Friction
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REVIEW ARTICLE

Recent advances in ocular lubrication

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Abstract: The ocular lubrication, where the eyelid constantly slides on the curved corneal surface, is considered as one of primary lubrication systems in bio-tribology. Under reliable lubrication conditions, sensitive ocular tissues remain intact from fatigue damage during spontaneous blink cycles. The tear film, evenly filled between cornea and conjunctiva, is a biological fluid with dynamic adjustment ability, which provides superior lubrication with the friction coefficient of below 0.01. However, the lubrication failure may result in a variety of uncomfortable symptoms such as inflammatory reactions, tissue damage and neurological abnormalities. Therefore, it is essential to clarify the fundamental mechanism of ocular lubrication, which helps to alleviate and even recover from various ocular symptoms. This review firstly demonstrates that the ocular components, containing lipids and mucins, contribute to maintaining the lubrication stability of tear film. Furthermore, the ocular lubrication state in various physiological environments and the physical effect on tear film dynamics are further discussed. As typical applications, the therapeutic agents of dry eye syndrome and contact lens with superior lubrication effects are introduced and their lubrication mechanisms are clarified. Finally, this review summarizes a series of the latest research inspired by ocular lubrication. Overall, this work will provide a valuable guidance on the theoretical research and extensive applications in the field of biological lubrication.

Keywords: bio-tribology; ocular lubrication; tear film; dry eye syndrome; tear film dynamics

1 Introduction

Friction is a physical phenomenon widely existing in nature and industry. Related friction, wear, and lubrication studies are widely conducted in the field of tribology, which involves machinery, transportation, aerospace, chemical, biological engineering and many other fields [1]. As an important branch of tribology, bio-tribology including teeth [2], joints [3], eyes [4] and some physiological adaptive and self-healing processes was first proposed by Dowson [5] in 1970. Lubrication is a physical phenomenon discovered following friction. At the same time, human tissues and organs secrete various kinds of biological mucus, which helps to reduce the friction and wear between the sliding surfaces, thus constituting human biological lubrication. In past studies, biological lubrication has played a crucial role in maintaining normal human body functions. Two lubrication modes were respectively revealed in the late 19th century (Tower and Reynolds) and early 20th century (Hardy and Doubleday): "Boundary lubrication" and "Fluid film lubrication" [6]. The lubrication mode is mainly affected by the thickness of lubricating layer and the roughness of contact surface. Boundary lubrication [7] and hydrodynamic lubrication [8] are main lubrication modes of living organisms, and friction in complex environments such as low sliding speed maybe two orders of magnitude higher than that under hydrodynamic lubrication [9]. Ocular lubrication is an important part of the biological lubrication system. During the blinking process, the ocular environment is mainly in hydrodynamic lubrication state, in which contact surfaces are completely separated by a layer

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of viscous fluid and the fluid film pressure is balanced with external load. Normal operation of ocular lubrication system depends on effective tear film lubrication, minimal friction and wear between cornea and eyelid. Lubrication failure may lead to a range of ocular diseases. Therefore, maintaining stable ocular lubrication is essential for protecting human visual health [10].

Under normal circumstances, the blinking frequency of human beings is about 15–20 times/min and the single blink cycle is within 100 ms. According to the thickness of corresponding shear region, the maximum shear rate is estimated around 10^4–10^5 1/s and the contact pressure applied to the cornea by the eyelids fall in the physiological range of 0.3–7 kPa [11, 12]. Thus ocular lubrication system is typically characterized by low load, high frequency and high shear rate. Stable tear film lubrication is essential for eye health and meanwhile tear film breakup (TBU) time often exceeds the blink interval. Among healthy subjects, TBU time is commonly estimated to be more than a minute, while this process occurs within only seconds for patients with dry eye syndrome (DES) [13]. As one of the most common diseases, the prevalence of DES has been increasing nowadays (up to 50% in some areas), and such cases are more common among contact lens (CL) wearers [14]. TFOS DEWS II redefined dry eye as *"Dry eye is a disorder of the tear film due to tear deficiency or excessive tear evaporation which causes damage to the interpalpebral the ocular surface and is associated with symptoms of ocular discomfort."* [15]. The clinical manifestations of DES include eye fatigue, foreign body sensation, dryness and other symptoms [16]. There are various treatment options for DES, including wetting agents, multiple-action tear substitutes and ocular surface modulators etc. Among them, dripping artificial tears on the ocular surface is the most direct and least invasive treatment method. Nowadays, eye drops such as cellulose derivatives, polyvinyl alcohol, hydroxypropyl guar gum, and sodium hyaluronate have been developed [17, 18]. However, conventional eye drops suffer from short residence time on the ocular surface and low bioavailability. Besides, frequent invasive intraocular injections may be accompanied by uncontrollable complications. Therefore, it is necessary to better understand the operation law of ocular lubrication system and further study the tribological behavior of the ocular surface. It will not only facilitate the development of various biomimetic lubricants and coatings for ocular devices, but also inspire new treatments for alleviating ocular inflammation.

In this review, recent advances in tribology research based on the ocular environment are discussed. Firstly, we introduce the structure and composition of natural ocular lubrication system, discuss the structure and composition of the tear film in detail, and analyze the viscoelastic properties, permeability and wettability of the ocular surface and the tear film. Then, based on film thickness, the lubrication state of the ocular surface is divided into boundary lubrication and hydrodynamic lubrication. The tear film dynamic behavior is analyzed from some factors such as surface tension, evaporation, viscosity and curvature, and then the effects of various factors on tear film stability are further discussed. After that, we summarize the research on natural and synthetic lubricants related to DES, the update of CL detection method and the optimization strategy of its surface lubrication properties. Finally, certain extended studies inspired by natural ocular lubrication system are summarized, which provide new insights into the study of ocular tribological behavior, mainly including contact models for Gemini hydrogels, gradient/composite gel network structure, hydrated lubricants and tribological dynamic regulation mechanism. In this review, based on the characteristics of natural ocular environment, tear film lubrication mechanism is theoretically explained by combining various physical effects. The application of ocular tribology is further enriched by the systematic research of water-based polymer materials and biological lubricating media. It is conducive to explore the advanced application and treatment prospects in the failure state of ocular lubrication, and it helps to provide theoretical guidance for ensuring human eye health.

2 Natural ocular lubrication system

2.1 Structure and composition of ocular lubrication system

Ocular lubrication system is a complex biological system with the cornea and conjunctiva as contact surfaces and the tears film as lubricant, which can maintain low coefficient of friction (COF), as shown in Fig. 1(a) [19, 20]. The cornea shows a convex structure including corneal epithelium, stroma and Descemet's membrane. The corneal epithelial consists of nonkeratinized stratified squamous epithelium and it has a symbiotic relationship with the overlying tear film. As the main body of the corneal structure, the corneal stroma accounts for about 80%–85% of its thickness, which can ensure the mechanical strength of the corneal layer and maintain the corneal curvature [21]. The conjunctiva can be divided into three regions: bulbar (covering the surface of the eye), palpebral (lining the undersurface of the eyelids) and the fornical region in between. The goblet cells in the conjunctiva provide mucins for tear film. The gradient mucin layer at sagittal section of retropalpebral recess shows dual, mirror-image structure [22]. Tear film covered on the ocular surface is divided into the mucus layer and the lipid layer, containing proteins, lipids, water, electrolytes, and other components. Tear film isolates the outermost corneal surface of the human eye from the eyelid, CL or the surrounding environment. It serves to protect the eye from the environment, lubricate the ocular surface, maintain a smooth surface for light refraction and protect the health of the conjunctiva and avascular cornea [23].

2.2 Composition and function of tear film

Tear film is a kind of biological fluid with complex components and intrinsic dynamic regulation ability, which can be divided into mucus layer and lipid layer according to its structure, as shown in Fig. 1(b) [24]. The water content of mucus layer in tear film is as high as 98% and it contains a variety of ions, including

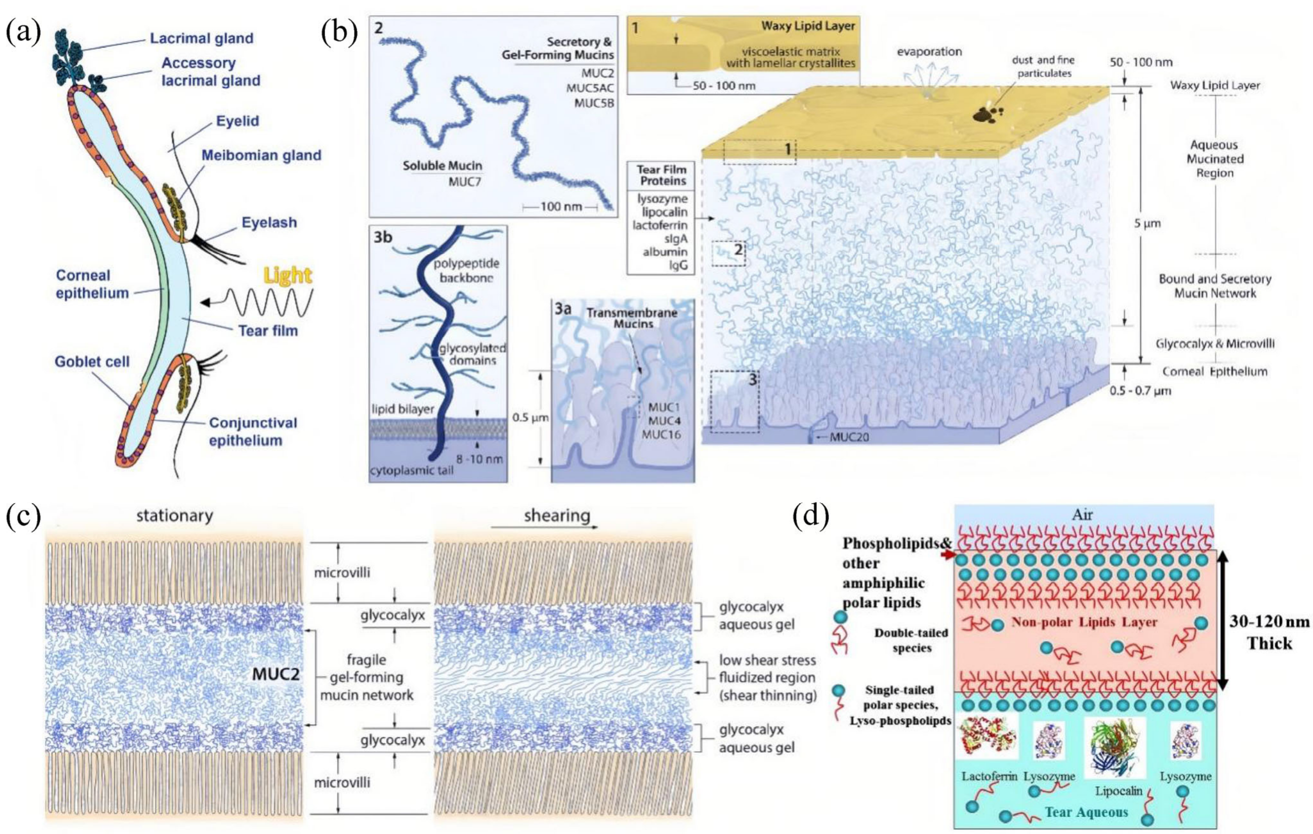

Fig. 1 (a) Schematic representation of ocular surface structure. Reproduced with permission from Ref. [19], © The Author(s) 2018. (b) A schematic of the corneal epithelium, tear film, mucins associated with the ocular surface, and the waxy lipid layer. Reproduced with permission from Ref. [24], © Elsevier Ltd. 2017. (c) Gel-forming mucin with a concentration gradient. Reproduced with permission from Ref. [28], © The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2021. (d) Inverted double-tailed tear lipid layer. Reproduced with permission from Ref. [29], © Elsevier B.V. 2016.

Na^+, K^+, Mg^{2+}, Ca^{2+}, Cl^-, HCO_3^-, CO_3^{2-}, etc., which maintain normal osmolarity and keep slightly alkaline of tear fluid. The average pH value of tear film is commonly in the range of 7.50 ± 0.23 [25, 26]. Tear film serves to lubricate and protect ocular surface, and meanwhile washes away foreign bodies existing between conjunctiva and cornea. Besides, its large mesh size allows for rapid transportation of gases, fluids, ions and nutrients to underlying cells [27].

The mucus layer of tear film exhibits a fine hierarchical multiscale mucin assembly structure with large mucin mesh size, high water content, low yield stress and good dynamic healing ability, which is used to maintain the hydration of the ocular surface. It can improve the lubrication and anti-adhesion properties between the corneal and conjunctival cells of the ocular surface during blinking. Mucin is a highly glycosylated glycoproteins with high molecular mass (>1 MDa). There are a large number of tandem repeat domains of poly clustered O-glycans in mucin, which are usually connected to the hydroxyl groups of serine or threonine via N-acetylgalactosamine [30, 31]. According to the structure and function, mucins can be divided into two categories: membrane-bound mucins and secreted mucins. The membrane-bound mucins form an anchoring layer and the secreted mucins are low-density, weakly physically cross-linked gel networks [32]. The apical plasma membrane of the ocular surface epithelium exhibits a microfolded structure that increases the specific surface area of epithelial cells. The membrane-bound mucins (MUC1 and MUC16) emanate from the tips of these structures and extend as far as 500 nm above the plasma membrane to form a unique glycocalyx structure, which convert the hydrophobic plasma membrane into a hydrophilic surface. Moreover, the glycocalyx and microvilli distributed on the surface of epithelial cells interact with the mucin layer, which further facilitates the anchoring of the base of the mucin layer on different epithelial cells of the ocular surface capsule [33]. The glycocalyx at ocular surface epithelium plays an important role in epithelial surface lubrication, hydration and barrier function. The secreted mucins with high molecular weight are usually homologous oligomers of mucin subunits arranged in flexible linear chains and it can be further divided into gel-forming mucin (MUC5AC) and soluble mucins (MUC7) [34]. As shown in Fig. 1(c), the gel-forming mucin presents a clear concentration gradient and its concentration gradually decreases away from the glycocalyx. Under shearing, the fragile mucin network yields in the low-concentration region (middle), fluidizes, and then undergoes shear thinning to maintain a low-friction interface during sliding. These mucins form gel-spanning networks through transient cross-links (hydrogen bonds and disulfide bonds) and even shorter-lived physical entanglements, with mild yielding and rapid recovery during and after sliding, respectively [28]. Besides, proteoglycan 4 (PRG4), also known as lubricin, is an amphiphilic mucin-like glycoprotein. It exhibits a semi-flexible rod-like structure and contains about 50% oligosaccharides. PRG4 is physically adsorbed to the epithelial surface through its hydrophobic globular end. The mucin-like domain composed of negatively charged hydrophilic sugar groups can form a brush-like structure, which enables tear film to achieve hydrophilic diffusion during blinking. It acts as a boundary lubricant between the corneal surface and the eyelid brush area in the absence of a thick fluid film. The combination of lubricin and galectin-3 further enhances its boundary lubrication activity, thereby effectively reducing the COF of the ocular surface [35, 36].

