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## 別添 5

## 研究成果の刊行に関する一覧表レイアウト

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著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
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## Importance of adaptive multimode lubrication mechanism in natural and artificial joints

Teruo Murakami

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# Importance of adaptive multimode lubrication mechanism in natural and artificial joints

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## Abstract

The healthy natural synovial joints maintain excellent load-carrying capacity and lubricating properties with extremely low friction and minimum wear even under heavily loaded conditions. The superior lubricating performance appears to be actualized by not single lubrication mode but the synergistic combination of various modes depending on the severity of operating conditions. This mechanism is called adaptive multimode lubrication and the application of this good working lubrication mechanism to artificial joints with soft layer is expected to contribute to remarkable improvement in longevity of joint prostheses. However, some of detailed mechanisms in natural synovial joints have not yet been clarified. In this article, the effectiveness of biphasic lubrication in natural synovial joints was examined by biphasic finite element analysis under both the on–off loading (migrating contact) and the continuous loading (continuous contact) to cartilage. Then, the method to suppress the gradual rising in friction for articular cartilage under the continuous loading is discussed. Finally, the effectiveness of fibre reinforcement in hydrogel artificial cartilage was examined in walking simulator test.

## Keywords

Biotribology, natural synovial joints, articular cartilage, artificial joints, artificial cartilage, adaptive multimode lubrication

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## Introduction

Application of joint replacements to patients with osteoarthritis or rheumatoid arthritis brings the recovery of walking ability and relief from severe pain. However, in certain cases of artificial joints composed of ultrahigh molecular weight polyethylene (UHMWPE) and metal or ceramic components, the revision operations are conducted due to the loosening of joint prostheses which is usually derived from wear debris induced osteolysis.<sup>1,2</sup> Therefore, the reduction of wear is strongly required for improvement in the longevity of artificial joints. In contrast, healthy natural synovial joints maintain very low friction and minimum wear for a long life, although some performances may be reduced by cartilage deterioration due to ageing. To establish low friction and low wear in artificial joints, we should elucidate the synergistic lubrication mechanism in natural synovial joints and then apply the effective lubrication mechanisms to artificial joint systems. In this article, the adaptive multimode lubrication mechanism<sup>3</sup> and related phenomena in natural synovial joints are first described. Then, the biphasic finite element (FE) analyses for reciprocating sliding of articular cartilage are conducted under both the on–off loading

and the continuous loading conditions. Next, the effective method to inhibit an increase in friction for sliding pair of articular cartilage and glass plate in repeated reciprocating tests under continuous loading condition is discussed. Subsequently, the improvement of lubrication performance in joint prostheses with compliant artificial cartilage is exhibited.

The first aim of this article is the elucidation of adaptive multimode lubrication mechanism in natural synovial joints, particularly from viewpoints of the biphasic lubrication considering loading conditions and the adsorbed film formation considering roles of lubricant constituents. The second aim is the evaluation of effectiveness in the application of superior lubrication mechanism in articular cartilage to artificial hydrogel cartilage in simulator test.

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### *Adaptive multimode lubrication in natural synovial joints*

The healthy synovial joints maintain excellent load-carrying capacity and lubricating properties with extremely low friction and minimum wear even under heavily loaded conditions in hip, knee and ankle joints. This superior lubricating performance appears to be actualized by not a single lubrication mode but the synergistic combination of various modes from the fluid film lubrication to boundary lubrication corresponding to the severity of rubbing conditions, as pointed out by Dowson.<sup>4</sup> He described that the major lubrication mechanism would seem to be some form of elastohydrodynamic action determined by sliding or squeeze film action between porous surfaces with boundary lubrication providing the surface protection in cases of severe loading and little movement.

The author first focused on the influence of elastic soft layer of articular cartilage on lubrication in natural joints. In the previous study using pendulum tester, the frictional behaviours were investigated for two-dimensional cylindrical hip joint models with and without 3 mm soft layer prepared as radial clearance of 0.1 mm for concave cup specimen with a radius of 25 mm.<sup>5</sup> To observe simultaneously the changes in contact conditions and amplitude of swing, the photoelastic method was applied, where epoxy resin with Young's modulus of 3.0 GPa was used approximately for elastic subchondral and cancellous bone model and polyurethane with Young's modulus of 10 MPa as soft layer corresponding to articular cartilage. The swing behaviours immediately after loading of 10 N/mm lubricated with paraffinic oil indicated that the joint model without soft layer shows rapid damping, i.e. high friction. In contrast, the existence of soft layer reduced the friction due to elastohydrodynamic lubrication (EHL) mechanism with enlarged contact zone. The average friction coefficients were estimated as 0.03–0.04 for model with soft layer, and 0.12 for model without soft layer for lubricant viscosity of 0.056 Pa s. Thus, the friction coefficient for low-viscosity lubricants is not so low compared with measured values of 0.003 to 0.02 for natural synovial joints. In natural joints, the viscosity of synovial fluid is reduced to a very low value as twice or several times of water viscosity as non-Newtonian property under a high shear rate of  $10^5$ – $10^6$  s<sup>-1</sup> during walking. This discrepancy indicates that simple soft-EHL modelling including elastic soft layer has not sufficiently elucidated the actual lubrication mechanism, although elastic deformation enhances the EHL film thickness.

