to higher viscosity oils, since surgical oils often have viscosity higher than or equal to 1 Pa s.

6.3 Droplet detachment

6.3.1 Texture Analyser experiments

In the B1 oil/aqueous/glass substrate case, the slides were left in the liquid bath after the formation of oil strands on the silane feature. The slide was then moved upwards and downwards in a regular periodic cycle to investigate the conditions under which the droplets would detach from the surface, and to see if the findings from Seevaratnam *et al.* (2010) predict the detachment of SiOil droplets (section 5.3.6). However, the pinned oils did not detach from the silane features under the conditions tested (see Table 6.2), not even with the lower viscosity oil nor at the maximum speed achievable by the Texture Analyser (40 mm/s).

Distance (mm)	5, 10
Substrate speed (mm/s)	20, 40
Latency time (ms)	50, 200

This experiment can be considered as an example of a Stokes' problem, which involves a fluid motion driven by the impulsive or oscillating motion of the boundary (Erdogan, 2000). The moving plate shears the fluid and sets it into motion, with the shear penetrating over a distance known as the Stokes boundary layer thickness:

$$\delta_{\text{Stokes}} = \sqrt{(2\nu)/\omega} \tag{6.6}$$

with v the kinematic viscosity of the fluid and $\omega/2\pi$ the frequency of the plate oscillation. In the Texture Analyser experiment, the frequency was equal to 2 Hz for a substrate speed of 20 mm/s. The Stokes boundary layer thicknesses calculated for the oil and aqueous phases were 12 and 0.44 mm, respectively. The penetration depth

in the aqueous phase was larger than the size of the pinned oil drop (10 to 100 μ m). Assuming a Stokes boundary layer thickness of 0.44 mm and a superficial velocity equal to the plate velocity (U = 40 mm/s), the shear rate in the aqueous phase around the pinning feature can be estimated from

$$\dot{\gamma} = \frac{U}{\delta_{\text{Stokes}}(\text{aqueous})}$$
(6.7)

giving a value of 90 s⁻¹.

Seevaratnam and co-workers (2010) investigated the onset of motion of silicone oil droplets (viscosity of 0.92 Pa s) subjected to a laminar shear flow of water in a rectangular channel. The experimental set-up is reproduced in Figure 6.24:





Seevaratnam et al. (2010) defined a dimensionless group, G, using eqn. (2.28):

$$G = \frac{Ca^2}{Re} = \frac{\mu_{\text{water}}{}^3 \overline{U}}{\gamma^2 \rho_{\text{water}} a_{\text{d}}}$$
(2.28)

with \overline{U} as the average velocity, given by Q/HW. This definition of *G* is not directly applicable to the Texture Analyser experiment, since the shear is concentrated in the Stokes boundary layer, in the vicinity of the oil droplet. Using the criterion defined by Seevaratnam *et al.* (2010), the analysis is revisited to calculate *G* around the droplet. The apparent shear rate at the wall on a rectangular channel can be approximated by 2U/H, where *U* is a characteristic velocity of the system, and gives a viscous stress at the wall equal to $2\mu_{water}U/H$. The capillary stress on the drop is γ/a_d . Assuming local inertia near the drop to be $\rho_{water}U^2$, a dimensionless group G_c is defined:

$$G_{\rm c} = \frac{Ca^2}{Re} \equiv \frac{\left(\frac{\rm viscous\ stress}{\rm capillary\ stress}\right)^2}{\frac{\rm inertia}{\rm viscous\ stress}} = \frac{\left(\frac{2\mu_{\rm water}U}{H}\right)^3}{\left(\frac{\gamma}{a_{\rm d}}\right)^2(\rho_{\rm water}U^2)} = \frac{8\mu_{\rm water}^3Ua_{\rm d}^2}{\gamma^2H^3} = 8\left(\frac{a_{\rm d}}{H}\right)^3G \quad (6.8)$$

This localized group is related to Seevaratnam *et al.*'s quantity by a geometrical factor, a_d/H , which captures geometric similarities.

