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RESEARCH ARTICLE

# Synovial fluid-inspired biomimetic lubricating microspheres: Zwitterionic polyelectrolyte brushes-grafted microgels

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**Abstract:** Synovial fluid is made up of various biomacromolecules, including hyaluronic acid, aggrecans, lubricins, and phosphatidylcholine lipid, which are assembled onto the surface of articular cartilage in a gel state. Among them, brush-like biomacromolecules or assemblies have a vital effect on human joint lubrication. Inspired by this, the combination of brush-like molecular structures and gel-like assembly may be an efficient approach for the synthesis of biomimetic lubricating matters. Learning from the lubrication system of human joints, poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) brushes grafted poly(N-isopropylacrylamide-co-acrylic acid) (poly(NIPAAm-co-AA)) microgels, abbreviated as MBs-g-MGs, were synthesized as one kind of biomimetic lubricating additives. It is worth noting that this bionic strategy considered both molecular structure and assembled form, which enabled this hairy microgel to achieve low friction in aqueous medium. Meanwhile, the effective lubrication was still achieved when using MBs-g-MGs at high temperature, indicating that this microgel maintains a good lubricating effect over a wide range of temperature. In addition, this kind of microgel possessed good biocompatibility, which laid the foundation for potential biomedical applications. Looking beyond, these biomimetic microgels may provide an effective lubricating effect for water-based sliding interfaces, especially in biomedical systems.

**Keywords:** biomimetic design; zwitterionic polyelectrolyte brushes; polymeric microgels; aqueous lubrication

## 1 Introduction

The biolubrication widely existed in human tissues, such as eyes, mouths, intestines, and knees [1]. Among them, the superlubricating ability of human joints has attracted much attention, which originates from the synergistic effect of the articular cartilage on the surface of the joint bones and synovial fluid in the joint cavity [2]. The surficial state of articular cartilage can be regarded as biohydrogels, which have excellent lubricating ability and bearing capacity [3, 4], while synovial fluid is made up of various lubricating biomacromolecules, including hyaluronic acid, mucins, lubricin, and phosphatidylcholine lipid [5–7]. Inspired by these biolubricating molecules and structures, biomimetic design of lubricating materials has evolved to be an interesting research hotspot [8–11]. One strategy is to mimic articular cartilage to design high-strength lubricating hydrogels, and the other strategy is to synthesize lubricating polymers by dissecting the biomacromolecules in synovial fluid. Compared with natural lubricating tissues, synthetic bionic lubricating materials have the tunability of components, structures, and functions, and can be endowed with functional

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and intelligent characteristics according to the purpose of application [12, 13]. In this work, our bionic idea was focused on the synthesis of biomimetic lubricating additives by learning from synovial fluid, in which the lubricating matters are brush-like or linear hydrophilic biomacromolecules, which are assembled in a gel state onto the surface of cartilages.

Since water is a natural medium of living systems, the lubrication in the human joint is very closely related to the hydration lubrication [14–16]. This lubrication theory provided a guideline for designing biomimetic lubricating polymers. Especially, it had been proved that polyzwitterionic brushes displayed a good lubricating effect in aqueous medium because of physiological pressure generated by molecular hydration [17]. In recent years, various biomimetic lubricating polymers have been synthesized for aqueous lubrication. In 2013, Wathier et al. [18] prepared a hydrophilic linear polyanion by imitating the molecular structure of hyaluronic acid. This polyanion showed excellent lubricating properties and good biocompatibility, making it promising to be a type of synovial supplement. In 2014, Banquy et al. [19] mimicked the lubricating protein lubricin and synthesized a triblock bottle-brush polymer. This polymer exhibited excellent aqueous lubricating properties under physiological conditions, and the coefficient of friction (COF) was at a low level ($10^{-3}$). In 2017, Faivre et al. [20] combined the molecular brushes and linear polymer to obtain a synergistic mixture. The entanglement between the two lubricating systems significantly enhanced the anti-wear performance of sliding interfaces. However, previous study was mostly focused on the imitation of molecular components and structures, lacking the consideration of gel-like assembly of natural molecules. To circumvent this challenge, microgels were introduced to design biomimetic lubricating materials.

Microgels are generally considered to be micro-nano-sized gel substances with high crosslinking degree and hydration and swelling ability [21]. Based on colloidal stability, viscoelasticity during shearing, and especially the unique spherical structure, microgels have been considered as a class of aqueous-based lubricant additives. Meanwhile, due to good biocompatibility, microgels have great potential for the applications in biolubrication. [22–25]. More importantly, if biomimetic lubricating polymers were integrated with microgels, the synthetic structure would enable the simultaneous biomimetic design of molecular configuration and gel-like assembly. Poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) was a zwitterionic polyelectrolyte with a similar molecular structure to phosphatidylcholine lipids. Meanwhile, the excellent biocompatibility made PMPC a promising material for biomedical applications [26, 27]. Especially in biolubrication (replacement joints and catheter), PMPC brush layer exhibits excellent aqueous-based lubricating properties [28, 29], which can achieve high-performance hydration lubrication due to the hydration layer around the zwitterionic phosphocholine groups [30, 31]. In 2020, Chen et al. [32] grafted PMPC onto silica nanoparticles, generating a slippery microsphere for osteoarthritis treatment. Notably, the superhigh modulus of silica cores may cause damage to joint tissues. In this case, soft microgels may be considered as a good alternative to the core of slippery microspheres.