The lipid layer of tear film is mainly composed of lipids secreted by the meibomian glands, including a thick non-polar phase (such as cholesterol, cholesterol esters, wax esters) adjacent to the air interface and a thin polar phase (such as omega-acyl hydroxy fatty acids (OAHFAs), phospholipids) adjacent to the water-mucin. The meibomian lipid layer shows strong interfacial viscoelasticity, which can stabilize tear film to prevent spontaneous dewetting and TBU. It plays a key role in delaying water evaporation and reducing the surface tension of tear film [37]. As shown in Fig. 1(d), for the lipid layer of tear film, the double-tailed amphiphilic molecules form an inverted bilayer at the air–lipid interface, while the monolayer containing lots of surfactants maintains low tension at the oil–water interface. The synergistic effect of them provides a positive diffusion coefficient for the lipid membrane [29]. A normal, efficient lipid layer should possess the following four characteristics: i) high evaporative resistance to prevent water loss and consequent hyperosmolarity; ii) respreadability to return to the original state after the compression-expansion cycle of the blink; iii) fluidity to avoid blocking the secretion of meibomian glands; iv) gel-like and incompressible structure to resist forces that may disrupt lipid layer [38].

2.3 Characteristics of tear film

Tear film is an important part of the ocular surface and good tear film stability is a critical guarantee to protect ocular surface epithelium from drying. Tear film stability is enhanced by the synergy between the tear components including mucin and lipid layer, and it is closely related to its viscoelasticity, permeability and wettability. Tear film is characterized by viscoelasticity. Based on weak non-covalent interactions, hydrogen bonds, van der Waals attraction and steric interactions among polymer molecules, secreted mucins form a unique dynamic gel layer on the ocular surface. The gel shows good shear-thinning properties, which decomposes with each blink and recovers at the end of the blink [39]. The viscosity of tear film has been shown to be non-Newtonian (i.e. dependent on the shear rate at which it is measured) and relatively low (in the range 1–10 mPa·s, compared to 1 mPa·s for water at 20°C) [40]. Gouveia et al. [31] concluded that human tear viscosity was a protein–protein and protein–lipid interaction type. They found pooled whole human tears showed shear-thinning behaviour, but the shear viscosity of the tear fluid decreased and changed to Newtonian viscosity after lipid removal. The wettability of the epithelial surface is usually determined by the intact structure of the glycocalyx and membrane-bound mucins, which can be studied by measuring contact angle of the corneal epithelial quantitatively [41]. The surface tension of the tear–air interface is influenced by surface-active polar lipids, depending on the binding of tear lipids to lipocalins. The surface tension of tear fluid in healthy individuals is 43.6 ± 2.7 mN/m, while it rises to 53.0–55.5 mN/m for the delipidised tear fluid [42]. Davidson and kuonen [43] believed that when lipids diffused on the surface, the surface tension of the tear film decreased, thereby drawing water into the tear film to increase its thickness. The soluble mucins in the mucus layer could also reduce the surface tension and enhance the water diffusion and cohesion, which improves tear film stability. Tear fluid osmolarity depends on the concentration of ions and solutes permeating the ocular surface. Tear fluid is hypoosmotic and normal tear film osmolarity ranges from 270 to 315 mOsm/L [44]. Previous studies have shown that evaporation would thin tear film and increase tear film osmolarity, with local osmolarity peaking as high as 800 to 900 mOsm/L in the interblink interval, resulting in associated pain and pro-inflammatory stress to the ocular surface [45]. The hyperosmolarity caused by the high evaporation rate of tear film is an important factor affecting tear film stability. Therefore, slowing down the evaporation of water and maintaining tear film hypoosmotic are the key to maintaining tear film stability.

3 Tear film lubrication theory

3.1 Ocular lubrication state

In classical tribology, the Stribeck curve [46] describes the relationship between COF, load, relative velocity and viscosity, corresponding to three different states of boundary lubrication, mixed lubrication and hydrodynamic lubrication respectively, as shown in Fig. 2(a) [47]. Tear film is a non-Newtonian fluid with shear-thinning properties, which does not follow classical Stribeck behavior, but can be used as a reference for research ideas. In general, the lubrication state of the ocular surface can be divided into hydrodynamic lubrication and boundary lubrication according to film thickness. Pult et al. [48] established a hydrodynamic model based on the human eyelid wiper model, as shown in Fig. 2(b). The upper eyelid is slightly lifted off the cornea by 1.1 mm during the closing phase, which ensures that the upper eyelid exerts significantly higher force on the ocular surface during the closing phase of the blink than the opening phase of the blink. The upper eyelid follows the corneal shape when closed and the eyelid edge remains perpendicular to the corneal tangent line, providing tangential velocity and normal load.

The lubrication state of tear film also varies in different physiological environments. Under normal

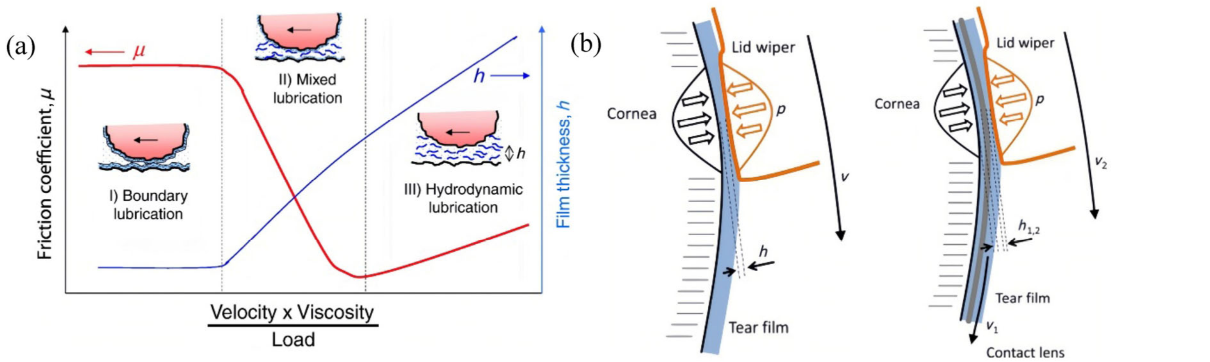

Fig. 2 (a) Stribeck curve. Reproduced with permission from Ref. [47], © Elsevier Ltd. 2010. (b) Lubrication model based on the human eyelid wiper model, which accounts for cornea interaction with lid velocity (v), lid pressure against the cornea (p) and tear film thickness (h), and lid-CL-cornea interaction with lid velocity (v_1, v_2), lid pressure against the cornea (p) and tear film thickness ($h_{1,2}$). Reproduced with permission from Ref. [48], © Elsevier Inc. 2015.

physiological conditions, hydrodynamic lubrication commonly occurs during the period of blink or saccade with high relative velocity. The fluid layer separates sliding surfaces and its shear strength depends on both relative velocity and tear viscosity. However, boundary lubrication is usually occurring at the start, end or return period of blink cycle and when eyes are stationary or gazing at a slow-moving object [48]. Cher [49] found that two mucosal layers were juxtaposed behind eyelids and meanwhile the dual mucus attached to epithelial surface was mirror-image. The interpalpebral mucus, wrapped by a lipid layer and attached to cornea, is much thicker than the retropalpebral mucus. During the relative movement of eyelid and cornea, the microvilli and glycocalyx grasp the basal gel of the mucoaqueous portion, which in turn drives tear fluid to form hydrodynamic lubrication. There are different forms of lubrication at the interface between CL and ocular environment. When the eyelid moves over CL during blinking, the tear film is separated and even consumed by CL, thereby introducing relative sliding on both sides of corneal epithelium and eyelid wiper. When wearing CL, there are two independent tribological regions between eyelid-lens and lens-cornea. Dunn et al. [50] proposed a numerical fluid model of the pressure and velocity between two sliding surfaces. Depending on the relative sliding velocity, the lubrication state between the eyelid and CL anterior surface points to hydrodynamic lubrication, while the lubrication state between the CL substrate curve and cornea is more likely to reach boundary lubrication. Particularly, stable hydrodynamic lubrication can be hardly formed due to the relative lack of aqueous tears, thus the ocular surface of DES patients is usually in the state of boundary lubrication. Lubricin, as a boundary lubricant, takes effects on preventing high shear stress to protect the ocular surface tissue [51, 52]. Mucins and mucinous glycoproteins with high surface activity can easily adhere to a variety of surfaces. Their conformations highly depend on the factors of substrate chemistry, surface charge, concentration and ionic strength. The hydrophobic surfaces can be turned into hydrophilic ones and generate strong steric repulsion, so as to promote the formation of boundary lubrication to reduce friction at relatively low sliding speeds [47].

3.2 Mechanism of tear film deposition and rupture

Tear fluid is distributed on the ocular surface and occupies three compartments, consisting of the meniscus and the tear film which are exposed to the atmosphere, as well as the fluid in the conjunctival fornices. Tear drainage is a complex physiological process that is realized through the cooperation of various systems. As shown in Fig. 3(a), tear fluid flows from the main and accessory lacrimal glands into the conjunctival sac, and then flows from the conjunctival sac into the tear meniscus. From the meniscus, the fluid flows into the canaliculi through the upper and lower punctal openings, then into the lacrimal sac, and finally exits through the opening of the nasolacrimal duct [53]. During normal blinking, the upper eyelid moves and forms a thin tear film on

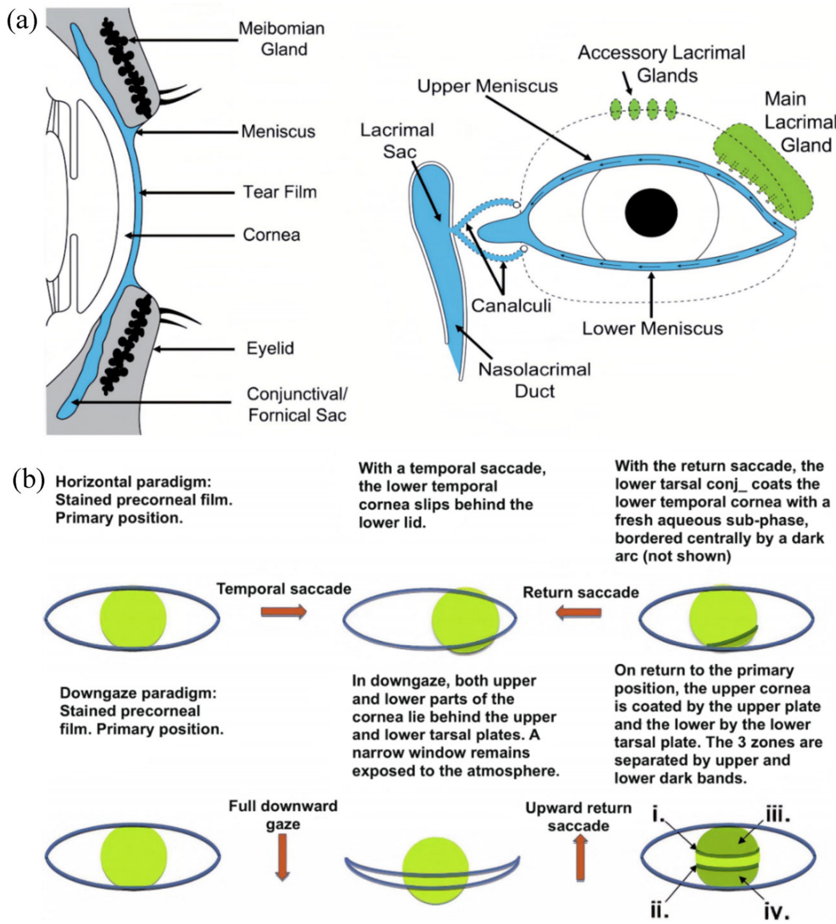

Fig. 3 (a) Sagittal view of tear distribution and schematic diagram of tear drainage system. Reproduced with permission from Ref. [53], © Elsevier Ltd. 2009. (b) Coating of the tear film during horizontal and vertical saccades. Reproduced with permission from Ref. [54], © Elsevier Inc. 2014.

exposed corneal and conjunctival surfaces, thereby reducing friction in the eye. Yokoi et al. [54] elucidated the tear film behavior during blinking, horizontal and vertical saccades, as shown in Fig. 3(b). During horizontal saccades, the lipid layer of tear film is combined with mucoaqueous subphase and adheres to the cornea in the form of a stable fluid shell. During vertical saccades, the lipid layer of tear film and the aqueous subphase may be disturbed by persistent blink suppression. The presence of the gel is indicated by the formation of upper and lower dark bands during blink suppression. The gel breaks down on the downstroke, recovers on the upstroke of each blink and remains stable with eyes open.

Rapid thinning of tear film is a critical contributor to its instability and many methods have been used to visualize or measure tear film thickness and its rate of flow. Imaging of tear film is an important tool for analyzing its dynamics. Non-invasive approaches can provide precise and rapid optical measurements. At present, various optical instruments such as optical microscopy, interferometry and optical coherence tomography (OCT) have been developed to analyze dynamic behavior of the tear film [55]. Since some parameters such as evaporation rate and osmolarity can't be accurately measured in the process of TBU, various mathematical models can be established to provide effective estimates, thereby greatly enriching the study of tear film dynamics [56]. Variation in tear film thickness on the ocular surface is determined by the direction of tear flow. Tear fluid may flow tangentially along the cornea surface and the tangential flow along the cornea surface is divided into: convergent type, radially flowing inwards and slowing down tear film thinning; divergent type, radially flowing outwards and promoting tear film thinning.