The local inertia near the drop can also be assumed to be given by $\rho_{water} U^2 \left(\frac{a_d}{H}\right)^2$ by taking the size of the droplet into account. A second dimensionless group G_c' is obtained:

$$G_{c}' = \frac{Ca^{2}}{Re} = \frac{\left(\frac{2\mu_{\text{water}}U}{H}\right)^{3}}{\left(\frac{\gamma}{a_{d}}\right)^{2} \left(\rho_{\text{water}}\left(U\frac{a_{d}}{H}\right)^{2}\right)} = \frac{8\mu_{\text{water}}^{3}U}{\gamma^{2}H} = 8\frac{a_{d}}{H}G$$
(6.9)

This group is again related to Seevaratnam *et al.*'s expression, with a weaker dependency on the geometric term. Table 6.3 summarises the experimental variables reported by Seevaratnam *et al.* (2010) and the parameters calculated using equations (6.8) & (6.9). They reported *G* values ranging from 1×10^{-7} to 2.5×10^{-6} and observed that the critical shear rate required to deform an oil droplet increased with increasing *G* (Figure 2.10). The *G*_c and *G*_c' values varied from 1.3×10^{-12} to 1.3×10^{-8} and from 1.0×10^{-8} to 2.5×10^{-6} , respectively.

The same calculations were performed for the Texture Analyser experiments and are summarized in Table 6.4, giving G_c values ranging from 1.1×10^{-13} to 2.6×10^{-6} for the oil-saline case, and 5.9×10^{-11} to 5.9×10^{-7} in the presence of surfactant. G_c ' values varied from 1.0×10^{-9} to 2.5×10^{-6} and 4.5×10^{-6} to 4.5×10^{-5} for both solutions respectively. Overall, these value ranges are comparable to the ones estimated from Seeveratnam *et al.* (2010), apart from the cases in presence of surfactant where G_c and G_c ' values were larger. Using the new estimations of Ca and G_c , a flow map was plotted with the values from Table 6.3 and Table 6.4 (Figure 6.25). The experimental conditions accessible with the Texture Analyser all lie in the no-detachment region, which would explain why droplets were not seen to detach in the dip-coating experiments.

Experimental values		Calculated parameters		
Н	5.3 mm	$A_{\rm s} = H * W$	3.9×10⁻⁵ m²	
W	7.3 mm	$\overline{U} = Q/A_{\rm s}$	0.13 – 0.52 m/s	
Q	300 – 1200 mL/min	$\dot{\gamma} = \overline{U}/H$	24 – 98 s ⁻¹	
Ý	32.5 – 193 s ⁻¹	Са	8.5×10 ⁻⁵ – 2.5×10 ⁻²	
$\mu_{ m water}$	0.001 Pa s	$\frac{\mu_{\rm water}{}^3\overline{U}}{\gamma^2\rho_{\rm water}}$	1.3×10 ^{−10} − 5.4×10 ^{−10} m	
$ ho_{ m water}$	1000 kg/m ³	a_{d}	0.054 – 5.4 mm	
γ	31 mN/m	$a_{\rm d}/H$	0.01 – 1	
Са	0.004 - 0.016	G _c	1.3×10 ⁻¹² – 1.3×10 ⁻⁸	
G	1×10 ⁻⁷ – 2.5×10 ⁻⁶	G_{c}	1.0×10 ⁻⁸ – 2.5×10 ⁻⁶	

 Table 6.3: Experimental variables and calculated parameters for Seevaratnam *et al.* (2010) study

Table	6.4:	Experimental	variables	and	calculated	parameters	for	the	Texture	Analyser
		experiments.								

Experimental values		Calculated parameters			
		$a_{\rm d}/\delta_{ m Stokes}$	0.011 – 0.11		
$\delta_{\mathrm{Stokes}}(\mathrm{aq})$	0.44 mm	$\dot{\gamma} = U/\delta_{\mathrm{Stokes}}$	90 s ⁻¹		
U	40 mm/s		Saline	TX-100	
$\mu_{ m aqueous}$	0.001 Pa s	Са	3.4×10 ⁻⁶ – 3.4×10 ⁻⁵	2.3×10 ⁻⁵ – 2.3×10 ⁻⁴	
$ ho_{ m aqueous}$	1000 kg/m ³	G	1.1×10 ⁻⁷ – 1.1×10 ⁻⁶	5.0×10 ⁻⁶ – 5.0×10 ⁻⁵	
γ	4 – 27 mN/m	G _c	1.1×10 ⁻¹³ – 2.6×10 ⁻⁶	5.9×10 ⁻¹¹ – 5.9×10 ⁻⁷	
a _d	5 – 50 mm	G_{c}	1.0×10 ⁻⁹ -2.5×10 ⁻⁶	4.5×10 ⁻⁶ – 4.5×10 ⁻⁵	



Figure 6.25: Flow map of the oil droplet behavior with each coloroured rectangle representing the value range of the experimental conditions. Data from Seeveratnam *et al.* (2010) represents oil of viscosity 0.92 Pa s with the red lines seprating the detachment region from non-detachment. Data from the Texture Analyser (TA) and test tube experiments were obtained for B1 oil (0.87 Pa s).