In this work, zwitterionic polyelectrolyte brushes-grafted microgels, MBs-g-MGs, were prepared according to a bionic strategy that combined brush-like polymer (PMPC brushes) with gel-like assembly (poly(NIPAAm-AA) microgels) (Fig. 1). In detail, the microgels with surface-initiated atom transfer radical polymerization (SI-ATRP) initiators, abbreviated as MGs-Br, were first synthesized, and then PMPC brushes were uniformly grafted on the microgels by SI-ATRP. The chemical components, colloidal morphology, interfacial behavior, and tribology property were systemically characterized. As one of the most important results, good interfacial lubrication was realized over a wide range of temperatures when using these hairy microgels as the lubricating additives, avoiding the influence caused by the gel phase transition of PNIPAAm segments. In addition, the cell experiments showed that MBs-g-MGs had good biocompatibility, which provided a basis for potential biomedical lubrication. Looking beyond, the combination of excellently lubricating polymers and soft microgels paves an extraordinary way for designing biomimetic lubricating materials with a specific function.

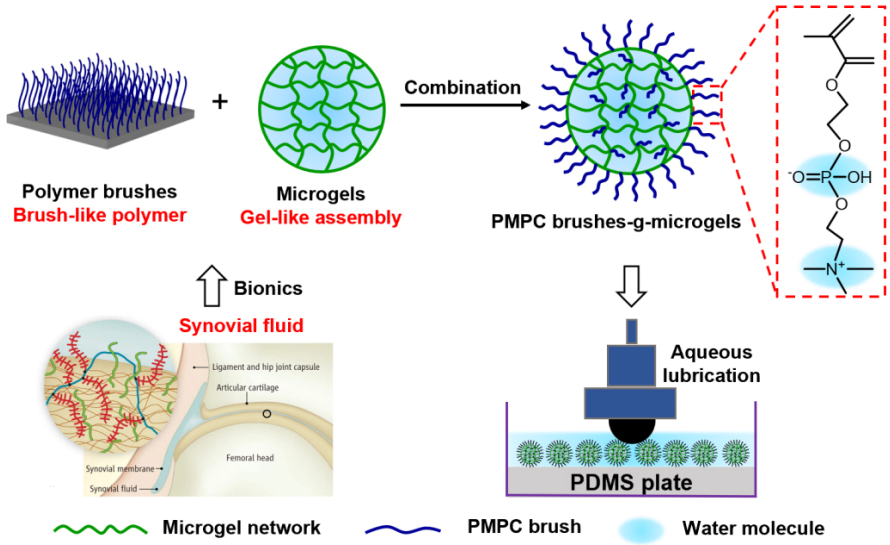


**Fig. 1** Schematic diagram illustrating the bionics design of PMPC brushes-g-microgels by learning from the synovial fluid on the surface of articular cartilage. Reproduced with permission from Ref. [33], © American Association for the Advancement of Science 2009.

## 2 Experimental

### 2.1 Materials

N-isopropylacrylamide (NIPAAm, 98%, TCI), 2-hydroxyethyl methacrylate (HEMA, 95%, TCI), 2-bromoisobutyryl bromide (98%, TCI), triethylamine (99%, TCI), 2-methacryloyloxyethyl phosphorylcholine (MPC, 96%, TCI), 2,2′-bipyridine (Bpy, 99%, TCI), N,N′-methylenebis(acrylamide) (MBA, 98%, Sigma-Aldrich), copper(I) bromide (CuBr, 99%, Sigma-Aldrich), potassium persulfate (KPS, 99%, Acros), acrylic acid (AA, > 99%, Aladdin), human hepatocellular carcinomas (HepG2 cells, Chinese Academy of Sciences), cell counting kit-8 (CCK-8, Beyotime), penicillin (Beyotime), streptomycin (Beyotime), phosphate buffered saline (PBS, Beyotime), Calcein-AM/PI double staining kit (Dojindo), fetal bovine serum (FBS, Gemini), trypsin-ethylenediaminetetraacetic acid (trypsin-EDTA, 0.25%, Amresco), and Dulbecco's Modified Eagle Medium (DMEM, High glucose, Gibco) were used. The pure water in the whole experimental process was obtained from the pure water machine (Ulupure) in the laboratory .