Tangential flow is driven by: i) capillarity, the pressure differences caused by surface tension and curvature at the tear/air interface; ii) the Marangoni effect, where surface concentration differences generate shear stresses on the tear/air interface; iii) intermolecular forces, such as van der Waals forces [57].

Tear fluid forms meniscus where the eyelid contacts the cornea. The upper meniscus follows the rise of the eyelids and deposits aqueous tears on the ocular surface epithelial. The distribution of aqueous tears thickness (h) at deposition is determined by the balance between the suction pressure of the upper meniscus and the reverse downward force due to the viscous resistance exerted on the tear fluid by the ocular surface epithelium, where $h = 1.338R(\eta U/\gamma)^{2/3}$ (γ: surface tension of the tears; R: radius of the meniscus; η: viscosity of the tears; U: velocity of the eyelid) [58, 59]. The fluid surface resembles a stretched rubber film and it tends to flatten if the fluid surface is curved. Thus, the concave fluid exerts a pulling force on the liquid below, while the convex fluid exerts pressure on the fluid below. Based on the comprehensive effect of surface tension and tear surface curvature, the tear film forms a pressure gradient flow through Laplace pressure or "capillary-suction" generated by the concave meniscus [60]. The meniscus at the edge of the eyelid draws fluid from the tear film, resulting in a localized thinning of the tear near the eyelid (i.e. "the black line"). The pressure difference in the tear near the meniscus is the driving force for the formation of the black line [61]. As the dividing line between the tear meniscus and the tear film, the black line is the thinnest area in the tear film and shows high tear film instability. Its formation is an important manifestation of initial thinning and rupture of the tear film. Allouche et al. [62] approximated the corneal surface as a spherical shape and explored the effect of corneal curvature on tear film dynamics. The study showed that the effect of curvature was weak in regions far from the upper eyelid. However, the interaction of curvature with gravity, capillarity and concentration gradient of surface polar lipids would affect the thinning rate and surface velocity of minimum film thickness (which occurred near the moving eyelid).

Small changes of temperature or composition at the fluid interface (often spontaneously generated) can lead to local changes of surface energy and prompt violent motion of the fluid. This phenomenon is known as the Marangoni effect [63]. The reverse movement phenomenon of the tear film after blinking is closely related to the Marangoni stress. Lin and Brenner [64] demonstrated theoretically that there may be the Marangoni convection in the tear film due to the diffusion of mucins, rather than the temperature drop of the tear film. So it can be inferred that the Marangoni effect is affected by changes of tear film composition. Polar lipids are insoluble surface substances that can alter the local surface tension of the tear film to smooth the tear film. To investigate the effect of polar lipids secreted by eyelid glands and presented on the tear film surface on the evolution of the precorneal tear film. Aydemir et al. [65] established two coupled nonlinear partial differential equations for the film thickness and the concentration of lipid under the lubrication limit. Through the numerical solution of the system, it was found that decreased Marangoni number would reduce tear film thickness and surface velocity, and it was observed that increased concentration of the lipid would increase ocular fluid flow. Zhong et al. [66] established a lipid globule-driven TBU mathematical model that reduced the tear/air surface tension by increasing the localized high surfactant concentration of streaks or globs. The result showed that the Marangoni effect would promote strong tangential flow away from the spheres thereby causing TBU.

Protein molecules are colloidal particles, so there is the inherent long-range van der Waals gravity among protein molecules. Due to the existence of the huge gravity, protein molecules tend to aggregate and combine with each other. The strength of van der Waals force is determined by Hamaker constant. Sharma and Ruckenstein et al. [67] suggested that the long-range van der Waals dispersion forces on the mucus layer would destabilize the mucus layer and eventually lead to the rupture of the mucus layer, which in turn exposed the aqueous and lipid layer on the hydrophobic cornea thereby causing TBU. Then, the intrinsic instability of the film was analyzed theoretically and experimentally. Furthermore, the TBU at the reduced wettability of the corneal epithelial surface, driven by long range van der Waals forces was further demonstrated by a thin film analog of the tear film mucus layer [68]. Based on the continuous mucin model and the heterogeneous mucin model, Dey et al. [69] and Choudhury et al. [70] explored the TBU driven by the van der Waals force, which respectively indicated the importance of mucins to the tear film stability. Blinking involves high shear rates in tear film and requires low tear viscosity to avoid damaging epithelial cells. Conversely, higher viscosity was required to resist drainage and TBU with eyes open. In Tiffany's early research, tear fluid was found to be shear thinning [71]. Zhang et al. [72] and Mehdaoui et al. [73]. carried out a dynamic modeling of mucus rheology, explained the delaying effect of the shear-thinning behavior on tear film thinning and then ensured the safe lubrication between the moving upper eyelid and corneal surface.

Not only the tear film instability caused by tangential flow, but also the excessive consumption of aqueous component in tears has attracted considerable attention in recent years. There are two main pathways for longitudinal flow of water. Respectively, water evaporates and flows through the cornea surface by osmosis. The evaporation in blink interval leads to increasing tear osmolality, resulting in the osmotic flow into the tear film. Braun et al. [74] studied the diffusion of lipid layer during blink cycle. During the downstroke of blink, lipids were compressed by the lower end of upper eyelid and usually released as thick and narrow lipid strips at the beginning of upstroke. The thicker non-polar lipid layer mainly acts as a barrier to decelerate water evaporation. In order to explore the effect of physiological non-polar lipids on tear film evolution, Bruna and Breward [75] established the interaction model considering water layer, surface reactive polar lipid and non-polar lipid layer. The study found that evaporation was commonly far away from eyelids. It would increase Marangoni number, thus promoting the diffusion of non-polar lipid layer and meanwhile increasing the thickness of water layer. Siddique and Braun [76] developed a tear film evaporation and rupture model that simulated the evaporation barrier by slowing dilution rate to increase surfactant concentration. The competition between the effect of increasing surfactant concentration to slowing down evaporation and lowering surface tension was studied in the lubrication theory with TBU. As for a spatially homogeneous thin film, the osmosis will slow the thinning rate of tear film and balance the mass loss of water owing to evaporation. Peng et al. [77] tested the regional evaporation-driven TBU hypothesis by a one-dimensional (1-D) model and illustrated the evolution of the thin aqueous tear film covering on cornea. Thus, the regional evaporation at the anterior surface of tear film was enhanced and the osmotic water flowed into the posterior surface. The fluorescence intensity imaging technology further demonstrated the competitive effect of osmosis and evaporation [78]. After that, a TBU model for evaporation and osmosis was proposed.

Figure 4 shows two types of TBU models as evaporation-driven and lipid globule-driven. The left column of the Fig. 4 shows evaporation-driven TBU. The loss of moisture into the air causes the decrease of tear film thickness $h(t)$ and the osmolarity $c(t)$ reacts inside the tear film, leading to osmosis at the tear/cornea interface. TBU occurs if the rate of evaporation is faster than the rate at which capillarity pushes the fluid into the thin area. The right column of Fig. 4 shows TBU is driven by polar lipids (surfactants). The Marangoni effect drives divergent flow away from the center, causing local tear film thinning but not hyperosmolarity [79]. With the further refinement of the model, Stapf et al. [80] established a tear film dynamics model with two mobile fluid layers (the aqueous and lipid layers) to explore the conditions of TBU. They comprehensively explored the effect of osmosis, evaporation as modified by the lipid and polar portion of the lipid layer, and analyzed the intrinsic effects of these physical effects and changes of initial conditions on the dynamical behavior of the system. To sum up, tear film thinning and rupture is a complex physiological process. Tangential flow based on capillarity, the Marangoni effect and long-range van der Waals forces, and longitudinal flow based on evaporation and osmosis all have varying degrees of influence on tear film thickness. The dynamic modeling of tear film is usually a combination of multiple mechanisms.

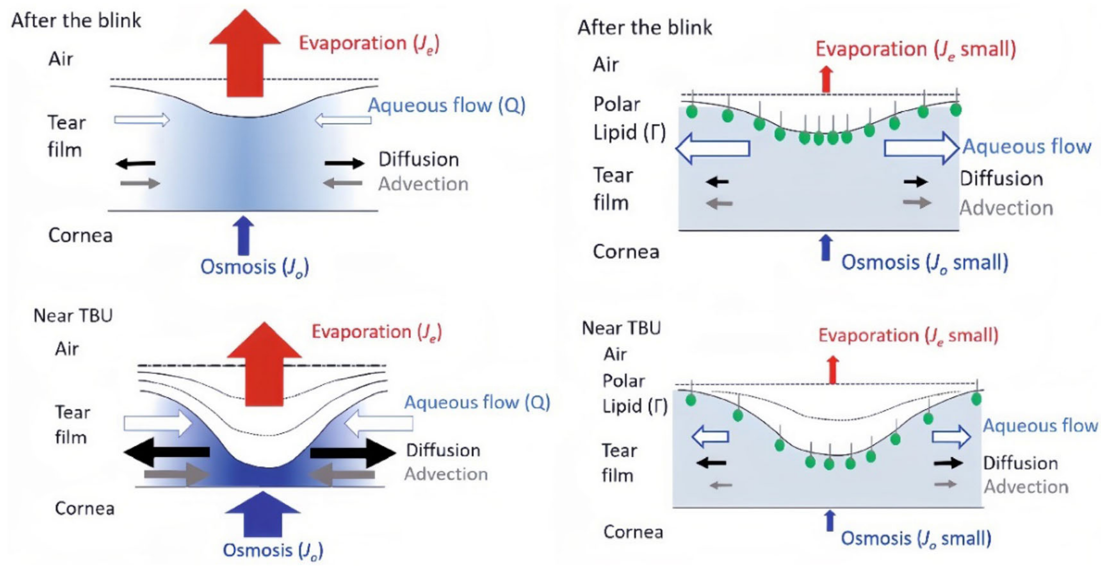

Fig. 4 Left column: evaporation-driven TBU, with increased evaporation leading to local thinning and hyperosmolarity; right column: lipid globule-driven TBU, that the Marangoni drives rapid divergent flow away from center, resulting in tear film thinning without hyperosmolarity, Reproduced with permission from Ref. [79], © Springer Nature Switzerland AG 2019.

4 Ocular tribology applications

4.1 Research on lubricants related to dry eye syndrome

DES is an ocular surface damaged and uncomfortable symptom caused by the imbalance of tear film homeostasis. TBU is the visible core manifestation of DES. Tear film instability and tear hyperosmolarity are the main factors in the development of DES. There are many polymer materials with excellent lubricating properties in the eye, which can be used for the treatment of DES. Crouzier et al. [81] compared the hydration of native and deglycosylated mucins. The study found the removal of glycans from mucins led to a significant weakening of hydration, whereas PEG-lectin conjugates restored hydration of the partially deglycomucin coating and improved its lubricity. Therefore, local complementation of defective mucus layers may provide new therapeutic options for patients with low mucus coverage, defective mucus production or glycosylation. As a natural boundary lubricant and anti-adhesion agent, PRG4 can be used as an effective eye drop for the treatment of DES. Seo et al. [12] developed a specialized in vitro model of evaporative DES that mimicked the multiscale structure organization of human ocular surface, biological phenotype and dynamically regulated environmental homeostasis. Treatment efficacy assessments suggested that lubricin could lubricate the ocular surface more effectively, as evidenced by significantly reduced static COF and dynamic COF. Mutated recombinant human PRG4 (rhPRG4) with truncated mucin domain, exhibits boundary lubrication capabilities similar to that of natural proteins on the ocular surface, with potential uses in dry eye therapeutics and CL coatings [82].

Treatment of DES heavily relies on the utilization of artificial tears. Formulations with enhanced hydration and lubrication, typically containing electrolytes, preservatives, thickener, buffers and water, contribute to maintaining osmotic equilibrium and normal pH range, improving adhesion effect of solution and reducing shear strength on the ocular surface. Recently, Bielory and Wagle [83] summarized a variety of available ocular lubricants, whose main properties are shown in Table 1. Mineral oil with high viscosity can form a relatively thick lubrication film on the ocular surface and slow down the evaporation of tear film. Water-based lubricants including glycerin, polyethylene glycol, methylcellulose, polyvinyl alcohol and hyaluronic acid, can easily combine with water molecules to form a protective film on the ocular surface, thus reducing shear strength between cornea and conjunctiva, and meanwhile alleviating discomfort

Table 1 Main properties of different ocular lubricants [83].

Component	Molecular formula	Molecular weight	Concentration range	Formulation
Mineral oil	$C_{25}H_{43}NO_3$	405.6	1%–42.5%	Ointment
Glycerin	$C_3H_5(OH)_3$	92.1	0.35–0.5%	Artificial tears
Polyethylene glycol	$HO[CH_2CH_2O]_nH$	$1.3–9\times10^4$	0.25%–0.4%	Artificial tears
Methylcellulose	$[C_6H_7O(OH)_3]_n$	$5\times10^3–1.4\times10^5$	0.2%–1.0%	Artificial tears
Polyvinyl alcohol	$(C_2H_3(OH)]_n$	300–8,000	0.5%–1.4%	Artificial tears
Hyaluronic acid	$[C_{14}H_{16}NO_6(OH)_5)]_n$	$1\times10^4–1.5\times10^6$	0.25%–1.5%	Artificial tears

symptoms. Among them, the properties of hyaluronic acid (HA) are similar to those of natural mucin in terms of chemical structure, molecular weight and rheology, therefore HA shows superior tribological properties and draws much attention.

HA is a naturally occurring, nonsulfated glycosaminoglycan with strong hydrophilicity and high molecular weight. It is composed of disaccharide units of glucuronic acid and N-acetyl-D-glucosamine and is mainly located in the extracellular matrix. HA can be used as a candidate material for ocular lubrication and it has been extensively studied in recent years [84]. The combination of HA and other polymers also plays an important role in enhancing lubricity and prolonging the duration of action. Rangarajan et al. [85] compared the differences of hydroxypropyl guar (HPG), HA, and HA/HPG dimers in cell hydration and surface retention, cell and cell barrier protection, and surface lubrication. The dual polymer formulation improved tissue hydration and lubrication, and significantly reduced hydrodynamic surface friction, which could be used to relieve DES-related symptoms. Černohlávek et al. [86] found that the COF of HA with medium molecular weight (natural and modified) was lower than that of high molecular weight HA. Amphiphilic HA-C12 could effectively reduce friction. Meanwhile, the combination of trehalose/HA or HA-C12 enhanced the mucoadhesiveness by about eighty times.