6.3.2 Test tube experiments

To achieve higher substrate speeds, a different experiment was conducted with the stepper motor device and test tubes coated with vertical line feature (section 5.3.6). Experiments were conducted with B1 oil - saline and 1 wt.% TX-100 in saline. The saccadic motion conditions are summarized in Table 6.5. The stepper motor generated angular velocities up to 1000° /s, corresponding to a surface rotation speed of nearly 174 mm/s, which was about 4 times the maximum speed in the Texture Analyser. Assuming the test tube surface underneath the pinned oil flat and the same aqueous Stokes boundary thickness as above, the shear rate can be estimated as 360 s^{-1} (4 × 90 s $^{-1}$). The saccadic-motion-induced aqueous shear flow was still not enough to overcome the adhesion of oil on silane features. None of the oil strands/drops formed on the silane features detached from the surface.

Table 6.5: Substrate saccadic motion conditions

Saccade amplitude (°)	10, 20, 30, 50
Maximum angular velocity (°/s)	400, 600, 800, 1000
Latency time (ms)	50, 200

The G_c and G_c' values were calculated and are summarized in Table 6.6. Figure 6.25 shows that the experimental conditions on the stepper motor are also situated below the detachment line. The flow map indicates that Ca = 0.01 is the minimum value required to potentially see droplet detaching, which corresponds to a velocity of at least 180 mm/s. Further experiments should be conducted at higher speed to find the detachment conditions for droplet size ranging from 10 to 100 µm.

Table 6.6: Parameters Ca, G_c and G_c' calculated for the test tube experiments.

	Saline	TX-100	
Са	1.5×10 ⁻⁴ – 1.5×10 ⁻³	9.9×10 ⁻⁴ - 9.9×10 ⁻³	
G _c	5.6×10 ⁻¹¹ – 5.6×10 ⁻⁷	2.6×10 ⁻⁹ – 2.6×10 ⁻⁵	
<i>G</i> _c ′	4.3×10 ⁻⁷ – 4.3×10 ⁻⁵	2.0×10 ⁻³ – 4.5×10 ⁻³	

Lu and coworkers extended the work of Seevaratnam *et al.* (2010) to higher liquid contact angles on the channel wall (2019). Increasing the contact angle (defined in the oil) decreased the critical shear rate required to remove the oil droplet from the wall under water shear flow (section 2.1.3.4). They found that for a given drop volume, an increase in the TPCA (defined in the oil) from 45° to 75° halved the critical shear rate (from 500 to 250 s⁻¹) to drive the motion of the droplet (Lu *et al.*, 2019). This was consistent with weaker oil/surface attraction. This pointed to the need for further investigation of moving contact line experiments with a surface coating of lower affinity to SiOil (and higher contact angles). It is also noteworthy that Seevaratnam, Lu and co-workers (2010, 2019) investigated the motion of droplets on homogeneous surfaces, which would be different to silane-printed surfaces. Further studies on the effect of irregular surfaces are necessary to understand the onset of motion of a droplet pinned on silane-printed substrates.

6.4 Emulsification in the eye-on-a-chip device

The moving contact line experiments with the lower viscosity silicone oil (A0.5 oil) and the feature-printed glass slides offer some insights into how the oil droplets were formed in the eye-on-a-chip device described in section 2.2.2.3.

Chan and co-authors (2015) attributed droplet formation due to the instability of the bulk interface between the aqueous layer and the oil phase, but the literature review of the thin aqueous layer hypothesis (section 2.2.2.3) indicated that this was unlikely to be the primary mechanism responsible for oil formation. Based on the results obtained with moving contact line experiments (sections 6.1 - 6.3), the surface emulsification mechanism could be a more plausible mechanism for oil formation in the eye-on-a-chip device.