### 2.2 Synthesis of HEMA-Br

The 2-(2-bromoisobutyryloxy)ethyl methacrylate (HEMA-Br) was synthesized with reference to the previous research [34]. Typically, HEMA (10.7 mL) and triethylamine (6.0 mL) were added into dichloromethane (35 mL) in 100 mL three-necked flask at 0 °C. After the removal of oxygen by bubbling nitrogen gas, 2-bromoisobutyryl bromide (9.88 mL) dissolved in dichloromethane (11.55 mL) was slowly added dropwise into the flask, which lasted about 30 min. The reaction was proceeded for 4 h at 0 °C. After the reaction was finished, the precipitate was filtered out and rinsed with dichloromethane. Subsequently, the supernatant was washed with saturated $Na_2CO_3$ and saturated NaCl solution three times. Finally, an appropriate amount of anhydrous $MgSO_4$ was added to the solution to remove the water, and a pale-yellow liquid was obtained for further use.

### 2.3 Synthesis of MGs-Br

The poly(NIPAAm-co-AA)-Br microgels (abbreviated as MGs-Br) were prepared by a modified emulsifier-free emulsion polymerization. In general, NIPAAm (0.8 g), AA (0.19 mL), and water (100 mL) were added into a three-necked flask with magnetic stirrer, ventilator, and condenser. After mixing well, the mixture of HEMA-Br (0.05 g) and ethanol (10 mL) was added into the flask. At room temperature, the solution was ventilated with nitrogen for 30 min, and then KPS (0.03 g) was added into the mixture as an

initiator. After 2 h of reaction at 75 °C, the synthetic colloidal solution was put into a dialysis membrane (8–12 kDa) and purified in 2 L of pure water for 72 h. The pure water was changed every 12 h.

### 2.4 Synthesis of MBs-g-MGs

The PMPC brushes-grafted poly(NIPAAm-co-AA) microgels (abbreviated as MBs-g-MGs) were synthesized by SI-ATRP. The MGs-Br solution (8 mL), MPC (0.5 g), and methanol (2.0 mL) were mixed well and poured into the polymerization tube. After removing the oxygen for 30 min, Bpy (0.065 g) and CuBr (0.0285 g) were added to the reaction quickly. The reaction was conducted for 2 h at room temperature. Similarly, the product was put into the dialysis membrane for purification.

### 2.5 Fabrication of PDMS plate

The polydimethylsiloxane (PDMS) plate was prepared in plastic petri dish using the commercial silicone elastomer kit (SYLGARD 184 silicone elastomer, Dow) and selected as the lower friction contact. The base fluid and curing agent were mixed at a 10:2 ratio (by weight), and then the mixture was poured into a petri dish, followed by the removal of bubbles under vacuum. After curing at 80 °C for 24 h, the PDMS plate was obtained for further use.

### 2.6 Characterization

The Fourier transform infrared (FTIR) spectrum was obtained on the FTIR spectrometer (Bruker, Germany). The X-ray photoelectron spectroscropy (XPS) measurement was performed by the X-ray photoelectron spectrometer (Al K$\alpha$ radiation; PHI 5000 VersaProbe III). The C 1s peak was shifted to 284.6 eV to adjust the peak position. The morphology was observed by the scanning electron microscope (SEM; FEI, Helios G4 CX, USA) and the transmission electron microscope (TEM; FEI, Talos F200X, USA). The distribution of elements was obtained by the energy-dispersive X-ray spectroscopy (attached to the TEM apparatus). The rheological properties of MBs-g-MGs were evaluated by the dynamic rotational rheometer (Anton-Paar, MCR302, Austria) at 25 °C. The hydrodynamic diameters ($D_h$) and $\zeta$-potential were measured by the dynamic light scattering (DLS) technique (Malvern Instruments, Zetasizer Nano ZS, UK). Meanwhile, the swelling ratio (SR) is an important index to evaluate the swollen/collapse transition of MBs-g-MGs, which can be calculated by Eq. (1):

$$\mathrm{SR} = \frac{V_{\mathrm{swollen}}}{V_{\mathrm{collapse}}} = \left(\frac{D_{\mathrm{h25℃}}}{D_{\mathrm{h50℃}}}\right)^3 \tag{1}$$

### 2.7 Tribological test

The tribological behavior of MBs-g-MGs was investigated by the universal mechanical tester (Bruker, UMT-3, USA) in the reciprocating mode. The $Si_3N_4$ ceramic ball (4.7 mm) was used as the upper friction contact, and the homemade soft PDMS plate (2 cm × 5 cm) was selected as the lower friction contact. The PDMS plate was fixed on the bottom of a transparent glass cuvette, and 2 mL of MBs-Br and MBs-g-MGs suspensions were added into the cuvette as the lubricating medium. The friction test was systematically conducted by changing the parameters of reciprocating frequency from 0.5 to 4.0 Hz, normal load from 0.25 to 1.0 N, and temperature from 25 to 50 °C. Among them, the temperature was controlled by the water bath temperature control device attached to the UMT-3.