As shown in Fig. 5(a), Lee et al. [87] established a heterobifunctional polymeric-peptide system that one end bounded to HA and the other end bounded to

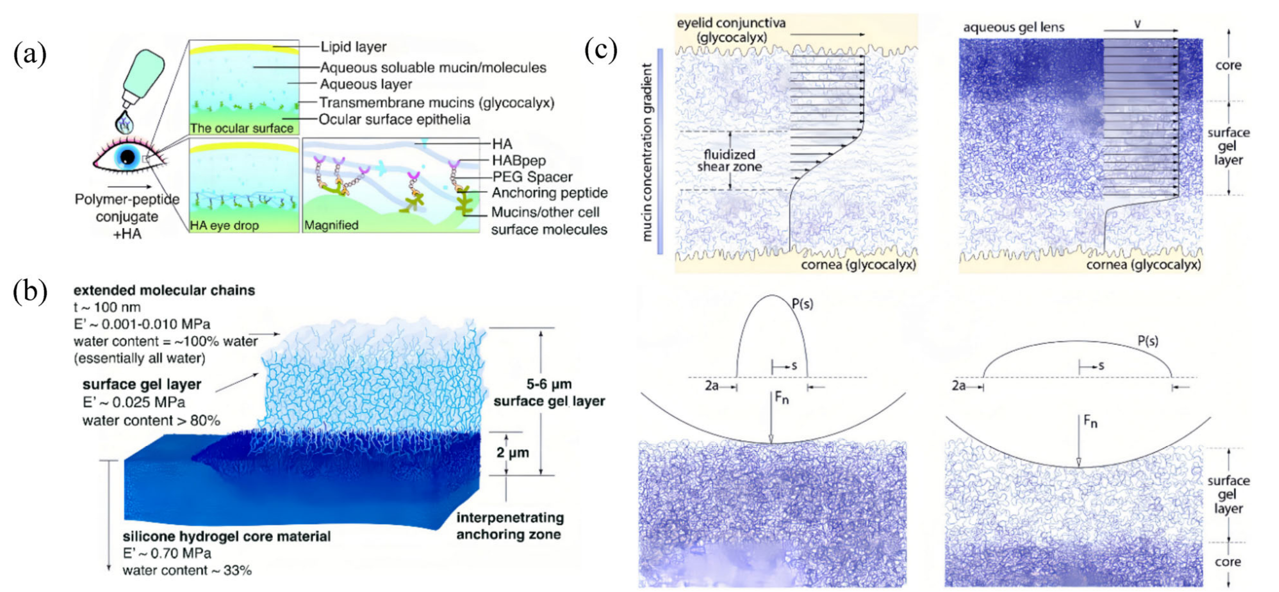

Fig. 5 (a) Schematic of the HA binding eye drop technology. Reproduced with permission from Ref. [87], © Elsevier Ltd. 2017. (b) Surface gel layer integrated into silicon hydrogel core. Reproduced with permission from Ref. [88], © The Author(s), under exclusive licence to Springer Science + Business Media New York 2012. (c) Gradient structure of natural tear film gel network and surface gel layer of CL. Reproduced with permission from Ref. [89], © The Author(s), under exclusive licence to Springer Science + Business Media, LLC, part of Springer Nature 2020..

sialic acid-containing glycosylated transmembrane molecules on ocular surface epithelium or type I collagen molecule in the matrix. HA solution was mixed with the polymer-peptide system, and it is showed on both ex vivo and in vivo tests that the combined peptide solution could make the ocular surface retain HA for a long time and maintain its stable lubricity. In addition to liquid lubricants, gel formulations are also candidates for the treatment of DES. Acar et al. [90] designed a novel liposome-based in situ gelling artificial tear formulation. In situ gelling polymer gellan gum contacted with certain ions present in tears could form gel to resist natural drainage and prolong the eye residence time of the formulation. Kim et al. [91] prepared a gelled hypotonic solution with a low concentration of thermosensitive triblock copolymer. When applied topically, the hypotonic formulation formed a thin, highly uniform transparent layer that fitted the ocular surface, which could enhance the intraocular absorption of hydrophilic and hydrophobic drugs and prolong drug contact with the ocular epithelium.

4.2 Tribological study of contact lens

The comfort of wearing CL is closely related to its tribological properties. With the development of science and technology, the measurement method of CL tribological properties is also updated and iterated. The tribological conditions of CL face a low contact pressure in the range of 3–5 kPa and a faster sliding velocity of about 120 mm/s. Rennie et al. [92] used a reciprocating tribometer to explore the effect of contact pressure and velocity on the COF of CL surface during the experiment. The result showed that the frictional force generated by CL was closely related to the viscoelastic dissipation of the material and the shear of the contact interface. Carvalho et al. [93] evaluated the energy dissipation in friction during the free vibration of CL. This technique had high sensitivity to low applied pressure and high sliding velocity, which could be used to measure the frictional force of CL. Roba et al. [94] established a biologically relevant measurement scheme to study the friction between the human eye and the CL in a simulated physiological environment. By optimizing the contact pair surface composition, lubricant solution, normal load and velocity parameters, ideal micro-tribology test scheme and device were established. With further research, it is found that the use of COF to classify soft materials such as CL has certain limitations. Sterner et al. [95] proposed a method to quantify the tribological properties of soft materials under boundary lubrication in terms of average work, which was defined the average work as the average value of a nonlinear function fitted to the friction versus normal force data, multiplied by a relevant sliding distance. The tribological properties of soft CL could be classified according to average work or the energy dissipated over a certain sliding distance.

Many myopic patients wear CL for a long time and the surface of CL interacts with corneal cells repeatedly. During the wearing process, it is easy to cause the wear of CL, which further leads to corneal cell damage. Therefore, it is crucial to evaluate the fatigue resistance of CL. Eftimov et al. [96] investigated the simultaneous evolution of critical material properties (such as water evaporation loss of water, water contact angle, COF) during rapid desiccation/ rehydration cycling for different silicone hydrogels, and analyzed the relationship among these properties at a timescale that matched the long-term wear of CL. Hofmann et al. [97] used human corneal epthelial structures and commercial CL to measure dynamic COF, related frictional force, frictional energy and corresponding cellular damage between the corneal epithelium and CL. The result showed that there was a moderate correlation between frictional energy and cellular damage, which could be caused by fatigue. Zhu et al. [98] developed and used a simple and representative test system and method to study the adhesion of different silicone CL on porcine cornea under the polished titanium alloy and dehydrating condition, which could be used to evaluate pre-clinical performance of long-lasting CL and its hydration capacity.

In order to further optimize the tribological performance of CL, the improvement of CL surface wettability and hydrophilicity has become the focus of research. The development of various surface wetting agents and modes of action helps to further improve the wearing safety and comfort. Silicone hydrogel is the main material of CL and the spontaneous adsorption of lubricant material on the surface of CL can form stable boundary lubrication. Samsom et al. [99, 100] evaluated the adsorption of PRG4 to silicone hydrogels by soaking–rinsing and western blotting, and they determined the boundary lubrication effect of PRG4 and HA in vitro eyelid-hydrogel and corneal-hydrogel biomechanical friction testing. The result showed that the biological boundary lubricants HA and PRG4 could effectively lubricate silicone hydrogels, providing inspiration for the future development and evaluation of new low-friction CL materials and lubricants. Rickert et al. [101] stably attached the transparent mucin layer to CL to establish a hydrophilic surface, which not only prevented lipid adsorption, but also adapted to the liquid environment. The mucin coating protects corneal tissue from wearing caused by the high frictional stress of the CL, which opens up enormous possibilities for various hydrophobic materials that are not suitable for CL applications [102]. The adsorption and grafting forms of polymer materials on CL surface can improve their surface properties to varying degrees. Korogiannaki et al. [103] studied the effect of the structure of (rhPRG4) /HA complex on CL properties. The rhPRG4-physisorbed/HA-grafted sample showed better antifouling and boundary lubrication properties on conventional hydrogel models, while the HA-physisorbed/rhPRG4-grafted sample exhibited improved surface wettability, antifouling, and water-retentive properties. In addition, the controlled release of lubricants in CL provides a new idea for optimizing their surface properties. Using molecular imprinting strategy. White et al. [104] prepared a silicone hydrogel CL releasing 120 kDa hydroxypropyl methylcellulose extendedly and controllably. The release of the re-wetting agent could refresh the lens surface on the ocular surface away from the lens, increasing the effectiveness of the re-wetting agent.

High water content and increased contact area of the surface gel layer are the main reasons for improving the lubrication performance of CL and reducing damage of ocular surface epithelial. Dunn et al. [88] constructed a thin and soft hydrogel surface layer with more than 80% water content on silicone hydrogel CL, as shown in Fig. 5(b). The soft surface hydrogel layer with low modulus and high water content could form boundary lubrication and exhibit low-friction sliding behavior, Whereas, pressure-induced collapse and dehydration of the soft-surface hydrogel layer were observed at pressures above 10–20 kPa. As shown in Fig. 5(c), Hart et al. [89] performed reciprocating sliding experiments on confluent monolayers of live human telomerase-immortalized corneal epithelial cells. They found that compared with ordinary lens, the lens surface containing the surface gel layer had larger polymer mesh size and higher water content, which could significantly reduce contact pressure and COF, thereby reducing the shear stress and cell damage [19].

5 Frontier exploration based on ocular tribology

A variety of natural or synthetic materials (inspired by nature) can be used in biological lubrication research to reduce cell damage caused by ocular friction, thereby relieving symptoms associated with DES. Starting from the structure, lubricating molecules and mechanisms of natural ocular lubrication system, the research on ocular tribology is further developed from the aspects of contact models to Gemini hydrogels, gradient/composite network structure, hydrated lubricants and friction dynamic regulation.

5.1 Contact models of Gemini hydrogels

Ocular lubrication system can withstand thousands of duty cycles per day without fatigue. Epithelial cells in the eye produce a polymer network that protects and lubricates the ocular surface, which can retain a lot of moisture. The friction and lubrication of the system occur between soft hydration surfaces. Its "twinned" structure features soft–soft contact, which can form a low shear layer at the symmetry plane, thus guaranteeing a stable, low COF [105, 106]. Inspired by such nanoporous biopolymer network lubrication systems, various Gemini (self-mated) hydrogel interface are constructed gradually. The influence of various factors on frictional properties of Gemini hydrogels is further explored by designing the hydrogel mesh size and component geometry, as well matching its osmolarity and mechanical properties.

Regarding Gemini hydrogels, their surface and interface characteristics (such as contact geometry, contact area, load, osmolarity, etc.) are the most intuitive factors to explore. Liu et al. [107] studied the tribological behavior of hydrogels with two different contact geometries (sphere-on-flat and flat-pin-on-flat) over a wide range of sliding velocities. As shown in Fig. 6(a), after normalizing frictional force by contact area, it was found that the shear stress of the sphere-on-flat configuration was lower than that of the flat-pin-on-flat configuration at high sliding speeds. This phenomenon was attributed to the larger equivalent hydrodynamic thickness in the convergent inlet region of the sphere-on-flat contact, which enhanced the water supply in the contact and promoted rehydration. Chau et al. [110] found that Gemini hydrogels with spherically-capped shell probe geometries was capable of generating load-independent friction over a range of low normal loads spanning 0.5 to 2.0 mN. To find out its cause, the contact geometry had large compliance, so that the contact area was proportional to the applied load. Urueña et al. [117] explored the influence of contact pressure and contact area on the friction behavior of hydrogel by varying the load over two orders of magnitude (0.1–20 mN) and the sliding velocity over four orders of magnitude (10 μm/s–100 mm/s). The COF of the hydrogel decreased with the increase of the applied load, which was consistent with the prediction of non-linear expansion of contact area with applied load and pressure-independent surface shear stress [111]. Interfacial mechanical properties of the material also play a crucial role in the tribological properties of hydrogels. Schulze et al. [112] investigated the effect of polymer osmolarity in the contact mechanics of hydrogels through a series of local indentation tests and volumetric compression tests. The study found that the hydrogel was incompressible when the pressure didn't exceed the osmolarity of the hydrogel. Rudge et al. [113] compared the tribological properties of two hydrogels with different surface roughness. The COF of hydrogels at low loads was related to roughness and Young's modulus, yet the COF of hydrogels remained constant on the length scale of roughness under high loads, depending mainly on the stiffness of the material. In addition, the dynamic measurement of the deformation behavior in the hydrogel contact area can better characterize its surface properties. McGhee et al. [114] established a method of slow confocal scanning by in situ dynamic equilibration, using 3D confocal laser-scanning microscopy to detect and image simultaneously. Fluorescent microbeads in the hydrogel and solution were used to generate images of the dynamic contact interface, which in turn revealed local and bulk deformation during the sliding.

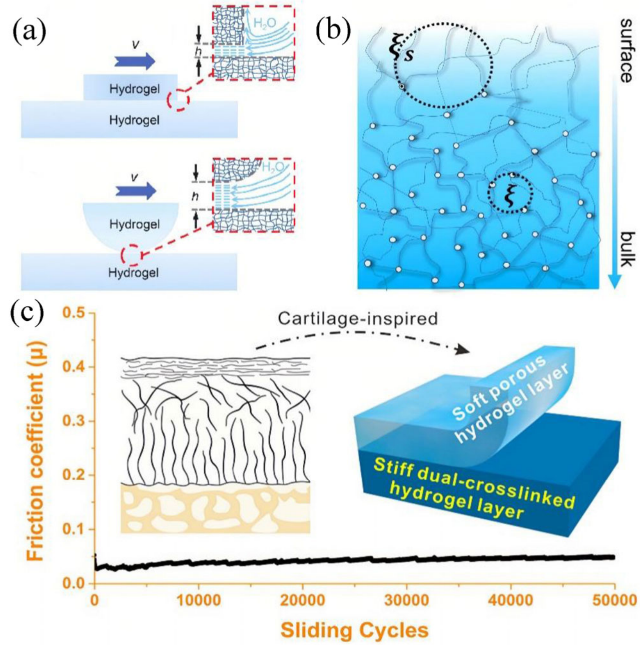

Fig. 6 (a) Schematic diagrams of the probable cause for the differences in high-speed friction for a flat-pin-on-flat configuration and sphere-on-flat configuration. Reproduced with permission from Ref. [107], © The author(s) 2020. (b) Hydrogel consisting of polymer chains permanently crosslinked or physically entangle. Reproduced with permission from Ref. [108], © Multidisciplinary Digital Publishing Institute 2020. (c) Bilayer hydrogels by employing an alkali-induced network dissociation strategy. Reproduced with permission from Ref. [109], © American Chemical Society 2020.