The cells coated on the PMMA walls of the eye-on-a-chip device could be considered as the topographical features on the retinal surface: they presented different surface wetting to the PMMA. During the saccadic motion of the device, presuming that the oil-aqueous TPCL exists on the test wall, the motion of the TPCL across the cells could lead to pinning of the contact line to the retinal cells and give rise to rivulet formation at the pinning sites. The break-up of the rivulet could then lead to primary and satellite droplet formation.

The pinned primary oil drops could be detached from the shearing flow of the aqueous phase in the device. According to the fluid dynamics analysis in Chapter 4, the oil drop on the surface would move at the same speed as the wall, and the aqueous phase was almost immobile away from the wall. These differences in velocity could create enough shear to cause the oil droplet to detach from its pinning point.

Chan and coworkers showed that oil droplets were formed faster with low viscosity oils (5 to 500 mPa s). This could arise from the formation of satellite droplets directly in the aqueous phase, as observed in the work with the A0.5 oil (Figure 6.23)). The satellite drops would then directly collect near the side walls of the disc as a result of centripetal acceleration which pushed them radially outwards. In the higher viscosity oil cases (1 to 5 Pa s), the satellite droplets may be pinned to the wall surface at first and then detached under a favorable aqueous shearing flow.

This surface emulsification mechanism would explain the formation of droplets in the eye-on-a-chip with the higher viscosity oils and the observation of droplets floating in the aqueous layers near the side walls. An eye-on-a-chip device was constructed as part of this project but there was not sufficient time to investigate these hypotheses further: this is the subject of ongoing work.

6.5 Summary

This section has presented experimental results for the motion and stability of the three-phase contact line passing over uniform and feature-printed substrates.

On bare and smooth slides, the motion of the TPCL depended on the substrate speed. At speed higher than or equal to the critical speed of entrainment, the TPCL moved at the same speed as the substrate. At a lower speed, the TPCL moved relative to the substrate. When the substrate stopped moving, the TPCL returned to its equilibrium position via an intrinsic buoyancy-driven force which depended only on the liquid properties (TPCA) and its distance from equilibrium.

Hydrophobic silane features of various dimensions and orientations were used as first approximation models of the surface roughness and chemical heterogeneities found on the retinal surface. A series of experiments with different feature widths and substrate motions showed that the TPCL motion was affected by the silane feature due to a higher affinity between the oil and the silane. When the TPCL moved across the feature, oil threads were formed and broke into smaller oil strands due to Rayleigh-type instabilities. The shape of the pinned oil strands/drops depended on the TPCA and interfacial tension: a TPCA of 35° gave a long half-cylinder shape whereas a TPCA of 110° yielded small spherical drops. The oil viscosity and the surface properties (TPCA, wettability) of the solid substrate also influenced the lengths of the oil segments. The experiments with the most viscous oil (B5 oil) did not give reliable results, indicating the need for a better surface cleaning and patterning method.

All the oil segments which formed adhered strongly to the silane coating and did not detach under the shearing flow of the aqueous phase. The experimental shear rates at the surface appeared to be too low to promote drop detachment. The A0.5 oil did give rise to satellite droplets in the aqueous phase, but since low viscosity oils (0.5 Pa s) are not used in retinal surgery, the results need further investigation. Overall, SiOil

adhered too strongly to the silane features even under the eye-like saccadic motion. These features had a surface energy (25.3 mN/m) lower than the rest of the uncoated substrate (69.2 mN/m for glass, 52.1 mN/m for plasma acrylic) and the difference might have been too high to be representative of the eye case. This requires further analysis of the surface properties of the retina and the features that are present in the eye chamber. A better understanding of the retinal surface would direct the choice of coatings to match the surface energies to the eye case and generate similar adhesion forces to the oil.

Chapter 7 Conclusions and recommendations for future work

7.1 Conclusions

7.1.1 Bulk emulsification

A novel spherical eye chamber model was used to study the stability of the SiOilaqueous interface under representative saccadic motions (Chapters 3 and 4). PIV studies of single-phase flow and numerical simulations showed that the difference in dynamic viscosities of the oil and aqueous phases resulted in different velocity profiles. The analytical model calculated the shear-stresses within the single-phase liquid in a spherical model, and the maximum shear stresses values were used to estimate the shear stress difference at the liquid-liquid interface. Numerical calculations of twophase flow showed that the maximum shear stress achievable at the interface under a typical eye saccade motion was around 10 Pa. This value was comparable to the analytical approximation of 3 - 15 Pa obtained on different planes of the spheres. These numerical simulations provided first estimates of the velocity profiles and shear stresses of the SiOil-aqueous system in a representative model of the eye chamber.