### 2.8 Cell culture and cytotoxicity assays

HepG2 cells were cultured with high glucose DMEM containing 10% FBS and 1% penicillin–stereptomycin solution at 37 °C in the 5% $CO_2$ incubator.

The cytotoxicity of MBs-g-MGs solution to HepG2 cells was detected by CCK-8 [35]. Typically, HepG2 cells were implanted in the 96 well plates, and the density was $1\times10^4$ cells/well. Then the cells were cultured with DMEM (200 μL) for 12 h. After the medium was discarded and washed 3 times with prewarmed sterile PBS, the fresh medium containing different concentrations of the MBs-g-MGs solution (0, 100, 200, 300, 400, 500, 600, 800, and 1,000 μg/mL) was subsequently added (total volume = 200 μL). The samples were incubated for 24 h, and then washed with PBS solution three times. Finally, the fresh medium containing 20 μL of CCK-8 was added and

further incubated for 2 h. The cell viability of the samples in each well was measured by the microplate reader (Thermo Fisher Scientific, Multiskan FC, USA) at the absorption value of 450 nm. The relative cell viability was calculated by Eq. (2):

$$\text{Cellviability} = \frac{V_{\text{sample}} - V_{\text{blank}}}{V_{\text{control}} - V_{\text{blank}}} \times 100\% \quad (2)$$

where $V_{\text{sample}}$ and $V_{\text{control}}$ are the absorption value the cells treated with and without MBs-g-MGs solution, respectively; and $V_{\text{blank}}$ is the absorption value of the cell-free well containing medium and CCK-8.

### 2.9 Live/dead cell staining

The biocompatibility of MBs-g-MGs solution for HepG2 was evaluated *in vitro* using live/death assay that was used to distinguish live/dead cells. The concentration of MBs-g-MGs was fixed at 500 μg/mL. The fluorescence images were obtained by the confocal laser scanning microscope (CLSM; Leica, TCS SP8, Germany). First, HepG2 cells were seeded at $4\times10^5$ cells/dish in 35 mm laser confocal dishes and incubated for 12 h (total volume = 2 mL). After the medium was discarded, HepG2 cells were washed with prewarmed sterile PBS three times. Then, HepG2 cells were incubated with DMEM containing the MBs-g-MGs materials (500 μg/mL) at 37 °C in the 5% $CO_2$ incubator for 24 h. After that, discard the medium and then wash three times with PBS buffer solution (pH = 7.4). The sample cells were further incubated in the prewarmed sterile PBS solution containing 0.5% Calcein-AM/PI staining solution at 37 °C in the 5% $CO_2$ incubator for 15 min (total volume of 2 mL). The fluorescence microscopic images were then obtained through the CLSM.

## 3 Results and discussion

### 3.1 Chemical component analysis

The chemical components of MGs-Br and MBs-g-MGs were characterized by the FITR and XPS in Fig. 2. As for the FTIR spectrum of MGs-Br (Fig. 2(a)), the absorption peak at 3,600–3,200 $cm^{-1}$ was assigned to the N–H group, and that at 1,643 $cm^{-1}$ was attributed to the C=O group. The double peaks at 1,387 and 1,365 $cm^{-1}$ were associated with the two $-CH_3$ groups in $-CH(CH_3)_2$ of NIPAAm. With regard to MBs-g-MGs, new peaks at 1,272 and 970 $cm^{-1}$ appeared, which were attributed to the P=O and P–O groups in PMPC brushes, respectively. The appearance of these two groups indicated the grafting of MPC onto the MGs-Br.