With further research, it was found that friction properties of Gemini hydrogels under different temperature states were significantly different. Using pNIPAAM hydrogels with tunable interfacial energy, Pitenis et al. [115] measured the relationship curve between COF and sliding velocity at two temperatures: 26 °C and 34 °C. The result showed that the COF was high and unstable at 34 °C, and the frictional force exceeded the strength of the pNIPAAM probe even at speeds below 1 mm s^{-1}. Temperature changes affect frictional properties of the system by changing two parameters that control gel friction dissipation, namely the mesh size of the gel and the viscosity of the solvent. To test the conjecture, McGhee et al. [116] measured the COF of hydrogels in the temperature range from −20 °C (253 K) to 20 °C (293 K) to study the potential friction dissipation mechanism during the sliding process of PAAm hydrogel. The result showed that the friction of Gemini hydrogel increased with the decrease of temperature, and the friction increased under contact sliding with both the increase of viscosity and the decrease of mesh size. The mesh size has an important effect on the hydrogel interfacial lubrication. Urueña et al. [117] controlled the elastic modulus E of the polymer network at low speed and the polymer relaxation time τ at high speed by adjusting the size of the polymer mesh. The transition of speed-independent friction state at low speed and speed-dependent friction state at high speed was obtained. Pitenis et al. [118] achieved superlubricity of Gemini hydrogels by adjusting the mesh size (magnitude), and the lowest measured COF was 0.0013. This phenomenon was attributed to the fact that under thermal fluctuation lubrication, the COF decreased monotonously with the increase of mesh size. Thermal fluctuations at the interface were sufficient to separate the surfaces, with solvent (water) shearing in this region being the main dissipation source. Dunn et al. [119] believed that it relaxed chains and suppressed thermal fluctuations when the Gemini interface slipped faster than the single-chain relaxation time. It reduced the ability of the polymer network to dissipate friction through polymer fluctuations, thereby increasing the COF of Gemini interface during high-speed sliding. It can be seen that thermal fluctuations are of great significance in reducing the frictional dissipation of hydrogels.

5.2 Gradient/composite network structure

Tear film model is a fine, layered, multiscale mucin assembly model. The mucus layer has dense glycocalyx structure and dispersed secreted mucins network. Gel-forming mucin is gel with gradient network structure, which forms a network hydrogel interface between the glycocalyx of the conjunctiva and corneal epithelium to provide mild shear and lubrication [28]. This interface is characterized by a very soft top surface and an increase of apparent modulus and polymer volume fraction with increasing sample depth. Therefore, the synergistic effect of mucin and glycocalyx in tear film inspires the study of new gradient/composite network structure copolymers.

Most nanocomposites used for interfacial tissue exhibit gradient design or layered design. Gradient design can simulate the gradual changes of physical and mechanical properties at native tissue interfaces and can provide seamless transitions between two tissue regions. Figure 6(b) is a schematic illustration of the gradient network hydrogel structure. The network size ξ (see dashed circle) can vary with the depth of the hydrogel due to the changes of crosslinking gradient and polymer concentration. The distance between two cross-linking points of the cross-linked network (marked as network size, ξ) depends on the polymer concentration and solvent quality, etc. This characteristic length determines the key properties of the hydrogel, such as osmolarity, elastic modulus, and viscoelastic relaxation [108]. Cross et al. [120] observed that from the GelMA region (4.0 ± 2.7 μm^2) moved to the interface area (16.9 ± 14.4 μm^2) and then to the MκCA region (75.3 ± 49.0 μm^2), the average pore area at the interface gradually increased. The prepolymers created a gradient by interdiffusion before irradiation crosslinking. Lin et al. [121] used 3D printed acrylonitrile-butadiene-styrene copolymer (ABS) as the mold. The formation of the bilayer structure of the hydrogel originated from the different crosslinking densities between the surface and bulk of ABS. Due to the continuous deactivation of free radicals from the active hydrogen of ABS, the polymerization degree of monomers on the ABS surface became smaller, and then the hydrogel showed a thin and porous top layer as well as a dense and tough bottom layer. In addition, a multi-layer/composite structure can be established by combining different materials to improve the bearing capacity of the hydrogel, so as to enhance the stiffness and mechanical strength of the hydrogel, avoid the destruction of its bulk structure during friction and form good, stable lubrication under high load. Based on the soft/hard combination strategy, Daniele Dini's team [122] developed a novel composite surface of ordered hydrogel nanofiber arrays, which was confined to an anodized aluminum (AAO) nanoporous template, and had potential applications in the fields of tissue engineering and medical devices.

5.3 Hydrated lubricants

Tear osmolarity is mainly determined by the concentration of electrolytes (such as Na^+, K^+, HCO_3^{335}, etc.) in the aqueous phase of tear film, and protein, sugar are secondary factors. Rapid thinning of tear fluid due to evaporation can lead to tear film instability, which in turn causes regional dryness and significant increase in tear film osmolarity [123]. Amphiphilic polar lipids act as surfactants which bring the hydrophilic aqueous phase into contact with non-polar lipids. The tear lipid film has high viscosity and low surface tension, which promotes tear film respreading after blinking and delays tearing evaporation. Lipids and electrolytes play an important role in maintaining ocular surface homeostasis. As a domain composed of negatively charged sugar chains, Lubricin forms a "polymer brush-like" lubrication layer on the surface of the cornea and conjunctiva, which can effectively reduce COF on the ocular surface [124, 125]. Likewise, natural or synthetic materials such as hydrated ions, liposomes, and amphiphilic block copolymers have a major part to play in hydration lubrication.

The basic concept of hydration lubrication mechanism was first proposed in the surface force balance (SFB) study in 2002. Raviv and Klein [126] measured the frictional force (average pressure $P \approx 0.3$ MPa) between mica surfaces in a highly concentrated salt solution under the hydration repulsion state, revealing the mechanism of hydration lubrication for the first time. Its core is the formation of strong hydration layer around polar groups, which can withstand large pressure without being squeezed out. It is further extended to other bases metal ions subsequently. Han et al. [127, 128] found the macroscopic hydration superlubricity behavior of monovalent (Li^+, Na^+, K^+), divalent (Mg^{2+}, Ca^{2+}, Sr^{2+}) and trivalent (Al^{3+}, Ce^{3+}, La^{3+}, Cr^{3+}) cations. After acid running-in, the above cations all could achieve stable superlubricity and the trivalent ions showed better superlubricity properties under the contact pressure of about 0.25 GPa. As a result, a new concentration-dependent hydration lubrication model was proposed, as shown in Fig. 7(a). The relationship formula among friction, load and film thickness ratio was established and the hydration lubrication theory of monovalent, divalent and trivalent ions was unified. The composite of hydrated ions and polymer solution is effective in cooperating lubrication. Li et al. [129] found that hydrated Na^+ ions would preferentially adsorb to the solid surface during friction, making the shear interface change from a polymer film/polymer film to a solid/polymer film. At the same time, it also generated hydration repulsion and low shear stress between the solid surfaces. The superlubricity of the PVA/NaCl mixture was attributed to a combination of hydration and hydrodynamic effects. The dissipation of frictional energy between the sliding solid surfaces in aqueous media can be carried out through different pathways. Gaisinskaya-Kipnis et al. [130]

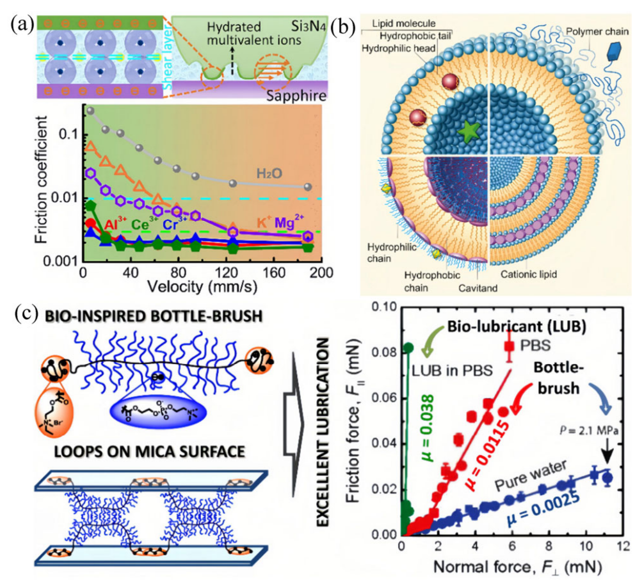

Fig. 7 (a) Schematic diagram of lubrication model: the superlubricity mechanism achieved by hydrated polyvalent ions between the Si_3N_4 spheres and sapphire discs. Reproduced with permission from Ref. [127], © American Chemical Society 2019. (b) Liposome structure. Reproduced with permission from Ref. [131], © The Author(s) 2012. (c) Adsorption of bottle brush polymer simulating lubricin on mica surface. Reproduced with permission from Ref. [132], © American Chemical Society 2014.

used SFB to study how this dissipation was mediated by a series of hydrated cations $M^+ = Li^+$, Na^+ and K^+ systematically. The study showed that lubrication could improve with the degree of ionic hydration and the size of the hydration shell was the primary cause of dissipation. Ma et al. [133] found that hydrated ions were trapped at a gap of 0.4–1 nm when the smooth charged surfaces of atoms slid over each other. Energy dissipation within the shear hydration shells was measured; dissipation modes of friction were separated; the viscous losses in the subnanometre hydration shells were identified. The result showed that viscous dissipation in the hydrated shells was 250 times higher than that of non-hydration water, thus revealing the origin of hydration lubrication.

Liposomes, known as phospholipid vesicles, are widely present in the synovial of biological joints and tear film as natural boundary lubricants. Liposomes are macromolecules composed of amphoteric phosphatidylcholine groups and non-polar aliphatic chains, with high surface activity and amphiphilic properties (hydrophilic head groups containing nitrogen and phosphorus, and long hydrophobic hydrocarbon tails). Liposomes usually exhibit a phospholipid bilayer or vesicle structure, as shown in Fig. 7(b) [127], whose excellent boundary lubrication properties are mainly attributed to the relative sliding between exposed highly hydrated head groups. HA, lubricin and phospholipids are ubiquitous molecules in synovial joints, which play a synergistic role in joint lubrication. Seror et al. [134] found that the boundary lubrication layer was formed by the composite of surface-anchored HA molecules and phosphatidylcholine lipids in joints, with a COF of 0.001 under the pressures of more than 100 atmospheres. Thus, the hydration mechanism of boundary lubrication for synovial joint was revealed. In addition to natural lipids, various synthetic lipids have also been gradually developed. Goldberg et al. [135] prepared small unilamellar vesicles (SUVs) of hydrogenated soy phosphatidylcholine (HSPC) lipids. The highly hydrated phosphatidylcholine groups exposed on the surface of the liposomes formed hydrated lubrication, and the vesicle adsorption layer was self-assembled into a close-packed adsorption layer on the solid surface. Dynamic COF can be reduced to 2×10^{-5} at pressures up to more than 100 atm. The lubricating ability of liposomes is closely related to the acyl chain length. Sorkin et al. [136] found that the lubricating ability of liposomes improved with the increase of the acyl chain length, but the trend was opposite in SUV dispersions. The difference originated from rapid self-healing of the softer surface layers (POPC and DMPC in liquid disordered phase), which made the robustness of DPPC or DSPC (both in their solid ordered phase) less important. The complexation of liposomes with other polymer materials helps to form a stable boundary lubrication layer, thereby effectively improving the lubrication properties of liposomes. Angayarkanni et al. [137] used SFB to examine the interaction between surface-adsorbed layers of PEO complexed and SUVs or PC lipid bilayers. Excellent lubrication was observed between the surfaces bearing PEO-PC, with the COF as low as 10^{-4}–10^{-3} at the contact stress of 6.5 MPa.

Affected by the amphiphilic characteristics of lubricin, the synthesis of amphiphilic block copolymers has become a research hotspot. Amphiphilic copolymers containing covalently-linked hydrophilic and hydrophobic blocks have unique self-assembly ability to form molecular ordered body. The hydrophobic segments in the polymer chain structure can be assembled on the surface of the hydrophobic substrate through hydrophobic interactions, while the hydrophilic segments form a boundary lubrication layer by extending outward to bind water molecules [138]. The high lubrication properties of polymer brushes were first reported in 1993/1994. Polystyrene brushes were formed by grafting the ends of amphiphilic chains to the mica surface. Under the contact pressure of 1 MPa, the COF of the copolymer could be effectively reduced to below 0.001 [139]. Depending on the chemistry properties and distribution of the side chains, amphiphilic multi-component molecular brushes can generally be divided into a variety of structural types such as AB, ABA or ABC block copolymer brushes, tadpole-type block grafting, xenografting, asymmetric and ring brushes [140]. The chemical composition, graft density, charge, uniformity, length and distribution of the main chain and side chain of the molecular brushes are different, and tribological properties of the brushes also have great differences.

Raviv et al. [141] reported the water lubrication behavior of poly (methyl methacrylate)-block-poly (sodium sulphonated glycidyl methacrylate) copolymer (PMMA-b-PSGMA) on the surface of hydrophobic mica. The PMMA chains segment could be anchored in situ on the hydrophobic mica surface, while the hydrophilic anionic PSGMA chains extended outward to form a "brush" structure, and the COF of the copolymer in water could be reduced to 0.0006. Banquy et al. [128] reported a bottle-brush polymer whose structure was similar to lubricin and assessed the interaction forces between two mica surfaces fully covered by the polymer using a surface forces apparatus, as shown in Fig. 7(c). The confined lubricating fluid obeyed Ammonton's law and exhibited a low COF of about 10^{-3} due to the strong shear thinning of the confined fluid and the osmotic repulsive forces that dominated the overall (dynamic and equilibrium) surface interactions.