Dowson and Jin<sup>6</sup> evaluated the possibility of fluid film formation during normal walking by considering the elastic deformation of surface asperity in numerical EHL analysis. In previous studies, minimum EHL film thickness for smooth compliant surface was predicted to be less than 1 µm during walking, and

maximum height of the undeformed surface roughness of articular cartilage was estimated to be 1–2 µm or more, and thus, the difficulty in fluid film lubrication was evaluated because of film parameter less than 3 as the ratio of minimum film thickness to composite roughness. In their analysis, however, the flattening of surface asperity in conjunction zone (load-carrying zone) was able to maintain a fluid film thickness of about 0.6 µm without interaction between the rubbing surfaces during walking. This lubricating mechanism was called micro-EHL, which indicates the possibility of fluid film lubrication during normal walking.

On the contrary, at start up after standing for a long time, some local direct contacts appear to occur between the rubbing cartilage surfaces. Under these thin film conditions, mixed lubrication and/or boundary lubrication modes are likely to prevail, and in addition, weeping lubrication<sup>7</sup> and boosted lubrication<sup>8</sup> may become effective. In boundary lubrication regime, the adsorbed films composed of glycoproteins,<sup>9</sup> proteins<sup>10</sup> and/or phospholipids<sup>11</sup> are likely to play roles in friction reduction and protection of surfaces. After removal of adsorbed films on cartilage surfaces, it was pointed out that non-fibrillar proteoglycan gel-like surface layer maintains a low friction due to its low shearing resistance and protects the cartilage bulk tissue.<sup>12</sup> Surface structure covered with adsorbed films on underlying proteoglycan gel-like layer<sup>13</sup> has one kind of fail-safe system in synovial joints. As mentioned above, the various lubrication modes appear to synergistically play important roles in the reduction of friction and wear, depending on the severity of operating conditions. This superior lubrication mechanism was called the adaptive multimode lubrication mechanism by Murakami.<sup>3,14</sup>

In addition to the previously described lubrication modes, the importance of biphasic lubrication<sup>15</sup> and hydration lubrication<sup>16</sup> has been indicated. The molecular lubrication mechanisms including polymer brush<sup>17,18</sup> has been explored.

On the viewpoint of biphasic lubrication,<sup>15,19–21</sup> it should be first recognized that articular cartilage has a high water content from 70% to 80% in tissue composed of type II collagen, proteoglycan and chondrocytes, and thus exhibits a time-dependent biphasic behaviour due to the simultaneous coexistence of solid and liquid phases.<sup>22</sup> It is also noted that lubrication mode depends on the extent of exudation and rehydration. The load support by interstitial fluid pressure in biphasic cartilage controls the friction and deformation. In this article, the difference in effectiveness of load support by interstitial fluid pressure under different loading conditions is examined by biphasic FE analysis previously reported by Sakai et al.<sup>23</sup>

Next, under operating condition where the effectiveness of biphasic lubrication will be reduced, the roles of alternate lubrication mechanisms are

discussed on the basis of reciprocating tests of articular cartilage against glass plate. In intimate local contact zone of hydrated cartilage surface, the effectiveness of rehydration and adsorbed films formed on proteoglycan gel layer at the uppermost superficial zone in articular cartilage was examined in repeated reciprocating tests, including the restarting processes after interruption and unloading to evaluate the influence of rehydration and roles of adsorbed film.<sup>24,25</sup>

### *Lubrication mechanism in artificial joints*

In most of joint prostheses composed of UHMWPE and metal, some direct contacts occur between the rubbing surfaces, which can produce wear debris in mixed or boundary lubrication modes. Although several new trials such as cross-linking of UHMWPE,<sup>26</sup> addition of vitamin E,<sup>27</sup> surface treatment by phospholipid polymeric brush-like layer to UHMWPE<sup>28</sup> and improvement of hard-on-hard bearing<sup>29,30</sup> have extended the life of joint prostheses; there are still unsolved problems on wear under severe contact conditions in various daily activities. Therefore, another promising method to establish no wear and low friction is required. The application of appropriate compliant artificial cartilage materials with properties similar to articular cartilage is expected to duplicate the superior load-carrying capacity and tribological properties of natural synovial joints. The fluid film formation is enhanced and the contact stress level is reduced due to the elastic deformation effect of low-modulus materials in joint prostheses, as described in 'Adaptive multimode lubrication in natural synovial joints'. Unsworth et al.<sup>31</sup> showed in hip prosthesis composed of metallic femoral head and acetabular cup lined with polyurethane of appropriate compliance and thickness that the fluid film lubrication can be achieved even with low-viscosity lubricants in experimental simulator tests. The polyurethane has sufficient mechanical strength, but the possibility of high friction lubricated with lubricant containing synovia constituents under thin film conditions<sup>32</sup> should be prevented. In contrast, poly(vinyl alcohol) (PVA) hydrogel with high water content is expected to reproduce similar multimode lubrication to natural joints.<sup>14,32</sup> At earlier stage (1988), the hip prosthesis with artificial cartilage layer of PVA hydrogel prepared by repeated freezing-thawing method with 85–90 wt% water content on the inner surface of the acetabular cup showed quite a similar low frictional behaviour to natural synovial joint, but did not attain the sufficient durability in the simulator test.<sup>33</sup> Meanwhile, the PVA hydrogel prepared through other synthetic process with lower water content had a better wear resistance in unidirectional pin-on-disc test and exhibited better shock-absorbing ability than traditional UHMWPE. However, wear increased in reciprocating test