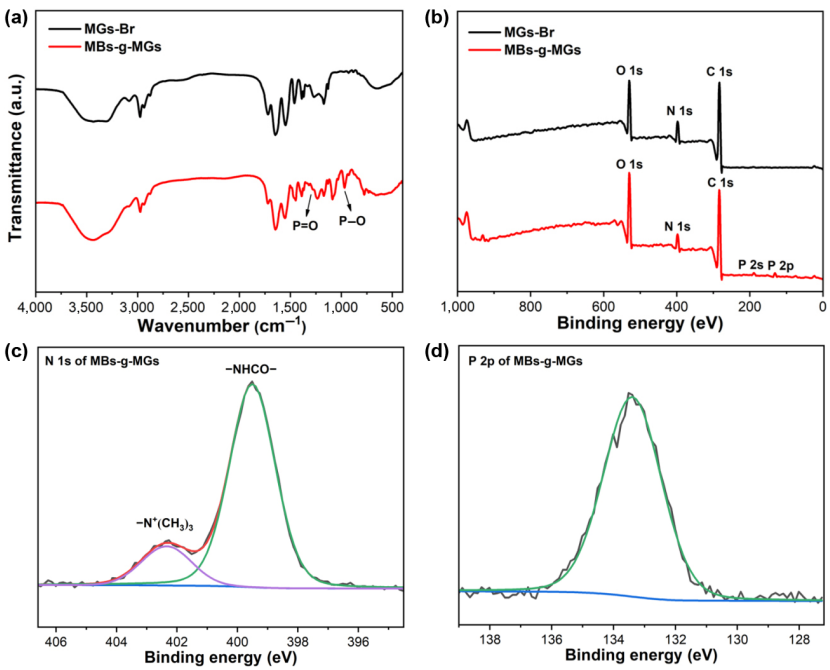


**Fig. 2** (a) FTIR spectra of MGs-Br and MBs-g-MGs. (b) XPS spectra of MGs-Br and MBs-g-MGs. (c) XPS deconvolution analysis of N 1s in MBs-g-MGs. (d) XPS deconvolution analysis of P 2p in MBs-g-MGs.

Furthermore, the XPS spectra in Fig. 2(b) displayed the change of elements between MGs-Br and MBs-g-MGs. It is clear that there were only signals of C, O, and N in the XPS spectrum of MGs-Br. After the grafting of PMPC brushes, the signals of P 2s and P 2p appeared at 189 and 131 eV, respectively. In Fig. 2(c), the deconvolution analysis of N 1s verified the existence of two types of N elements, where the signals at 402 and 399 eV were assigned to the N element of $-N^{+}(CH_3)_3$ in NIPAAm and –NHCO– in MPC, respectively. Figure 2(d) shows the deconvolution analysis of P 2p associated with MPC. These results further demonstrated that the successful grafting of PMPC brushes onto MGs-Br.

### 3.2 Morphology observation

The morphologies of MGs-Br and MBs-g-MGs were observed by the TEM and SEM. The MGs-Br had a spherical structure with a diameter of ~350 nm (Fig. 3(a)). From the corresponding energy-dispersive X-ray spectra (EDXS) (Fig. 3(b)), the signal of the Br element indicated that HEMA-Br was successfully polymerized with NIPAAm and AA, providing a basis for the subsequent SI-ATRP. After the grafting of PMPC brushes, the diameter of MBs-g-MGs was increased to ~450 nm (Fig. 3(c)). Notably, the signal of P element appeared at the corresponding EDXS (Fig. 3(d)). From the morphology obtained by the SEM, it is clear that MGs-Br was a typical colloidal structure (Fig. 4(a)) with a narrow size distribution by measuring particle diameter in a large area (Fig. 4(b)). Interestingly, the MBs-g-MGs displayed a special "donut-like" structure (Fig. 4(c)), which may be caused by dehydration collapse of PMPC brushes during the drying process. The histogram of size distribution in Fig. 4(d) shows that MBs-g-MGs were also uniformly synthesized, indicating that it was reliable that the polymer brushes were grown from the microgel base with the SI-ATRP initiator.

### 3.3 Hydration ability investigation

Since the hydration capacity has an important influence on the effect of aqueous lubrication, the ζ-potential and $D_h$ of MGs-Br and MBs-g-MGs were measured by the DLS technique. As shown in Fig. 5(a), the ζ-potential of MGs-Br was ca. −11.7 mV, which was attributed to the negatively charged AA component. After the grafting of PMPC brushes, the ζ-potential of MBs-g-MGs trended to be electrically neutral because of the presence of zwitterions. Figure 5(b) shows the change of hydrodynamic diameters of MGs-Br and MBs-g-MGs at different temperatures. For MGs-Br, the diameter was decreased from ~1,089 to ~341 nm as the temperature rose from 25 to 50 °C. This volume shrinkage behavior originated from the hydrophilic–hydrophobic transition of PNIPAAm segments, which