Hydrated ions, liposomes and amphiphilic block copolymers can achieve good lubrication effects under different friction conditions, and exhibit extremely low COF under certain loads and speeds. The core idea is to form a firm hydration shell around charged ions or polar groups, which can support large normal stress without being squeezed out, and form a slip layer with extremely low shear stress at the mutual sliding interface, thus forming hydration lubrication.

5.4 Dynamic regulation of friction

Tear film is a thin mucin network with dynamic regulatory properties that transforms from a gel-like fluid at low shear stress to a low viscosity fluid at high shear rate. Sol-gel transition in mucin solution is reversible and the transition point can be tuned by parameters including pH, temperature, and ionic strength [142]. Traditional hydrogels composed of permanent covalent cross-links are irreversibly broken upon shearing. Yet there are a large number of disulfide bonds in the mucin network, which can rapidly restore their cross-link density through the recombination of their transient interactions [143]. It is the dynamic recombination ability that provides mucus with the viscoelasticity needed to mediate shear stress and adhere to epithelial cells. The phenomenon has led to the investigation of tunable frictional behavior of water-based polymer materials. The polymer friction phenomenon based on non-covalent and dynamic covalent interactions are as follows.

Non-covalently cross-linked hydrogels are mainly bonded through hydrogen bonds, metal ions coordination, host-guest interactions, π–π stacking and van der Waals forces. Compared with stable and strong covalent interactions, non-covalent interactions are often in a dynamic state of breaking and reforming, which makes this kind of hydrogel show macroscopic properties such as reversible/dynamic sol-gel transition, stimuli-responsiveness and tunable strength of molecular association [144]. The researchers obtained a variety of copolymer materials with tunable friction properties by controlling factors such as pH, temperature, light, ions and force. Inspired by fish skin, Wu et al. [145] changed the molecular chain conformation of responsive hydrogels to achieve ultra-low COF by sequentially adjusting pH and temperature, and could reversibly switch the three COF levels in different states for many times. Chen et al. [146] reported a near-infrared photothermal microgel which could be used as a smart lubricating additive for regulating interfacial friction, as shown in Fig. 8(a), and it could achieve reversible adjustment of interfacial friction under the effect of NIR irradiation. Semi-convertible hydrogels composed of stable covalent frameworks and stimuli-responsive supramolecular networks could switch between solid–liquid states under UV and visible light stimulation to achieve reversible photoresponsive lubrication regulation [147]. Hua et al. [148] investigated the tunable friction behavior of chitosan-silver ion hydrogels by adding Cl^- or excess Ag^+, dynamically and reversibly adjusting the COF between the two phases. Superlubricity could be achieved with both solution and gel typed lubricants under elastohydrodynamic lubrication. Since the equilibrium of weak non-covalent interactions is easily disrupted, Zhang et al. [149] developed a thixotropic supramolecular hydrogel whose viscosity decreased with the applied shear, and the viscosity would recover in time when the shear was stopped. So the gel-sol transition could be controlled by the shear forces and then the lubrication properties of the hydrogel interface could be adjusted. Based on the above studies, Wu et al. [150] summarized the latest research progress of controllable interfacial friction

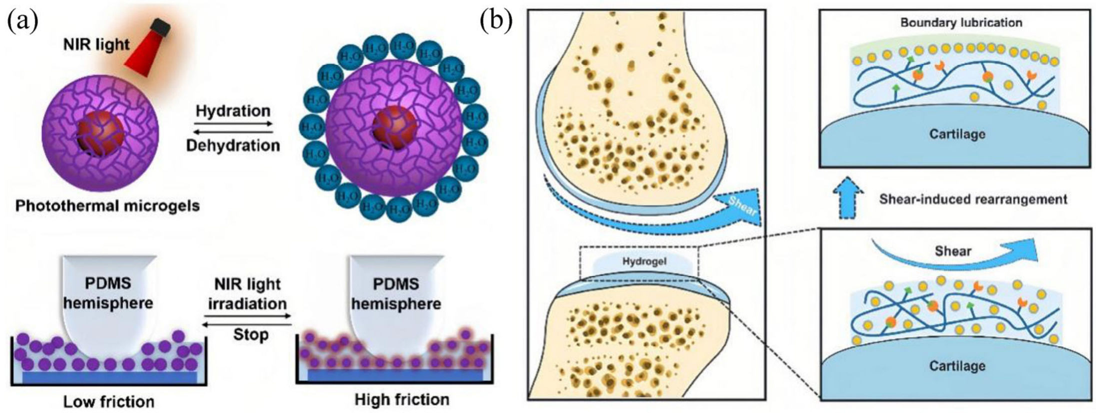

Fig. 8 (a) NIR-light modulation of interfacial friction in PTMGs. Reproduced with permission from Ref. [146], © American Chemical Society 2021. (b) shear-induced rearrangement of liposome structure to form a boundary layer. Reproduced with permission from Ref. [151], © Elsevier B.V. 2022.

on solid/solid and solid/liquid surfaces, and analyzed the effects of external stimuli (such as solvent, electrolyte, pH, temperature, light, electric potential, magnetic field, etc.) on surface chemistry, interfacial charge and topography at the friction interface, thereby triggering the transition of the friction properties of environmentally sensitive materials.

Covalently cross-linked hydrogel polymer networks synthesized by traditional chemical methods are usually irreversible, and hydrogels tend to exhibit relatively brittle properties and are prone to fatigue or damage. However, dynamic covalent bonds (such as boronic esters, disulfides and imine/hydrazone bonds, etc. [152]) will dynamically break and reform according to external stimuli. They show good dynamic reversibility, and provide shear thinning and self-healing properties for hydrogels [153]. Dynamic covalent bonds combine the properties of covalent bonds and non-covalent bonds, that is, they can be formed and broken reversibly like non-covalent bonds and can also be as strong and durable as covalent bonds [154]. Yu et al. [155] developed an analytical theory based on polymer networks, which could mechanically simulate the constitutive behavior and interfacial self-healing behavior of dynamic polymer networks. They predicted the stress-stretching behavior of pristine, self-healing dynamic polymer networks and healing strength that changes with healing time. In the field of lubrication research, as shown in Fig. 8(b), Lei et al. [145] incorporated liposomes into HA hydrogels with dynamic covalent bonds, enabling them to recombine in response to shear. The internal liposomal microreservoirs in the HA matrix continuously released lipids on the sliding surface, forming a boundary layer to provide stable lubrication. Zhang et al. [156] hierarchically self-assembled sodium thioctate into a highly ordered supramolecular layered network. By combining the unique dynamic covalent ring-opening polymerization of sodium thioctate and the evaporation-induced interface confinement effect, a supramolecular layer that could bind water molecules as structural water was constructed, and it was used as an interlayer lubricant to adjust the mechanical properties and self-healing ability of materials.

6 Summary and Outlook

This review focuses on recent advances in ocular lubrication. Normal operation of ocular lubrication system depends on tear film stability. Tear film is attached to the cornea in a gel state without shearing and the gel is decomposed at high shear rates during the blinking process. The eyelid and cornea contact and slide to form good hydrodynamic lubrication, and low shear stress protects the cornea from fatigue damage under high-frequency blinking conditions. For the people wearing CL and DES patients with tear film homeostasis imbalance, the ocular lubrication state is boundary lubrication and the friction between ocular sliding surfaces usually keeps higher. TBU occurs when critical thickness of tear film is reached. TBU is affected by various physical effects such as capillarity, the Marangoni effect, van der Waals forces and evaporation. Short-lived TBU is a typical symptom of DES. Natural and synthetic polymers for bio-boundary lubrication are of great significance for the treatment of DES, and the study of various gel preparations also provides a theoretical guidance for long-term lubrication of ocular surface. As a medical device in direct contact with ocular surface, the tribological properties of CL directly affect ocular lubrication stability. Therefore, the research on the surface coating of CL can help to optimize their interface properties, thereby avoiding ocular inflammation caused by long-term wearing of CL. What's more, inspired by natural ocular lubrication system, this paper discusses contact models for Gemini hydrogels, gradient (composite) gel network structure, various hydrated lubricants and hydrogel tribological behavior changes based on dynamic interactions such as non-covalent and reversible covalent. It has some reference significance to the development of ocular lubricants and ocular lubrication theories.

Finally, certain potential points related to ocular lubrication are proposed as follows; i) To further understand the origin of the ocular friction, it is necessary to conduct in-depth research on the behavior of ocular friction dissipation. How to realize dynamic monitoring of microscopic changes such as friction dissipation? ii) There are two types of lubrication states in the eye: hydrodynamic lubrication and boundary lubrication. How is mutual transformation mechanism during blinking? iii) Tear film stability is affected by different factors such as evaporation, osmolarity and tangential flow. How to explore the influence of various physical effects on the evolution mechanism of tear film systematically for tear film rupture phenomena such as black lines, black dots and stripes? vi) Natural tear fluid has the characteristics of gel-sol transformation and shear thinning to meet the specific working conditions of ocular lubrication system. How to improve the compatibility of various synthetic lubricants to the ocular environment and ensure their lubrication effect? In summary, the exploration for these issues will greatly facilitate the research on ocular tribology and improve the ability to regulate ocular lubrication stability. Thereby, it is quite necessary to further investigate ocular tribological behavior in the future.

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Declaration of competing interest

The authors have no competing interests to declare that are relevant to the content of this article.

References

[1] Luo J B, Liu M, Ma L R. Origin of friction and the new frictionless technology—Superlubricity: Advancements and future outlook. *Nano Energy* **86**: 106092 (2021)

[2] Zheng Y, Bashandeh K, Shakil A, Jha S, Polycarpou A A. Review of dental tribology: Current status and challenges. *Tribol Int* **166**: 107354 (2022)

[3] Seror J, Zhu L Y, Goldberg R, Day A J, Klein J. Supramolecular synergy in the boundary lubrication of synovial joints. *Nat Commun* **6**: 6497 (2015)

[4] Holly F J, Holly T F. Advances in ocular tribology. *Adv Exp Med Biol* **350**: 275–283 (1994)

[5] Dowson D. Whither tribology? *Wear* **16**(4): 303–304 (1970)

[6] Dowson D. Bio-tribology. *Faraday Discuss* **156**: 9–30 (2012)

[7] Hsu S M. Boundary lubrication: Current understanding. *Tribol Lett* **3**(1): 1–11 (1997)

[8] Zakharov S M. Hydrodynamic lubrication research: Current situation and future prospects. *J Frict Wear* **31**(1): 56–67 (2010)

[9] Gellman A J, Spencer N D. Surface chemistry in tribology. *Proc Inst Mech Eng Part J J Eng Tribol* **216**(6): 443–461 (2002)

[10] Jin Z M, Dowson D. Bio-friction. *Friction* **1**(2): 100–113 (2013)

[11] Hart S M, McGhee E O, Urueña J M, Levings P P, Eikenberry S S, Schaller M A, Pitenis A A, Sawyer W G. Surface gel layers reduce shear stress and damage of corneal epithelial cells. *Tribol Lett* **68**(4): 106 (2020)

[12] Seo J, Byun W Y, Alisafaei F, Georgescu A, Yi Y S, Massaro-Giordano M, Shenoy V B, Lee V, Bunya V Y, Huh D. Multiscale reverse engineering of the human ocular surface. *Nat Med* **25**(8): 1310–1318 (2019)

[13] Bertsch P, Bergfreund J, Windhab E J, Fischer P. Physiological fluid interfaces: Functional microenvironments, drug delivery targets, and first line of defense. *Acta Biomater* **130**: 32–53 (2021)

[14] Stapleton F, Alves M, Bunya V Y, Jalbert I, Lekhanont K, Malet F, Na K S, Schaumberg D, Uchino M, Vehof J, et al. TFOS DEWS II epidemiology report. *Ocul Surf* **15**(3): 334–365 (2017)

[15] Craig J P, Nichols K K, Akpek E K, Caffery B, Dua H S, Joo C K, Liu Z G, Nelson J D, Nichols J J, Tsubota K, et al. TFOS DEWS II definition and classification report. *Ocul Surf* **15**(3): 276–283 (2017)

[16] Bron A J, de Paiva C S, Chauhan S K, Bonini S, Gabison E E, Jain S, Knop E, Markoulli M, Ogawa Y, Perez V, et al. TFOS DEWS II pathophysiology report. *Ocul Surf* **15**(3): 438–510 (2017)

[17] Ang B C H, Sng J J, Wang P X H, Htoon H M, Tong L H T. Sodium hyaluronate in the treatment of dry eye syndrome: A systematic review and meta-analysis. *Sci Rep* **7**(1): 9013 (2017)

[18] Labetoulle M, Benitez-Del-Castillo J M, Barabino S, Herrero Vanrell R, Daull P, Garrigue J S, Rolando M. Artificial tears: Biological role of their ingredients in the management of dry eye disease. *Int J Mol Sci* **23**(5): 2434 (2022)

[19] Rodriguez Benavente M C, Argüeso P. Glycosylation pathways at the ocular surface. *Biochem Soc Trans* **46**(2): 343–350 (2018)

[20] Madl A C, Fuller G F, Myung D. Modeling and restoring the tear film. *Curr Ophthalmol Rep* **8**(4): 281–300 (2020)

[21] Sridhar M S. Anatomy of cornea and ocular surface. *Indian J Ophthalmol* **66**(2): 190–194 (2018)

[22] Ramos T, Scott D, Ahmad S. An update on ocular surface epithelial stem cells: Cornea and conjunctiva. *Stem Cells Int* **2015**: 601731 (2015)

[23] Ohashi Y, Dogru M, Tsubota K. Laboratory findings in tear fluid analysis. *Clin Chim Acta* **369**(1): 17–28 (2006)

[24] Pitenis A A, Urueña J M, Hormel T T, Bhattacharjee T, Niemi S R, Marshall S L, Hart S M, Schulze K D, Angelini T E, Sawyer W G. Corneal cell friction: Survival, lubricity, tear films, and mucin production over extended duration *in vitro* studies. *Biotribology* **11**: 77–83 (2017)

[25] Masmali A M, Purslow C, Murphy P J. The tear ferning test: A simple clinical technique to evaluate the ocular tear film. *Clin Exp Optom* **97**(5): 399–406 (2014)