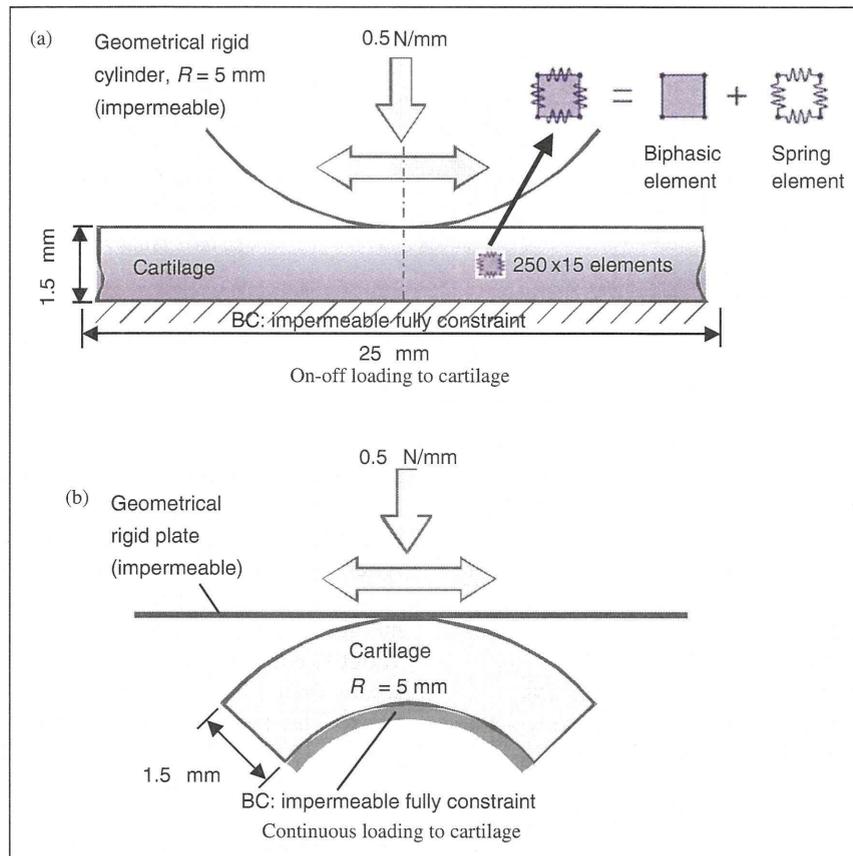
including thin film condition at stroke ends.<sup>34</sup> The simplified knee prosthesis model with soft layer of PVA hydrogel prepared by repeated freezing-thawing method with high water content of 79 wt% and Young's modulus of 1.1 MPa exhibited superior lower friction in walking simulator test lubricated with hyaluronate (HA) solution containing serum proteins than the model with polyurethane layer as described above.<sup>32</sup> However, an increase in protein concentration in the HA solution increased wear of PVA in reciprocating test of PVA hydrogel against itself under severe conditions.<sup>35</sup> Even in this reciprocating test, at certain combination of albumin and  $\gamma$ -globulin in lubricants, it was found that the wear was remarkably reduced, where the layered adsorbed film formation was confirmed.<sup>35</sup> The fluorescent images of adsorbed films after testing indicated the optimum adsorbed film formation as layered structure at minimum wear and low friction conditions. Furthermore, the corresponding adsorbed film formation during reciprocation was confirmed by *in situ* visualization.<sup>36–38</sup> But, further improvement of tribological performance of hydrogel artificial cartilage is required for various physiological conditions. The possibility of further improvement by fibre reinforcement in tribological property of PVA hydrogel in artificial joints is examined in this article.

For clinical application, the *in vivo* study for post-operative 2 years on biocompatibility and stability of meniscal function including mechanical properties of PVA hydrogel artificial meniscus of high water content in rabbit joint<sup>39</sup> suggests a satisfactory possibility of PVA hydrogel meniscal replacement treatment. The authors confirmed the good wear resistance of PVA hydrogel cartilage implanted in femoral condyle as hemi-arthroplasty in rabbit knee joint as a preliminary evaluation.<sup>40</sup>

## **Materials and methods**

### *Biphasic FE analysis for articular cartilage during reciprocating motions*

In biphasic lubrication, the keeping of high ratio of load support by interstitial fluid pressurization due to very low permeability of cartilage tissue is capable to reduce friction. In the biphasic FE analysis, the changes in interstitial fluid pressure and stress in solid phase in the two models in reciprocating motion were examined. Detailed analysis method is described in the previous paper by Sakai et al.,<sup>23</sup> and the important fundamental method and different terms are described in this article. The biphasic FE analysis was carried out using inhomogeneous depth-dependent apparent Young's modulus of solid phase,<sup>41,42</sup> strain-dependent permeability (compaction effect)<sup>43,44</sup> and collagen reinforcement in tensile strain.<sup>44</sup> In this study, the differences in biphasic behaviours were examined under different loading



**Figure 1.** Biphase FE models for reciprocating sliding under two kinds of loading conditions.

conditions for two models, as shown in Figure 1, in the reciprocating tests at sliding speed 4 mm/s and stroke 8 mm at a constant load of 0.5 N/mm. For model (a) under on-off loading to articular cartilage, the reciprocating sliding of cylindrical impermeable rigid specimen was simulated on the biphase cartilage flat plate specimen of 1.5 mm thickness where the contact region migrates on the cartilage surface, similar to that described in the previous paper.<sup>23</sup> In contrast, for model (b) under continuous loading to articular cartilage, the reciprocating sliding of impermeable rigid plate specimen was simulated on the biphase cartilage cylindrical specimen of 1.5 mm thickness where the continuous contact is maintained on the top area of the articular cartilage.