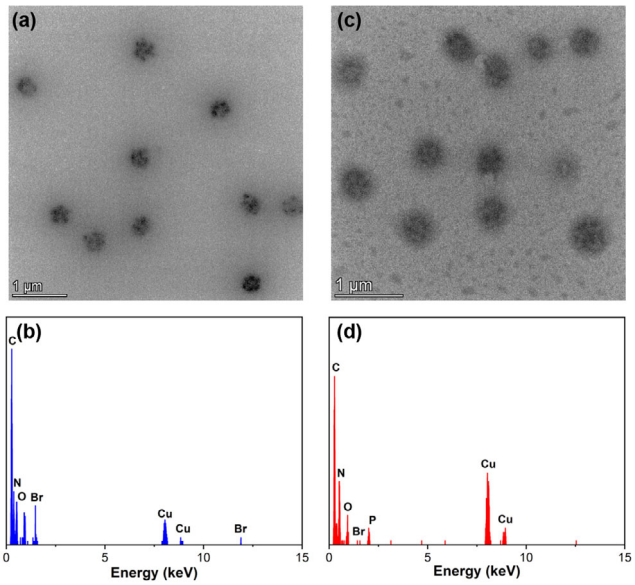


**Fig. 3** TEM images and corresponding EDXS of (a, b) MGs-Br and (c, d) MBs-g-MGs.

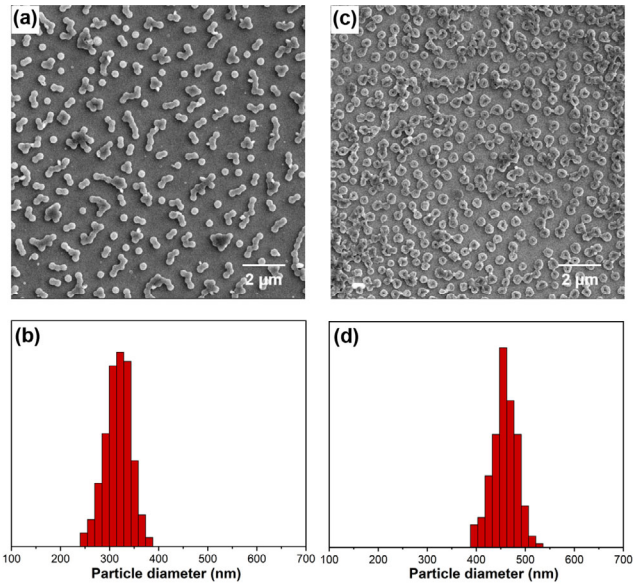


**Fig. 4** SEM images and corresponding size distribution histograms of (a, b) MGs-Br and (c, d) MBs-g-MGs.

enabled microgels a thermosensitive property. For MBs-g-MGs, the diameter was ~1,248 nm at 25 °C and decreased to ~458 nm at 50 °C, suggesting that there was a still thermosensitive phase shrinkage. Compared with MGs-Br, the diameters of MBs-g-MGs at 25 and 50 °C both had an increase because of the grafting of hydrated PMPC brushes. After calculation, the SRs of MGs-Br and MBs-g-MGs were 32.57 and 20.23, respectively, which means that both MGs-Br and MBs-g-MGs have good swelling and hydration ability. As illustrated in Fig. 5(c), another difference to note is that the surface of MBs-g-MGs kept hydrophilic though the temperature changed, which benefited from the ionized PMPC shell. However, this hydrophilicity over a wide range of temperature could not be realized by MGs-Br. These results indicated that the MBs-g-MGs could be hydrated well in aqueous medium, and the construction of hydrated layer is significant in hydration lubrication. More importantly, the zwitterions had a stronger hydrated ability than anions or cations and could anchor more water molecules surrounding themselves, which was beneficial for hydration lubrication.

The rheological behavior of MBs-g-MGs suspension was also investigated (Fig. 5(d)), since the change trend of colloidal viscosity during the shearing process had an important influence on the lubricating performance. It is found that the viscosity of MBs-g-MGs suspension had a non-negligible increase with the increase of shearing rate. This shear thickening character had a positive effect on the friction surface, which could overcome the thinning phenomenon of lubricants during the friction process.

### 3.4 Tribological study

The tribological behaviors of MGs-Br and MBs-g-MGs were investigated by the UMT-3 in the reciprocating mode. As we all know, the surface of human joint is covered by a layer of viscoelastic and cushioning joint cartilage. To simulate this friction situation, a soft homemade PDMS plate was employed as the lower friction contact. Meanwhile, the $Si_3N_4$ ceramic ball was selected as the upper friction contact in order to avoid the corrosion of steal balls in a watery environment. The relationship between frequency and COF was first studied (Fig. 6(a)). The change in reciprocating frequency essentially represents the change in sliding speed. During the test process, the COFs of pure water were always high. When using MGs-Br as the lubricating additives, the COF was reduced compared with pure water, suggesting that MGs-Br had a certain lubricating effect. Remarkably,