Experiments with the RBFs showed that the oil-aqueous interface formed standing waves under saccadic motion. Higher saccade amplitudes and velocities, and lower latency time, generated larger waves, because they increased the effect of inertia and decreased the time for the liquid to recover to rest before the next saccade pulse. Other factors such as bulk liquid properties, interfacial properties, chamber geometry and saccadic motion parameters were investigated. The chemical surfactant (TX-100) modelled the effect of surface active molecules on the interface: the reduction in interfacial tension led to a less stable interface. The presence of a lens or a buckle indentation in the eye chamber gave rise to larger deformations, related to the more complex flow around the indent. No oil droplets were formed over the range of conditions studied, indicating that the bulk emulsification was not the main mechanism responsible for SiOil emulsification in eyes.

7.1.2 Surface emulsification

The contact line motions on a flat solid substrate were investigated to study the surface emulsification hypothesis.

The motion and stability of the oil-aqueous TPCL on a solid substrate depended on the presence of surface features, physical properties, presence of surfactant and the substrate speed. Silane coatings on the solid substrate presented higher affinity to the oil phase and dragged the TPCL more than the bare substrate. The TPCL formed an oil film on the feature in water which subsequently broke into smaller oil strands due to Rayleigh-type instabilities. The pinned oil shape depended on the surface free energies and contact angles, and its dimensions depended on the feature width and substrate speed. The oil strand dimensions increased with increasing feature width and substrate speed. Horizontal line features gave rise to rivulets between the pinning point and the liquid-liquid meniscus. The instability of the rivulet led to a primary oil drop on the pinning site and satellite drops. The satellite drops were pinned to the substrate for the 1 Pa s oil case, but were readily detached in the aqueous phase for the 0.5 Pa s oil.

The pinned oils were strongly adhered to the saline coating, and did not detach from the surface even under eye-saccadic motions. The shear rates generated by the Texture Analyser (90 s⁻¹) or the stepper motor set-up (360 s^{-1}) were not high enough to deform and detach the droplet from the silane coating. The surface energies chosen in this work (glass and silane) presented a large difference in wetting which prompted the oil to preferentially attach to the silane coating. Confirmation of the surface-driven emulsification mechanism therefore requires further evidence.

7.2 Future work

7.2.1 Experimental investigation

Although oil droplets were formed on silane features, detachment of the droplets requires further investigation to validate the surface emulsification hypothesis. In order to achieve this:

(1) Silane coatings presented a surface free energy (8.0 mN/m) significantly lower than glass (54.8 mN/m) and its hydrophobic groups had a higher affinity with the oil. Alternative materials presenting a smaller surface energy difference from glass and a lower affinity with the oil should be investigated. This could allow the formation and detachment of the oil droplets. Characterisation of the retinal surface should be also conducted in order to find a material that has a similar surface properties to the retina.

- (2) Other methods of making surface features could be tried, such as surface lithography or laser machining. Instead of having a chemical feature, topographical features could be studied. This would decouple the effect of feature dimensions from its surface properties.
- (3) The number of feature geometries, dimensions and orientation could be extended to investigate the effect of surface heterogeneities on the stability of the TPCL and extend the dataset.
- (4) In the case of rivulet formation with alternative materials, the satellite drop dimensions, location and flow dynamics could be further investigated by varying the substrate speed, feature dimensions and orientations.
- (5) The aqueous flow-induced motion of a sessile droplet on a heterogeneous surface could be investigated and compared to the results on a homogeneous surface.
- (6) The moving contact line experiments could be complemented by numerical models that would study the effect of more complex surface features and properties.

Another suggestion would be to develop a synthetic basement membrane to achieve a more suitable alternative to model the retinal surface. More characterisation of the retinal surface is needed to inform the selection of surface features. Initial studies could start with synthetic membranes of collagen and laminin. These synthetic hydrogels have been used to grow epithelial cell culture and could be used to grow retinal cells (Cruz-Acuña and García, 2017; Rofaani *et al.*, 2020).