Two-dimensional biphase FE analysis was conducted using commercial package ABAQUS (6.8-4), which was evaluated as an appropriate software for the biphase analysis.<sup>45</sup> The biphase tissue was modelled by CPE4RP (four-node bilinear displacement and pore pressure, reduced integration with hourglass control) elements and the mesh size was chosen as  $0.1 \text{ mm}^2$ . The horizontal and vertical fibrils were represented by spring element SPRINGA (axial spring between two nodes, whose line of action is the line joining the two nodes) of the software, in which the spring elements were configured to generate reaction

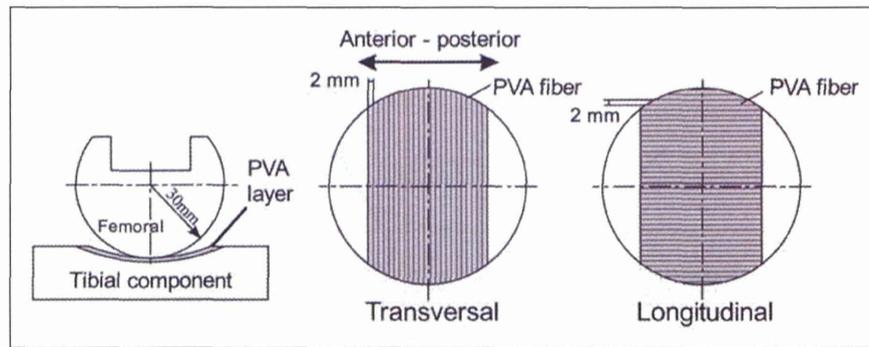
force only in the tensile direction. The stiffness  $K$  of the spring elements was simplified to the uniform value over the tissue and both in horizontal and vertical directions.

The bottom surfaces of the cartilage models were fixed and impermeable, where no flow was allowed through them. Material properties were specified by curve fitting comparing FE calculation with experimental time-dependent reaction force of the cylindrical indenter. The other surfaces were not fixed and basically permeable except for the contact region. The friction coefficient for solid-to-solid contact  $\mu_{eq}$  between the geometrical rigid indenter and the solid phase<sup>18</sup> was set to 0.2. In this study, the management of the surface seepage for exuding water content was implemented by user subroutine of ABAQUS using FLOW function (user subroutine to define non-uniform seepage coefficient and associated sink pore pressure for consolidation analysis).

The variables for the curve fitting on FE calculation were as follows:

total apparent Young's modulus:  $E_0 = 0.83 \text{ MPa}$   
 depth-dependent Young's modulus at depth  $x$

$$E(x) = (\varepsilon_0/\varepsilon)E_0 \quad (1)$$



**Figure 2.** PVA specimens for simulator test. PVA: poly(vinyl alcohol).

local strain at depth  $x$

$$\varepsilon(x) = 0.462e^{-6.53x} + 0.0284 \quad (2)$$

Poisson's ratio:  $\nu = 0.125$

initial permeability:  $k_0 = 58.9 \times 10^{-15} \text{ m}^4/\text{Ns}$

minimum permeability:  $k_{\min} = 5.0 \times 10^{-15} \text{ m}^4/\text{Ns}$

compaction effect of permeability:  $M = 22$

initial void ratio:  $e_0 = 4.0$  (80% interstitial fluid)

spring stiffness:  $K = 17.5 \text{ MPa}$

seepage coefficient:  $1 \text{ mm}^3/\text{Ns}$  for flow and  $0 \text{ mm}^3/\text{Ns}$  for no flow

The strain dependence of permeability  $k$  is estimated by the following formula above the minimum limit, where  $e$  is the current void ratio<sup>44</sup>

$$k = k_0 \exp(M(e - e_0)/(1 + e_0)) \quad (3)$$

In simulation of reciprocating test, a load of  $0.5 \text{ N/mm}$  was applied by rigid cylindrical or flat plate indenter with a ramp time of 1 s and then the load was held constant for further 508 s. Initial horizontal position of the indenter was at the centre of the cartilage tissue surface. The reciprocation of rigid cylinder or flat plate was started immediately after loading and continued for 508 s, 127 cycles at a period of 4 s.