[26] Yamada M, Mochizuki H, Kawai M, Yoshino M, Mashima Y. Fluorophotometric measurement of pH of human tears *in vivo*. *Curr Eye Res* **16**(5): 482–486 (1997)

[27] Pitenis A A, Urueña J M, McGhee E O, Hart S M, Reale E R, Kim J, Schulze K D, Marshall S L, Bennett A I, Niemi S R, et al. Challenges and opportunities in soft tribology. *Tribol Mater Surf Interfaces* **11**(4): 180–186 (2017)

[28] Pedro D I, Nguyen D T, Rosa J G, Diodati N, Kim J, Bowman J I, Olson R A, Urueña J M, Sumerlin B S, Sawyer W G. Gel-forming mucin improves lubricity across model gemini epithelial cell interfaces. *Tribol Lett* **69**(4): 155 (2021)

[29] Svitova T F, Lin M C. Dynamic interfacial properties of human tear-lipid films and their interactions with model-tear proteins *in vitro*. *Adv Colloid Interface Sci* **233**: 4–24 (2016)

[30] Hattrup C L, Gendler S J. Structure and function of the cell surface (tethered) mucins. *Annu Rev Physiol* **70**: 431–457 (2008)

[31] Gouveia S M, Tiffany J M. Human tear viscosity: An interactive role for proteins and lipids. *Biochim Biophys Acta* **1753**(2): 155–163 (2005)

[32] Downie L E, Bandlitz S, Bergmanson J P G, Craig J P, Dutta D, Maldonado-Codina C, Ngo W, Siddireddy J S, Wolffsohn J S. CLEAR—Anatomy and physiology of the anterior eye. *Cont Lens Anterior Eye* **44**(2): 132–156 (2021)

[33] Uchino Y. The ocular surface glycocalyx and its alteration in dry eye disease: A review. *Invest Ophthalmol Vis Sci* **59**(14): DES157–DES162 (2018)

[34] Hori Y. Secreted mucins on the ocular surface. *Invest Ophthalmol Vis Sci* **59**(14): DES151–DES156 (2018)

[35] Schmidt T A, Sullivan D A, Knop E, Richards S M, Knop N, Liu S H, Sahin A, Darabad R R, Morrison S, Kam W R, et al. Transcription, translation, and function of lubricin, a boundary lubricant, at the ocular surface. *JAMA Ophthalmol* **131**(6): 766 (2013)

[36] Samsom M, Chan A, Iwabuchi Y, Subbaraman L, Jones L, Schmidt T A. *In vitro* friction testing of contact lenses and human ocular tissues: Effect of proteoglycan 4 (PRG4). *Tribol Int* **89**: 27–33 (2015)

[37] Bai Y Q, Ngo W, Khanal S, Nichols J J. Characterization of the thickness of the tear film lipid layer in meibomian gland dysfunction using high resolution optical microscopy. *Ocul Surf* **24**: 34–39 (2022)

[38] King-Smith P E, Bailey M D, Braun R J. Four characteristics and a model of an effective tear film lipid layer (TFLL). *Ocul Surf* **11**(4): 236–245 (2013)

[39] Georgiev G A, Eftimov P, Yokoi N. Contribution of mucins towards the physical properties of the tear film: A modern update. *Int J Mol Sci* **20**(24): 6132 (2019)

[40] Tiffany J M. Tears in health and disease. *Eye* **17**(8): 923–926 (2003)

[41] Cope C, Dilly P N, Kaura R, Tiffany J M. Wettability of the corneal surface: A reappraisal. *Curr Eye Res* **5**(10): 777–785 (1986)

[42] Nagyová B, Tiffany J M. Components responsible for the surface tension of human tears. *Curr Eye Res* **19**(1): 4–11 (1999)

[43] Davidson H J, Kuonen V J. The tear film and ocular mucins. *Vet Ophthalmol* **7**(2): 71–77 (2004)

[44] Herbaut A, Liang H, Denoyer A, Baudouin C, Labbé A. Tear film analysis and evaluation of optical quality: A review of the literature. *J Fr Ophtalmol* **42**(2): e21–e35 (2019)

[45] Braun R J, Gewecke N R, Begley C G, King-Smith P E, Siddique J I. A model for tear film thinning with osmolarity and fluorescein. *Invest Ophthalmol Vis Sci* **55**(2): 1133 (2014)

[46] Lu X B, Khonsari M M, Gelinck E R M. The stribeck curve: Experimental results and theoretical prediction. *J Tribol* **128**(4): 789–794 (2006)

[47] Coles J M, Chang D P, Zauscher S. Molecular mechanisms of aqueous boundary lubrication by mucinous glycoproteins. *Curr Opin Colloid Interface Sci* **15**(6): 406–416 (2010)

[48] Pult H, Tosatti S G P, Spencer N D, Asfour J M, Ebenhoch M, Murphy P J. Spontaneous blinking from a tribological viewpoint. *Ocul Surf* **13**(3): 236–249 (2015)

[49] Cher I. A new look at lubrication of the ocular surface: Fluid mechanics behind the blinking eyelids. *Ocul Surf* **6**(2): 79–86 (2008)

[50] Dunn A C, Tichy J A, Urueña J M, Sawyer W G. Lubrication regimes in contact lens wear during a blink. *Tribol Int* **63**: 45–50 (2013)

[51] Rabiah N I, Sato Y, Kannan A, Kress W, Straube F, Fuller G G. Understanding the adsorption and potential tear film stability properties of recombinant human lubricin and bovine submaxillary mucins in an *in vitro* tear film model. *Colloids Surf B Biointerfaces* **195**: 111257 (2020)

[52] Samsom M, Iwabuchi Y, Sheardown H, Schmidt T A. Proteoglycan 4 and hyaluronan as boundary lubricants for model contact lens hydrogels. *J Biomed Mater Res B Appl Biomater* **106**(3): 1329–1338 (2018)

[53] Gaffney E A, Tiffany J M, Yokoi N, Bron A J. A mass and solute balance model for tear volume and osmolarity in the normal and the dry eye. *Prog Retin Eye Res* **29**(1): 59–78 (2010)

[54] Yokoi N, Bron A J, Georgiev G A. The precorneal tear film as a fluid shell: The effect of blinking and saccades on tear film distribution and dynamics. *Ocul Surf* **12**(4): 252–266 (2014)

[55] Bai Y Q, Nichols J J. Advances in thickness measurements and dynamic visualization of the tear film using non-invasive optical approaches. *Prog Retin Eye Res* **58**: 28–44 (2017)

[56] Braun R J. Dynamics of the tear film. *Annu Rev Fluid Mech* **44**: 267–297 (2012)

[57] Zhong L, Braun R J, Begley C G, King-Smith P E. Dynamics of fluorescent imaging for rapid tear thinning. *Bull Math Biol* **81**(1): 39–80 (2019)

[58] Cher I. Fluids of the ocular surface: Concepts, functions and physics. *Clin Exp Ophthalmol* **40**(6): 634–643 (2012)

[59] Yokoi N, Georgiev G A. Tear-film-oriented diagnosis for dry eye. *Jpn J Ophthalmol* **63**(2): 127–136 (2019)

[60] Sharma A, Tiwari S, Khanna R, Tiffany J M. (1998) Hydrodynamics of meniscus-induced thinning of the tear film. *Lacrimal Gland, Tear Film, and Dry Eye Syndromes 2*. Boston, MA: Springer US: 425–431

[61] Miller K L, Polse K A, Radke C J. Black-line formation and the "perched" human tear film. *Curr Eye Res* **25**(3): 155–162 (2002)

[62] Allouche M, Abderrahmane H A, Djouadi S M, Mansouri K. Influence of curvature on tear film dynamics. *Eur J Mech B* **66**: 81–91 (2017)

[63] Scriven L E, Sternling C V. The Marangoni effects. *Nature* **187**: 186–188 (1960)

[64] Lin S P, Brenner H. Marangoni convection in a tear film. *J Colloid Interface Sci* **85**(1): 59–65 (1982)

[65] Aydemir E, Breward C J W, Witelski T P. The effect of polar lipids on tear film dynamics. *Bull Math Biol* **73**(6): 1171–1201 (2011)

[66] Zhong L, Ketelaar C F, Braun R J, Begley C G, King-Smith P E. Mathematical modelling of glob-driven tear film breakup. *Math Med Biol A J IMA* **36**(1): 55–91 (2019)

[67] Sharma A, Ruckenstein E. Mechanism of tear film rupture and formation of dry spots on cornea. *J Colloid Interface Sci* **106**(1): 12–27 (1985)

[68] Sharma A, Khanna R, Reiter G. A thin film analog of the corneal mucus layer of the tear film: An enigmatic long range non-classical DLVO interaction in the breakup of

thin polymer films. *Colloids Surf B Biointerfaces* **14**(1–4): 223–235 (1999)

[69] Dey M, Vivek A S, Dixit H N, Richhariya A, Feng J J. A model of tear-film breakup with continuous mucin concentration and viscosity profiles. *J Fluid Mech* **858**: 352–376 (2019)

[70] Choudhury A, Dey M, Dixit H N, Feng J J. Tear-film breakup: The role of membrane-associated mucin polymers. *Phys Rev E* **103**: 013108 (2021)

[71] Tiffany J M. The viscosity of human tears. *Int Ophthalmol* **15**(6): 371–376 (1991)

[72] Zhang Y L, Matar O K, Craster R V. Rupture analysis of the corneal mucus layer of the tear film. *Mol Simul* **30**(2–3): 167–172 (2004)

[73] Mehdaoui H, Abderrahmane H A, Bouda F N, Koulali A, Hamani S. 2D numerical simulation of tear film dynamics: Effects of shear-thinning properties. *Eur J Mech B* **90**: 128–136 (2021)

[74] Braun R J, King-Smith P E, Begley C G, Li L F, Gewecke N R. Dynamics and function of the tear film in relation to the blink cycle. *Prog Retin Eye Res* **45**: 132–164 (2015)

[75] Bruna M, Breward C. The influence of non-polar lipids on tear film dynamics. *J Fluid Mech* **746**: 565–605 (2014)

[76] Siddique J I, Braun R J. Tear film dynamics with evaporation, osmolarity and surfactant transport. *Applied Mathematical Modelling* **39**(1): 255-269 (2015)

[77] Peng C C, Cerretani C, Braun R J, Radke C J. Evaporation-driven instability of the precorneal tear film. *Adv Colloid Interface Sci* **206**: 250–264 (2014)

[78] Braun R J, Driscoll T A, Begley C G, King-Smith P E, Siddique J I. On tear film breakup (TBU): Dynamics and imaging. *Math Med Biol A J IMA* **35**(2): 145–180 (2018)

[79] Braun R J, Driscoll T A, Begley C G. Mathematical models of the tear film. Ocular Fluid Dynamics. Cham: Birkhäuser, 2019: 387–432.

[80] Stapf M R, Braun R J, King-Smith P E. Duplex tear film evaporation analysis. *Bull Math Biol* **79**(12): 2814–2846 (2017)

[81] Crouzier T, Boettcher K, Geonnotti A R, Kavanaugh N L, Hirsch J B, Ribbeck K, Lieleg O. Modulating mucin hydration and lubrication by deglycosylation and polyethylene glycol binding. *Adv Materials Inter* **2**(18): 1500308 (2015)

[82] Samsom M L, Morrison S, Masala N, Sullivan B D, Sullivan D A, Sheardown H, Schmidt T A. Characterization of full-length recombinant human Proteoglycan 4 as an ocular surface boundary lubricant. *Exp Eye Res* **127**: 14–19 (2014)

[83] Bielory L, Wagle P. Ocular surface lubricants. *Curr Opin Allergy Clin Immunol* **17**(5): 382–389 (2017)

[84] Aragona P, Simmons P A, Wang H P, Wang T. Physicochemical properties of hyaluronic acid-based lubricant eye drops. *Translational Vision Science & Technology* **8**(6): 2 (2019)

[85] Rangarajan R, Kraybill B, Ogundele A, Ketelson H A. Effects of a hyaluronic acid/hydroxypropyl guar artificial tear solution on protection, recovery, and lubricity in models of corneal epithelium. *J Ocul Pharmacol Ther* **31**(8): 491–497 (2015)

[86] Černohlávek M, Brandejsová M, Štěpán P, Vagnerová H, Hermannová M, Kopecká K, Kulhánek J, Nečas D, Vrbka M, Velebný V, et al. Insight into the lubrication and adhesion properties of hyaluronan for ocular drug delivery. *Biomolecules* **11**(10): 1431 (2021)

[87] Lee D, Lu Q Z, Sommerfeld S D, Chan A, Menon N G, Schmidt T A, Elisseeff J H, Singh A. Targeted delivery of hyaluronic acid to the ocular surface by a polymer-peptide conjugate system for dry eye disease. *Acta Biomater* **55**: 163–171 (2017)

[88] Dunn A C, Urueña J M, Huo Y C, Perry S S, Angelini T E, Sawyer W G. Lubricity of surface hydrogel layers. *Tribol Lett* **49**(2): 371–378 (2013)

[89] Hart S M, McGhee E O, Urueña J M, Levings P P, Eikenberry S S, Schaller M A, Pitenis A A, Sawyer W G. Surface gel layers reduce shear stress and damage of corneal epithelial cells. *Tribol Lett* **68**(4): 106 (2020)

[90] Acar D, Molina-Martínez I T, Gómez-Ballesteros M, Guzmán-Navarro M, Benítez-Del-Castillo J M, Herrero-Vanrell R. Novel liposome-based and *in situ* gelling artificial tear formulation for dry eye disease treatment. *Cont Lens Anterior Eye* **41**(1): 93–96 (2018)

[91] Kim Y C, Shin M D, Hackett S F, Hsueh H T, Silva R L E, Date A, Han H, Kim B J, Xiao A, Kim Y, et al. Gelling hypotonic polymer solution for extended topical drug delivery to the eye. Nat *Biomed Eng* **4**(11): 1053–1062 (2020)

[92] Rennie A C, Dickrell P L, Sawyer W G. Friction coefficient of soft contact lenses: Measurements and modeling. *Tribol Lett* **18**(4): 499–504 (2005)