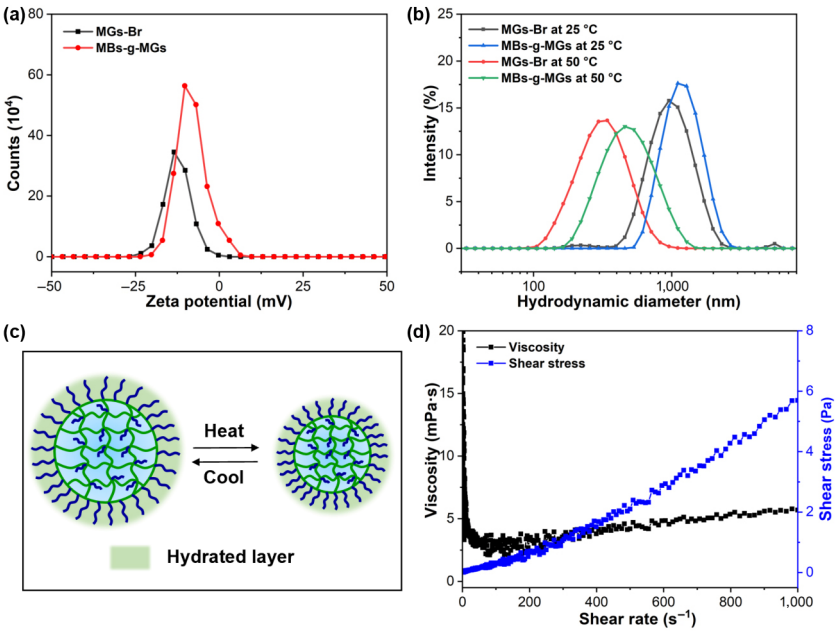


**Fig. 5** (a) ζ-potentials of MGs-Br and MBs-g-MGs. (b) Hydrodynamic diameters of MGs-Br and MBs-g-MGs at 25 and 50 °C. (c) Schematical diagram illustrating the phase shrinkage and the surficial wetting change at different temperatures. (d) Viscosity and shear stress vs. shear rate curve of MBs-g-MGs suspension.

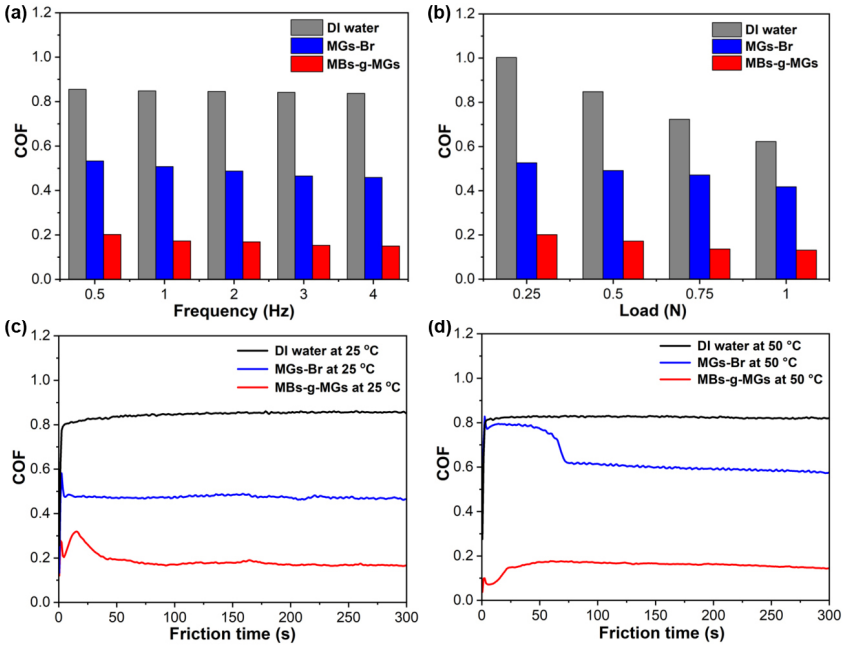


**Fig. 6** (a) COFs of MGs-Br and MBs-g-MGs as a function of frequency with pure water as the reference (temperature: 25 °C, normal load: 0.5 N, and amplitude: 2.0 mm). (b) COFs of MGs-Br and MBs-g-MGs as a function of normal load with pure water as the reference (temperature: 25 °C, frequency: 1.0 Hz, and amplitude: 2.0 mm). Friction curves of MGs-Br and MBs-g-MGs at (c) 25 °C and (d) 50 °C with pure water as the reference (normal load: 0.5 N, frequency: 1.0 Hz, and amplitude: 2.0 mm).

when MBs-g-MGs was introduced onto sliding interfaces instead of MGs-Br, the COF showed an obvious decrease in comparison with pure water. When increasing the frequency, the COF was slightly decreased, which was in line with the trend of boundary lubrication in the Stribeck curve. These results indicated that the MBs-g-MGs displayed a good lubricating performance in aqueous medium, which was originated from the strong hydration effect of PMPC brushes. The hydrated layer surrounding the MBs-g-MGs enabled hydration lubrication to come into effect. Figure 6(b) shows the relationship between the COF and normal load. It can be clearly seen that the COF of MBs-g-MGs was always smaller than those of pure water and MGs-Br under any normal load. Also, with the increase of normal load, the COF of MBs-g-MGs was reduced to some extent. This result still verified the good lubricating effect of MBs-g-MGs suspension. Notably, the soft PDMS plate collapsed and unloaded part of applied force when increasing the normal load, which reduced the frictional resistance like articular cartilage.