### Improvement of tribological performance of artificial cartilage

In the walking simulator test, the simplified knee prosthesis models composed of stainless steel cylindrical femoral component of radius 30 mm and axial length 60 mm, and tibial component with PVA hydrogel layer in 2 mm thickness as a concave surface of radius 60 mm were used (Figure 2).<sup>46</sup> To examine the performance of fibre-reinforced PVA, three kinds of PVA sheets of thickness 2 mm were prepared, i.e. pure PVA and fibre-reinforced PVA in transversal and longitudinal directions to anterior–posterior, as shown in Figure 2. As reinforcing fibre, long-fibre PVA of diameter

0.34 mm and strength 1.9 N was used. PVA fibre was located at the centre in thickness and at definite intervals of 2 mm between the adjacent fibres. After arrangement of fibre network, PVA solution was cast in and gelled by repeated freezing–thawing method. Young's modulus of fibre-reinforced PVA is about five times larger as 5.8 MPa in longitudinal direction than 1.2 MPa in transversal direction or pure PVA. The simulator testing was conducted under normal walking condition for flexion–extension motion and phase-dependending tibial-axis load according to the condition in draft of ISO-14243 (1998). The internal–external rotation and anterior–posterior movement were constrained to evaluate the frictional behaviours in sliding motion through load cell. HA solution containing 0.7 wt% albumin and 1.4 wt%  $\gamma$ -globulin was used, because this lubricant showed very low wear and low friction in reciprocating test of sliding pair of PVA against itself.<sup>35,47</sup>

## Results

### Biphase FE analysis for articular cartilage during reciprocation motions

The changes in interstitial fluid pressure and Mises stress of solid phase in simulated reciprocating tests based on biphase FE analysis are shown for the on–off loading to articular cartilage (migrating contact area) and for the continuous loading to articular cartilage (continuous contact) in Figures 3 and 4, respectively. It is noticed under on–off loading condition in Figure 3 that the interstitial fluid pressure is high at start and a high level of pressure is maintained even after 508 s, 127 reciprocating cycles. In addition, Mises stress is low at start and the stress distribution is a little changed but stress level is not so much changed after 508 s, 127 cycles. This fact suggests that most of the loading is supported by interstitial fluid pressure in reciprocating sliding with sufficient stroke length.<sup>48</sup> As pointed out in the previous paper,<sup>23</sup> the model including the spring reinforcement exuded the interstitial fluid in the forward surface of the indenter, whereas the fluid flow in the backward region was

drawn into the cartilage tissue. On the contrary, the continuous loading to the cartilage had a large influence on time-dependent biphasic behaviours. It is remarkably noted under continuous loading to articular cartilage in Figure 4 that the interstitial fluid pressure at start is considerably high and Mises stress at start is low, but after 508 s, 127 reciprocating cycles, the fluid pressure almost disappears and high Mises stress concentrates in the cartilage surface zone. Furthermore, it is worth noting that the contact area increases from the initial contact area, while the contact area under on-off loading maintains almost initial area in size.

To compare the changes in load supports by fluid pressure and vertical stress in solid phase, the supporting forces by fluid pressure and vertical stress in solid phase were estimated and the percentages of fluid load support were calculated in Figure 5. It is confirmed

that the fluid load support maintains from 90% at start to 83% after 508 s in reciprocation motion under on-off loading condition, but under a continuous loading condition, the load support by interstitial fluid pressure decreases from 91% at start to 27% after 508 s as time-depending phenomenon. The maintaining of fluid pressure under on-off loading is considered to be due to recovery of deformation with rehydration during off-loading phase, as indicated by a previous paper.<sup>23</sup>

In the biphasic FE analysis for reciprocating sliding, the friction coefficient  $\mu_{eq}$ <sup>15</sup> for solid-on-solid contact is assumed as 0.2. Therefore, the time-depending changes in friction coefficient  $\mu_{eff}$  can be estimated using the formula by Ateshian et al.<sup>19,21</sup>

$$\mu_{eff} = \mu_{eq}(1 - (1 - \Psi)W^P/W) \tag{4}$$

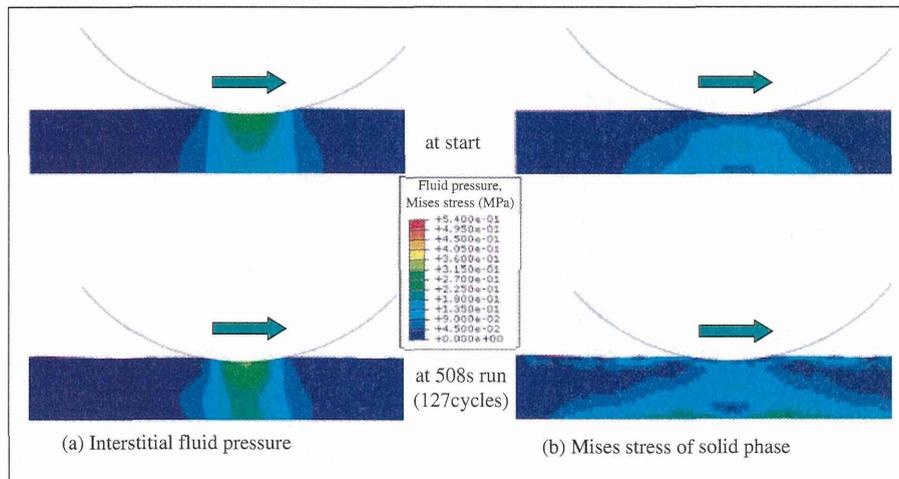


Figure 3. Changes in interstitial fluid pressure and Mises stress of solid phase in the reciprocating test under on-off loading to the cartilage.