[93] Carvalho A L, Vilhena L M, Ramalho A. Study of the frictional behavior of soft contact lenses by an innovative method. *Tribol Int* **153**: 106633 (2021)

[94] Roba M, Duncan E G, Hill G A, Spencer N D, Tosatti S G P. Friction measurements on contact lenses in their operating environment. *Tribol Lett* **44**(3): 387 (2011)

[95] Sterner O, Aeschlimann R, Zürcher S, Scales C, Riederer D, Spencer N D, Tosatti S G P. Tribological classification of contact lenses: From coefficient of friction to sliding work. *Tribol Lett* **63**(1): 9 (2016)

[96] Eftimov P B, Yokoi N, Peev N, Paunski Y, Georgiev G A. Relationships between the material properties of silicone

hydrogels: Desiccation, wettability and lubricity. *J Biomater Appl* **35**(8): 933–946 (2021)

[97] Hofmann G, Jubin P, Gerligand P, Gallois-Bernos A, Franklin S, Smulders N, Gerhardt L C, Valster S. *In-vitro* method for determining corneal tissue friction and damage due to contact lens sliding. *Biotribology* **5**: 23–30 (2016)

[98] Zhu D K, Liu Y P, Gilbert J L. Micromechanical measurement of adhesion of dehydrating silicone hydrogel contact lenses to corneal tissue. *Acta Biomater* **127**: 242–251 (2021)

[99] Samsom M, Chan A, Iwabuchi Y, Subbaraman L, Jones L, Schmidt T A. *In vitro* friction testing of contact lenses and human ocular tissues: Effect of proteoglycan 4 (PRG4). *Tribol Int* **89**: 27–33 (2015)

[100] Samsom M, Iwabuchi Y, Sheardown H, Schmidt T A. Proteoglycan 4 and hyaluronan as boundary lubricants for model contact lens hydrogels. *J Biomed Mater Res B Appl Biomater* **106**(3): 1329–1338 (2018)

[101] Rickert C A, Wittmann B, Fromme R, Lieleg O. Highly transparent covalent mucin coatings improve the wettability and tribology of hydrophobic contact lenses. *ACS Appl Mater Interfaces* **12**(25): 28024–28033 (2020)

[102] Winkeljann B, Boettcher K, Balzer B N, Lieleg O. Mucin coatings prevent tissue damage at the cornea–contact lens interface. *Adv Materials Inter* **4**(19): 1700186 (2017)

[103] Korogiannaki M, Samsom M, Matheson A, Soliman K, Schmidt T A, Sheardown H. Investigating the synergistic interactions of surface immobilized and free natural ocular lubricants for contact lens applications: A comparative study between hyaluronic acid and proteoglycan 4 (lubricin). *Langmuir* **37**(3): 1062–1072 (2021)

[104] White C J, McBride M K, Pate K M, Tieppo A, Byrne M E. Extended release of high molecular weight hydroxypropyl methylcellulose from molecularly imprinted, extended wear silicone hydrogel contact lenses. *Biomaterials* **32**(24): 5698–5705 (2011)

[105] Dunn A C, Sawyer W G, Angelini T E. Gemini interfaces in aqueous lubrication with hydrogels. *Tribol Lett* **54**(1): 59–66 (2014)

[106] Bonyadi S Z, Hasan M M, Kim J, Mahmood S, Schulze K D, Dunn A C. Review: Friction and lubrication with high water content crosslinked hydrogels. *Tribol Lett* **68**(4): 119 (2020)

[107] Liu W R, Simič R, Liu Y H, Spencer N D. Effect of contact geometry on the friction of acrylamide hydrogels with different surface structures. *Friction* **10**(3): 360–373 (2022)

[108] Shoaib T, Espinosa-Marzal R M. Advances in understanding hydrogel lubrication. *Colloids Interfaces* **4**(4): 54 (2020)

[109] Qu M H, Liu H, Yan C Y, Ma S H, Cai M R, Ma Z F, Zhou F. Layered hydrogel with controllable surface dissociation for durable lubrication. *Chem Mater* **32**(18): 7805–7813 (2020)

[110] Chau A L, Urueña J M, Pitenis A A. Load-independent hydrogel friction. *Biotribology* **26**: 100183 (2021)

[111] Urueña J M, McGhee E O, Angelini T E, Dowson D, Sawyer W G, Pitenis A A. Normal load scaling of friction in gemini hydrogels. *Biotribology* **13**: 30–35 (2018)

[112] Schulze K D, Hart S M, Marshall S L, O'Bryan C S, Urueña J M, Pitenis A A, Sawyer W G, Angelini T E. Polymer osmotic pressure in hydrogel contact mechanics. *Biotribology* **11**: 3–7 (2017)

[113] Rudge R E D, Scholten E, Dijksman J A. Natural and induced surface roughness determine frictional regimes in hydrogel pairs. *Tribol Int* **141**: 105903 (2020)

[114] McGhee E O, Pitenis A A, Urueña J M, Schulze K D, McGhee A J, O'Bryan C S, Bhattacharjee T, Angelini T E, Sawyer W G. *In situ* measurements of contact dynamics in speed-dependent hydrogel friction. *Biotribology* **13**: 23–29 (2018)

[115] Pitenis A A, Urueña J M, Schulze K D, Nixon R M, Dunn A C, Krick B A, Sawyer W G, Angelini T E. Polymer fluctuation lubrication in hydrogel gemini interfaces. *Soft Matter* **10**(44): 8955–8962 (2014)

[116] McGhee E O, Urueña J M, Pitenis A A, Sawyer W G. Temperature-dependent friction of gemini hydrogels. *Tribol Lett* **67**(4): 117 (2019)

[117] Urueña J M, Pitenis A A, Nixon R M, Schulze K D, Angelini T E, Gregory Sawyer W. Mesh size control of polymer fluctuation lubrication in gemini hydrogels. *Biotribology* **1–2**: 24–29 (2015)

[118] Pitenis A A, Manuel Urueña J, Cooper A C, Angelini T E, Gregory Sawyer W. Superlubricity in gemini hydrogels. *J Tribol* **138**(4): 042103 (2016)

[119] Dunn A C, Pitenis A A, Urueña J M, Schulze K D, Angelini T E, Sawyer W G. Kinetics of aqueous lubrication in the hydrophilic hydrogel Gemini interface. *Proc Inst Mech Eng H* **229**(12): 889–894 (2015)

[120] Cross L M, Shah K, Palani S, Peak C W, Gaharwar A K. Gradient nanocomposite hydrogels for interface tissue engineering. *Nanomedicine* **14**(7): 2465–2474 (2018)

[121] Lin P, Zhang R, Wang X L, Cai M R, Yang J, Yu B, Zhou F. Articular cartilage inspired bilayer tough hydrogel prepared by interfacial modulated polymerization showing excellent combination of high load-bearing and low friction performance. *ACS Macro Lett* **5**(11): 1191–1195 (2016)

[122] Ma S H, Scaraggi M, Wang D A, Wang X L, Liang Y M, Liu W M, Dini D, Zhou F. Nanoporous substrate-infiltrated hydrogels: A bioinspired regenerable surface for high load bearing and tunable friction. *Adv Funct Materials* **25**(47): 7366–7374 (2015)

[123] Stahl U, Willcox M, Stapleton F. Osmolality and tear film dynamics. *Clin Exp Optom* **95**(1): 3–11 (2012)

[124] Bayer I. Advances in tribology of lubricin and lubricin-like synthetic polymer nanostructures. *Lubricants* **6**(2): 30 (2018)

[125] Navarro L A, French D L, Zauscher S. Advances in mucin mimic synthesis and applications in surface science. *Curr Opin Colloid Interface Sci* **38**: 122–134 (2018)

[126] Raviv U, Klein J. Fluidity of bound hydration layers. *Science* **297**(5586): 1540–1543 (2002)

[127] Han T Y, Zhang C H, Li J J, Yuan S H, Chen X C, Zhang J Y, Luo J B. Origins of superlubricity promoted by hydrated multivalent ions. *J Phys Chem Lett* **11**(1): 184–190 (2020)

[128] Han T Y, Zhang C H, Luo J B. Macroscale superlubricity enabled by hydrated alkali metal ions. *Langmuir* **34**(38): 11281–11291 (2018)

[129] Li S W, Bai P P, Li Y Z, Jia W P, Li X X, Meng Y G, Ma L R, Tian Y. Extreme-pressure superlubricity of polymer solution enhanced with hydrated salt ions. *Langmuir* **36**(24): 6765–6774 (2020)

[130] Gaisinskaya-Kipnis A, Ma L R, Kampf N, Klein J. Frictional dissipation pathways mediated by hydrated alkali metal ions. *Langmuir* **32**(19): 4755–4764 (2016)

[131] Safinya C R, Ewert K K. Liposomes derived from molecular vases. *Nature* **489**: 372–374 (2012)

[132] Banquy X, Burdyńska J, Lee D W, Matyjaszewski K, Israelachvili J. Bioinspired bottle-brush polymer exhibits low friction and Amontons-like behavior. *J Am Chem Soc* **136**(17): 6199–6202 (2014)

[133] Ma L R, Gaisinskaya-Kipnis A, Kampf N, Klein J. Origins of hydration lubrication. *Nat Commun* **6**: 6060 (2015)

[134] Seror J, Zhu L Y, Goldberg R, Day A J, Klein J. Supramolecular synergy in the boundary lubrication of synovial joints. *Nat Commun* **6**: 6497 (2015)

[135] Goldberg R, Schroeder A, Silbert G, Turjeman K, Barenholz Y, Klein J. Boundary lubricants with exceptionally low friction coefficients based on 2D close-packed phosphatidylcholine liposomes. *Adv Mater* **23**(31): 3517–3521 (2011)

[136] Sorkin R, Kampf N, Zhu L Y, Klein J. Hydration lubrication and shear-induced self-healing of lipid bilayer boundary lubricants in phosphatidylcholine dispersions. *Soft Matter* **12**(10): 2773–2784 (2016)

[137] Angayarkanni S A, Kampf N, Klein J. Surface interactions between boundary layers of poly(ethylene oxide)-liposome complexes: Lubrication, bridging, and selective ligation. *Langmuir* **35**(48): 15469–15480 (2019)

[138] Narumi A, Matsuda T, Kaga H, Satoh T, Kakuchi T. Synthesis of amphiphilic triblock copolymer of polystyrene and poly(4-vinylbenzyl glucoside) via TEMPO-mediated living radical polymerization. *Polymer* **43**(17): 4835–4840 (2002)

[139] Klein J, Kumacheva E, Mahalu D, Perahia D, Fetters L J. Reduction of frictional forces between solid surfaces bearing polymer brushes. *Nature* **370**(6491): 634–636 (1994)

[140] Ivanov I V, Meleshko T K, Kashina A V, Yakimansky A V. Amphiphilic multicomponent molecular brushes. *Russ Chem Rev* **88**(12): 1248–1290 (2019)

[141] Raviv U, Giasson S, Kampf N, Gohy J F, Jérôme R, Klein J. Lubrication by charged polymers. *Nature* **425**(6954): 163–165 (2003)

[142] Curnutt A, Smith K, Darrow E, Walters K B. Chemical and microstructural characterization of pH and [Ca^{2+}] dependent sol-gel transitions in mucin biopolymer. *Sci Rep* **10**(1): 8760 (2020)

[143] Lai S K, Wang Y Y, Wirtz D, Hanes J. Micro- and macrorheology of mucus. *Adv Drug Deliv Rev* **61**(2): 86–100 (2009)

[144] Xue K, Liow S S, Karim A A, Li Z B, Loh X J. A recent perspective on noncovalently formed polymeric hydrogels. *Chem Rec* **18**(10): 1517–1529 (2018)

[145] Wu Y, Pei X W, Wang X L, Liang Y M, Liu W M, Zhou F. Biomimicking lubrication superior to fish skin using responsive hydrogels. *NPG Asia Mater* **6**(10): e136 (2014)

[146] Chen Z, Feng Y, Zhao N, Shi J Q, Liu G Q, Liu W M. Near-infrared photothermal microgel for interfacial friction control. *ACS Appl Polym Mater* **3**(8): 4055–4061 (2021)

[147] Wang J, Zhang X W, Zhang S, Kang J Y, Guo Z C, Feng B Y, Zhao H, Luo Z, Yu J, Song W L, et al. Semi-convertible hydrogel enabled photoresponsive lubrication. *Matter* **4**(2): 675–687 (2021)

[148] Hua J, Björling M, Larsson R, Shi Y J. Friction control of chitosan-Ag hydrogel by silver ion. *ES Mater Manuf* **16**: 30-36 (2021)

[149] Zhang X W, Wang J, Jin H, Wang S T, Song W L. Bioinspired supramolecular lubricating hydrogel induced by shear force. *J Am Chem Soc* **140**(9): 3186–3189 (2018)

[150] Wu Y, Wei Q B, Cai M R, Zhou F. Interfacial friction control. *J Advanced Materials Interfaces* **2**(2): 1400392 (2015)

[151] Lei Y T, Wang X K, Liao J Y, Shen J L, Li Y L, Cai Z W, Hu N, Luo X J, Cui W G, Huang W. Shear-responsive boundary-lubricated hydrogels attenuate osteoarthritis. *Bioact Mater* **16**: 472–484 (2022)

[152] Wojtecki R J, Meador M A, Rowan S J. Using the dynamic bond to access macroscopically responsive structurally dynamic polymers. *Nat Mater* **10**(1): 14–27 (2011)

[153] Wu M, Peng Q Y, Han L B, Zeng H B. Self-healing hydrogels and underlying reversible intermolecular interactions. *Chin J Polym Sci* **39**(10): 1246–1261 (2021)

[154] Wilson A, Gasparini G, Matile S. Functional systems with orthogonal dynamic covalent bonds. *Chem Soc Rev* **43**(6): 1948–1962 (2014)

[155] Yu K H, Xin A, Wang Q M. Mechanics of self-healing polymer networks crosslinked by dynamic bonds. *J Mech Phys Solids* **121**: 409–431 (2018)

[156] Zhang Q, Deng Y X, Luo H X, Shi C Y, Geise G M, Feringa B L, Tian H, Qu D H. Assembling a natural small molecule into a supramolecular network with high structural order and dynamic functions. *J Am Chem Soc* **141**(32): 12804–12814 (2019)

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