Another direction of research would be the thin aqueous layer hypothesis that has been excluded in this thesis. Further experimental studies with the eye-on-a-chip device should be carried out to validate or not the surface emulsification hypothesis. However, results should be interpretated with care when generalizing them to 3D spherical eye chamber models.

7.2.2 Clinical interpretations of the experimental results

The bulk experimental investigation showed that a higher viscosity oil and a higher oil level of fill provided a more stable and deformation-resistant interface. By considering the difficulty of injecting high viscosity oil (5 Pa s) in the eye chamber, the lower viscosity oil (1 Pa s) could still be used for the retinal repair surgery. The experiments showed the oil-aqueous interface was still stable for the lower viscous case even under the most severe eye motion scenarios.

The surface emulsification studies showed that a smoother retinal surface would be more favourable to a stable interface. More clinical research to investigate the effect of tearing, inflammation, laser treatment or cryotherapy on the retinal surface roughness and properties, is recommended.

The presence of surfactant in the study mimicked the effect of surface-active molecules, such as proteins, in the eye chamber. The presence of these surfactants decreased the interfacial tension, which decreased the stability of the liquid-liquid interface. The surfactant also promoted spherical drop formation on surface features during the contact line motion, which meant the need of a lower critical shear rate to move the drop, leading to easier oil droplet formation in the aqueous phase. Clinical research could be undertaken to study the liquid and interfacial properties of fluids collected from the patient eyes. The comparison between eyes without and with emulsification could give some insights into why some patients experience emulsification.

The addition of the scleral buckle in the eye chamber model increased the deformation of the bulk interface between the oil and aqueous phases. The scleral buckle could also be considered as topographical feature (bump) on the eye chamber. The effect of the scleral buckling on the SiOil emulsification mechanisms need further investigation.

Appendices

Appendix A: PIV image processing

The vector calculation is executed on the DaVis software via the 'Processing' dialog. The first step consists of using the 'Load' button to add evaluation parameters in the 'Operation List'. The parameters are:

- a geometrical mask (sphere in this study) to eliminate outliers incorrect velocity vectors that have length or direction significantly different from the rest of the neighbouring vectors.
- 2) In the 'Vector calculation parameter', set the iterations to single pass, the interrogation windows to 64 X 64, overlap to 50%, and the correlation function to 'standard FFT'.

To achieve more precise results and higher spatial resolution, change the following parameters:

- Change the iterations to "multi-pass(decreas. size)"
- Set the initial interrogation window size to 64 X 64, iteration: 2, overlap: 50%
- Set the final interrogation window size to 32 x 32, , iteration: 3, overlap: 75%
- Set the initial pass(es) to standard FFT correlation function
- Set the final pass(es) to normalised correlation function

Once the resulting vectors looks reasonable, configure the vector postprocessing parameters.

- Select median filter as remove & replace
- 2 * r.m.s neighbors
- Remove groups with less than 5 vectors

Depending on the result, readjust the parameters. Increase the neighbor factor (e.g. 2.5) if too many good vectors have been removed, but reduce the factor to 1.5 if too many bad vectors remain. Once a suitable factor for the r.m.s neighbors is found, use this value as a start value for the median filter "strongly remove & iteratively replace" evaluation. Finally, select "Display settings" to choose a suitable vector length and color to display the calculated vector field.

Appendix B: Image Analysis for Chapter 6 results in ImageJ

Recorded videos of TPCL motion on a silane-printed substrate in the Texture Analyser were analysed on ImageJ. The image frame at the instant right after the TPCL moved across the printed features was selected to characterise the size of the formed silicone oil droplets.

Crop the selected image to the area of interest, then convert the image to grey scale. Apply a threshold to create a binary version of the image with only two pixel intensities: black = 0 and white = 255. The substrate appears as a white background and the droplets as a dark circle. This processing step didn't change the droplet size significantly.

Then use the 'Particle Analyzer' in-built functionality and the default properties to measure the number, the position, and the surface area of the detected circles. The surface area of the detected circles was used to calculate the diameter of the oil droplet. The same image analysis was performed with three experimental repetitions, and the mean value and the standard deviation of all these three sets of results were used to plot the figures in Chapter 6.

Similar image processing was used to analyse oil segments. The only change is in 'Particle Analyzer' step where the circularity was defined as 0 - 0.1 which is closer to a segment configuration. The width and height were recorded.

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