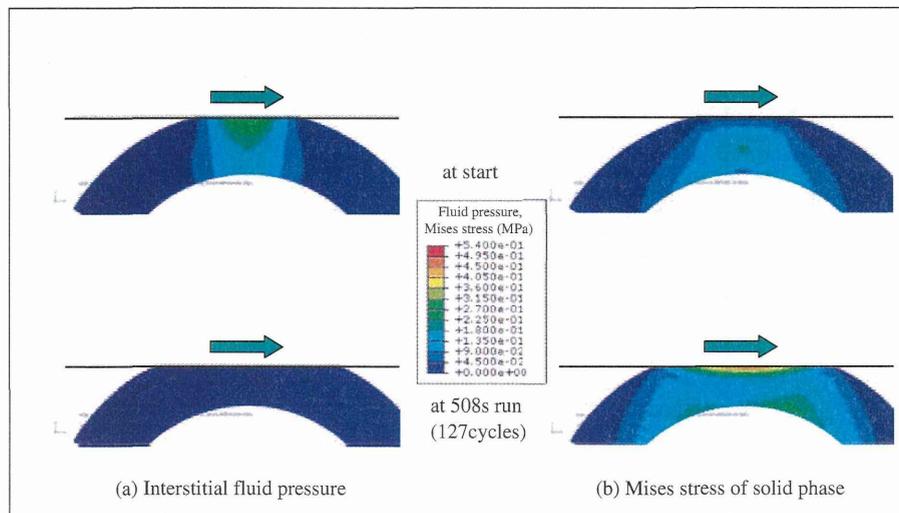
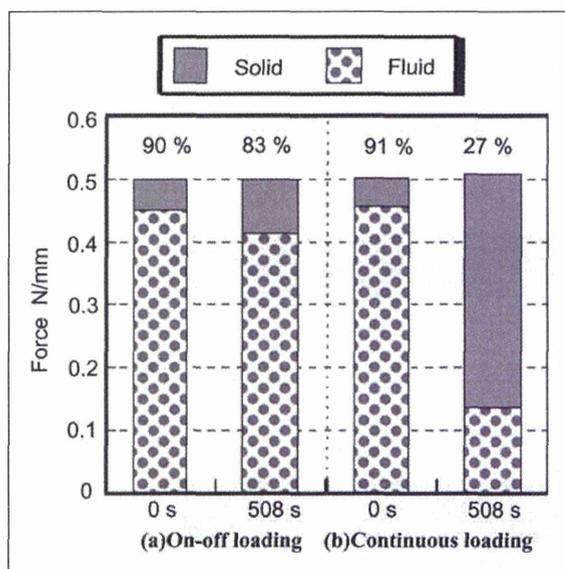


Figure 4. Changes in interstitial fluid pressure and Mises stress of solid phase in the reciprocating test under continuous loading to the cartilage.

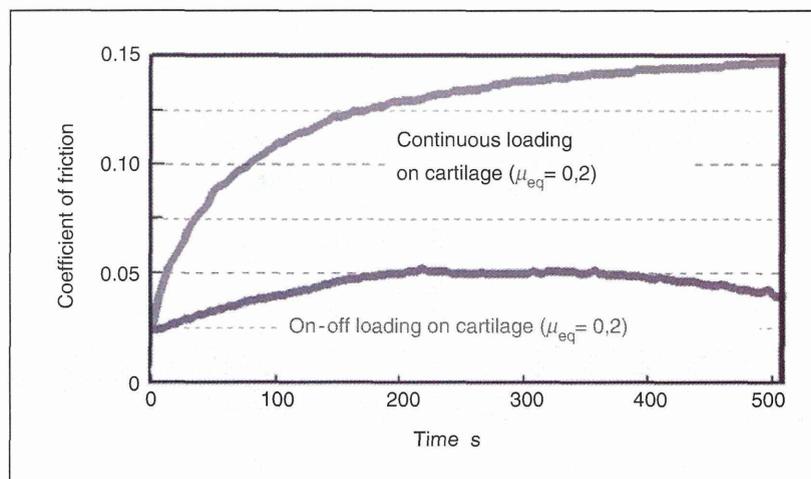
where  $W$  is the total load support,  $W^p$  the load support by fluid pressure and  $\Psi$  the fraction of contact area of solid phase.

The estimated frictional behaviours are shown in Figure 6. The friction for on-off loading condition shows a little increase but is not so much changed. In contrast, the friction for continuous loading gradually increases from an initial low value and approaches to equivalent friction coefficient, although the friction level depends on the assumed value of 0.2 for solid-to-solid friction coefficient. The gradual increase in friction under continuous loading corresponds to the previous studies.<sup>15,19,21</sup>

As described above, the biphasic lubrication mechanism is expected to be effective in reciprocating



**Figure 5.** Load support by interstitial fluid pressure and stress in solid phase for on-off loading and continuous loading to cartilage (percentages of load support by fluid pressure are shown with graph).