Since the MBs-g-MGs had a thermosensitive property, the change in the COF was investigated at 25 and 50 °C, respectively (Figs. 6(c) and 6(d)). As for MGs-Br, the COF at 50 °C (0.598) was higher than that at 25 °C (0.492). The increase in temperature caused the dehydration of MGs-Br, which reduced the effect of hydration lubrication and increased the COF. At the same time, this microgel collapsed and became harder, thereby enhancing the role of the micro-bearings. The comparison of the COFs at different temperatures was attributed to the result of the balance between hydrophilic–hydrophobic transition and swelling–shrinking behavior. As for MBs-g-MGs, the COF at high temperature was slightly reduced in comparison with low temperature. Though the increase in temperature led to the dehydration of PNIPAAm segments in MBs-g-MGs, the shell of PMPC brushes kept highly hydrated at different temperatures. In this case, the hydration lubrication of the MBs-g-MGs surface, which directly contacted with the friction interface, was still effective. Thus, as aqueous lubricating additives, this hairy microgel could achieve low friction over a wide range of temperature. In a word, the bionic strategy of the combination of brush-like polymer and microgels plays an effective role in the design of aqueous lubricating additives.

### 3.5 *In vitro* cytotoxicity

As the lubricating material was prepared based on the biomimetic system, the cytotoxicity of MBs-g-MGs has a good guiding significance for further biological applications. To this end, the toxicity of the MBs-g-MGs against HepG2 cells was first investigated via the CCK-8 assay. As shown in Fig. 7(a), when the concentration of MBs-g-MGs in the culture medium reached 1,000 μg/mL, the viability of HepG2 cells was still as high as 97.4%, which indicated that MBs-g-MGs showed no apparent cytotoxicity to HepG2 cells. Also, the low concentration of MBs-g-MGs had a certain promotion effect on cell proliferation. Furthermore, the cell live/dead staining was conducted to intuitively characterize the viability of HepG2 cells incubated with MBs-g-MGs (500 μg/mL) for 24 h. Compared with blank control, it can be seen from the CLSM images in Fig. 7(b) that the density of cell proliferation was increased slightly after the addition of MBs-g-MGs to culture medium. The good biocompatibility of MBs-g-MGs to HepG2 cells laid a foundation for their biomedical lubrication.

## 4 Conclusions

In summary, one kind of biomimetic lubricating additives, MBs-g-MGs, was successfully synthesized by learning from the molecular structure and assembly form of biomacromolecules in synovial fluid. The interfacial low friction was achieved when using MBs-g-MGs in aqueous lubrication. Though the increase in temperature caused a phase transition of microgel base, a low friction was still realized at high temperature, indicating that MBs-g-MGs could play a lubricating role in a wide temperature range. These results originated from high hydration of zwitterionic PMPC brushes and gel state of poly(NIPAAm-co-AA) microgel base, which synergistically reduced the friction in aqueous lubrication. Also, this hairy microgel displayed good biocompatibility to cells. In a word, the integration of lubricating polymer with soft colloid provides an effective bionic strategy for the synthesis of micro-nano additives for aqueous lubrication.

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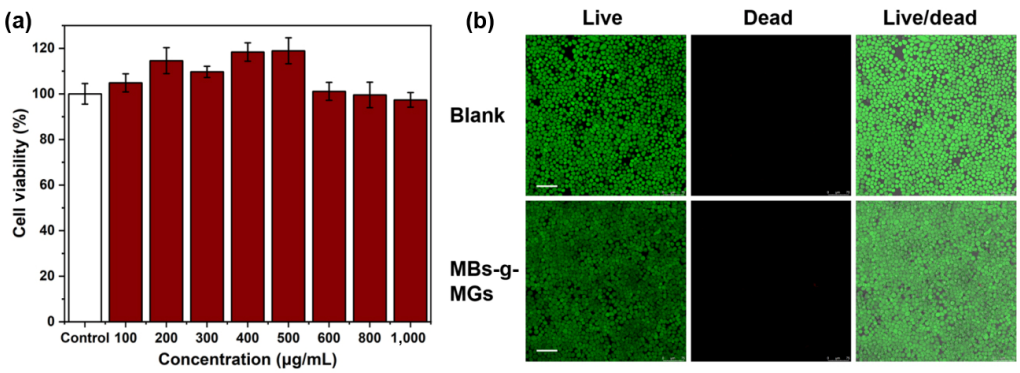


**Fig. 7** (a) Cell viability of HepG2 cells incubated with different concentrations of MBs-g-MGs for 24 h. (b) Live/dead staining of HepG2 cells after incubation with MBs-g-MGs for 24 h detected by the CLSM. Scale bar: 75 μm.

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