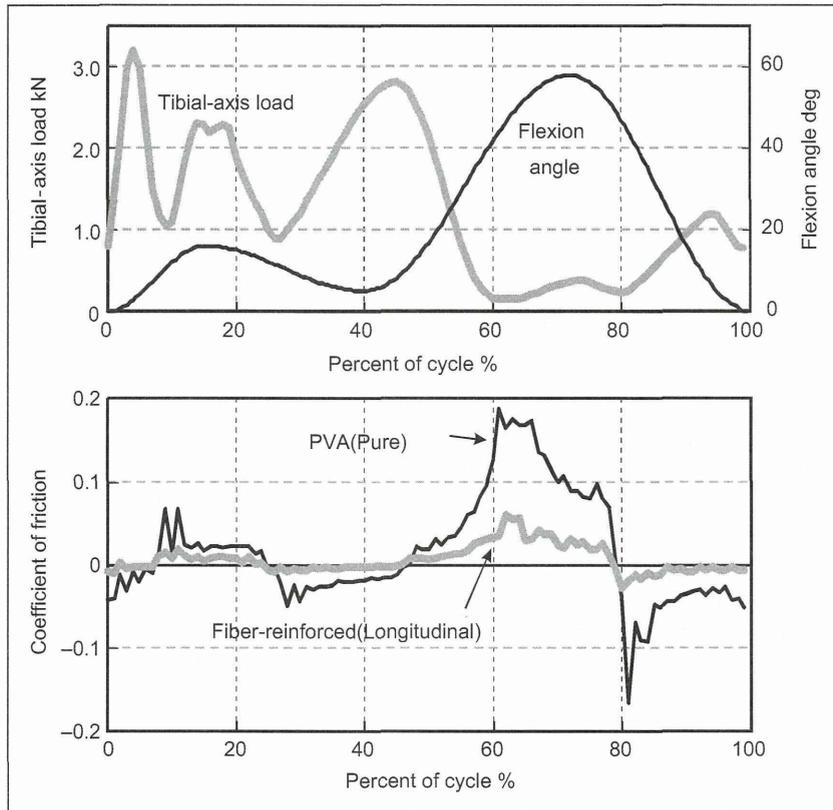


**Figure 6.** Estimated friction behaviours based on biphasic friction for on-off loading and continuous loading to cartilage in reciprocating motion.

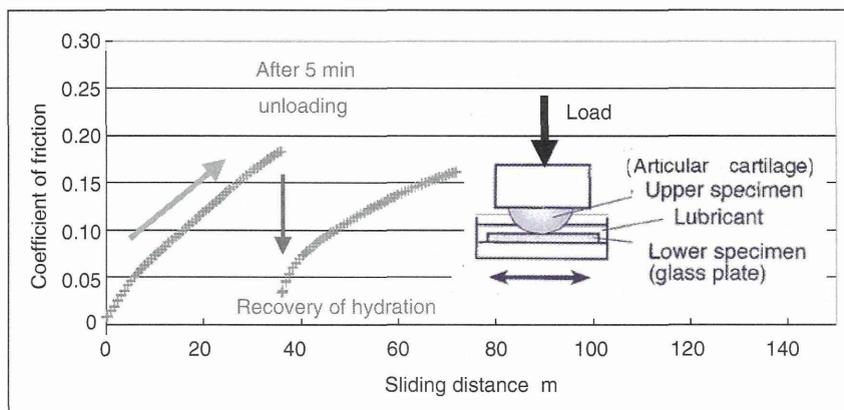
sliding where the contact region of cartilage specimen migrates for the cartilage specimen. However, in reciprocating sliding of cartilage under continuous loading, the interstitial fluid pressurization diminishes with exudation of fluid from the cartilage at a constant load, and thus, the effect of biphasic lubrication is gradually decreased. In the latter case, the alternate lubrication mechanisms become important from the viewpoint of adaptive multimode lubrication, and new findings are discussed on the basis of the previous experimental results of friction tests in 'Discussion'.

### Improvement of tribological performance of artificial cartilage

Figure 7 shows the frictional behaviours of simplified knee prostheses composed of metallic cylindrical femoral component and tibial component with PVA hydrogel layer in the walking simulator test.<sup>46</sup> HA solution containing 0.7 wt% albumin and 1.4 wt%  $\gamma$ -globulin as one of the optimum composition seems to be effective in maintaining a low friction level during stance phase under high load. For comparison of three models during stance and swing phases, pure PVA shows the largest friction, and fibre-reinforced PVA in the longitudinal direction exhibits the lowest friction (Figure 7). The fibre-reinforced PVA in the transversal direction showed a little higher friction than in longitudinally reinforced PVA. As discussed in the previous paper<sup>23</sup> on biphasic FE analysis, the reinforcement by collagen fibre in the surface zone was effective to maintain the interstitial pressurization during reciprocating sliding. The experimental result in Figure 7 indicates the possibility of application of biphasic lubrication mechanism in natural articular cartilage to hydrogel artificial cartilage. However, the further investigation for actual lubrication mechanism in fibre-reinforced hydrogel is required, including synergistic lubrication with



**Figure 7.** Frictional behaviours of simplified knee prostheses with PVA layer in the simulator. PVA: poly(vinyl alcohol).



**Figure 8.** Frictional behaviour in repeated reciprocating test for ellipsoidal articular cartilage specimen against glass plate lubricated with saline.

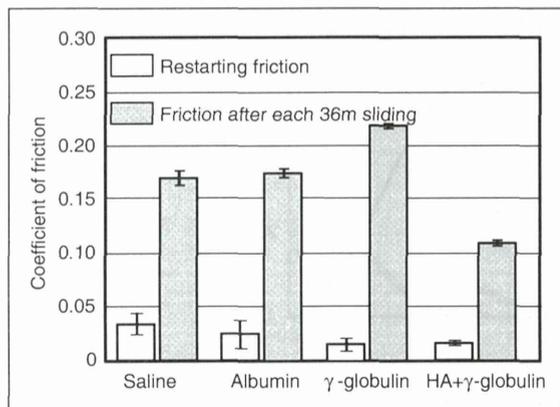
appropriate lubricants and surface properties as discussed below.

## Discussion

### *Biphasic FE analysis for articular cartilage during reciprocation motions*

As shown in biphasic FE analysis (Figures 3 and 5), the high interstitial fluid pressure can be maintained accompanied with low Mises stress in the solid phase

during repeated reciprocating motions at sufficiently long stroke of 8 mm under on-off loading to articular cartilage (migrating contact area), which enables the unloaded region in the cartilage to rehydrate. In contrast, after 127 cycles in the reciprocating test under continuous loading to the same region of cartilage, the interstitial fluid pressure was remarkably reduced, and Mises stress substantially increased and the deformation proceeded for larger load support by solid phase, as shown in Figures 4 and 5. For the latter condition under continuous loading, friction gradually increased to a high level (Figure 6). In this FE



**Figure 9.** Influence of proteins and HA on changes in friction during repeated reciprocating test for articular cartilage. HA: hyaluronate. Error bars indicate standard deviation.

analysis, friction coefficient  $\mu_{eq}$  for solid-on-solid contact is assumed as 0.2. In healthy synovial joints, the lubricating constituents in the synovial fluid and on uppermost superficial cartilage are likely to maintain  $\mu_{eq}$  at a lower level than 0.01 and prevent the rising of friction as adsorbed film formation in a fail-safe system in case the interstitial fluid pressurization has subsided.

In repeated reciprocating tests of 36 m sliding with unloading for 5 min for an intact ellipsoidal cartilage specimen against a flat glass plate, time-dependent frictional behaviours were observed, as shown in Figure 8.<sup>24,25</sup> An intact ellipsoidal cartilage with a subchondral layer was carefully prepared from the femoral condyle in a porcine knee joint (6–7 months old), after it was brought with protective joint capsule and synovial fluid to the laboratory from the slaughterhouse. In saline, the gradual increase from an initial low friction was observed as suggested by a curve under continuous loading in Figure 6, but friction at 36 m sliding did not attain the equilibrium state. Furthermore, it is noticed in Figure 8 that the restarting friction immediately after reloading is reduced from the previous high friction before unloading. The level of restarting friction indicates the extent of recovery of biphasic and hydration lubrications after rehydration of the cartilage, and the state of adsorbed film formation appears to control this frictional behaviour. For example, the addition of a single protein such as albumin or  $\gamma$ -globulin improved the restarting friction but did show higher friction than saline at each 36 m sliding, as shown in Figure 9, where the restarting tests were carried out three times.<sup>24,25</sup> In contrast, a combination of HA as a viscous constituent and  $\gamma$ -globulin as a protein exhibited lower friction at restart and at 36 m sliding (Figure 9). This fact suggests the possibility of sustaining of low friction with appropriate lubricant composition even under continuous loading conditions. For example, Nakashima et al.<sup>35</sup> first found the good

lubricating performance of this composition of proteins as 1.4 wt% albumin and 0.7%  $\gamma$ -globulin (A/G ratio = 2:1) or 0.7 wt% albumin and 1.4 wt%  $\gamma$ -globulin (A/G ratio = 1:2) in reciprocating tests of PVA hydrogel against itself. The elucidation of effect of lubricant compositions containing proteins, HA, phospholipids and other lubricating constituents on low friction and minimum wear for articular cartilage will be reported in future study.

### Improvement of tribological performance of artificial cartilage

To improve the tribological performance of artificial hydrogel cartilage, the approaches of optimization for biphasic properties of hydrogel and lubricating properties of lubricant constituents are required. The effectiveness of fibre-reinforced structure in the PVA hydrogel in a simulator (Figure 7) is one successful example to mimic natural mechanism in articular cartilage. The lowering of friction during high-load stance phase at low sliding speed is a noticeable phenomenon.

Recently, the authors' research group found that the network structure of PVA gels cross-linked by microcrystallites has important roles in time-dependent friction and deformation behaviours in reciprocating tests for two kinds of PVA hydrogel materials prepared by repeated freezing–thawing method and cast-drying method. It is worth noting that the cast-drying PVA hydrogel with uniform microstructure maintains superior low friction even under continuous loading condition.<sup>49</sup>

In the previous studies,<sup>35–38</sup> the effectiveness of optimum layered adsorbed film formation to minimize the wear of PVA hydrogel has already been reported. In this article, HA solution containing 1.4 wt% albumin and 0.7 wt%  $\gamma$ -globulin was used as an optimum lubricant. To evaluate the actual adsorbed film formation, the changes in conformation of proteins<sup>50</sup> should be considered in rubbing conditions. In further study, the mechanism for the optimum adsorbed film formation on PVA hydrogel should be elucidated in comparison with optimum adsorbed films on articular cartilage.

As discussed above, the superior lubrication mechanisms with a high load-carrying ability in natural synovial joints are expected to apply to the appropriate lubricating mechanism and biphasic structure with surface property providing the surface protection in cases of severe loading and little movement in hydrogel materials as artificial cartilage. In development of artificial hydrogel cartilage with superior lubricity, it is considered that the viewpoint of adaptive multi-mode lubrication becomes important.

The clinical application of PVA hydrogel as artificial cartilage for high-load joints is the final target, but at the present stage, the establishment for appropriate design for not only low friction but also zero wear is required. The conditions for zero wear will be