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Protein-mediated boundary lubrication in arthroplasty

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Abstract

Wear of articulated surfaces can be a major lifetime-limiting factor in arthroplasty. In the natural joint, lubrication is effected by the body's natural synovial fluid. Following arthroplasty, and the subsequent reformation of the synovial membrane, a fluid of similar composition surrounds the artificial joint. Synovial fluid contains, among many other constituents, a substantial concentration of the readily adsorbing protein albumin. The ability of human serum albumin to act as a boundary lubricant in joint prostheses has been investigated using a pin-on-disc tribometer. Circular dichroism spectroscopy was employed to follow the temperature- and time-dependent conformational changes of human serum albumin in the model lubricant solution. Effects of protein conformation and polymer surface hydrophilicity on protein adsorption and the resulting friction in the boundary lubrication regime have been investigated. Unfolded proteins preferentially adsorb onto hydrophobic polymer surfaces, where they form a compact, passivating layer and increase sliding friction—an effect that can be largely suppressed by rendering the substrate more hydrophilic. A molecular model for protein-mediated boundary friction is proposed to consolidate the observations. The relevance of the results for in vivo performance and ex vivo hip-joint testing are discussed.

Keywords: Albumin; Protein adsorption; Protein conformation; Joint replacement; Arthroplasty; Friction; Interface; Polyethylene; Hydrophilicity

1. Introduction

By virtue of our modern lifestyle, more than one-third of the readers of this article will likely experience the failure of their native hip joint(s)—sooner or later [1]. Fortunately, hip-joint arthroplasty is on hand to deal with this condition. A major unsolved problem, however, is the mechanical wear of the artificial joint, which limits the lifetime to about 10–15 years [2]. While most lubrication of the healthy natural joint relies on a film of synovial fluid (SF), the artificial joint consists of synthetic materials and is mainly lubricated in the mixed and boundary regimes [3]. In a widely used arthroplastic design [4], the acetabular cup consists of a linear of ultra-high-molecular-weight poly(ethylene) (UHMWPE), and the femoral head is a polished metal or ceramic ball. The wear [2] of the UHMWPE lining is generally regarded as the key lifetime-limiting factor. Up to 100,000 μm-sized wear particles are released per footstep. Such wear particles can activate the immune system [5] as well as be deposited into the surrounding tissue [6]. These factors can ultimately lead to osteolysis and mechanical loosening of the implant [7]. In this study, we investigated boundary lubrication mediated by naturally occurring amphiphilic molecules—an aspect that has received recent attention [8–11].

From an engineering standpoint, SF can be regarded as an aqueous electrolyte solution containing proteins, lipids and hyaluronic acid [12]. SF is also important for implants since a few weeks into the healing process, it surrounds the artificial joint. The predominant lubrication mode is in the mixed and boundary regimes [13]. In this study, we focus on the role of the most abundant protein in SF—human serum albumin (HSA). A screening study involving proteins and lipids was used

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to identify the molecules relevant for boundary lubrication. In agreement with previous studies [14], we identified HSA as a constituent with a significant effect on sliding friction. We wanted to focus on the boundary lubrication properties of the HSA component adsorbed onto poly(ethylene). Poly(ethylene) is considerably more hydrophobic than natural cartilage, and therefore proteins are expected to adsorb in very different ways onto the two surfaces. In a previous pin-on-disc study [15], we indeed found that the friction of UHMWPE versus ceramic was reduced in a HSA solution after the polymer was transiently rendered more hydrophilic. An oxygen RF-plasma treatment of the polymer surface was used to achieve the desired hydrophilicity. The use of more permanently hydrophilic surfaces by changing the bulk polymer chemistry was shown to be impractical, using available materials, due to their inferior mechanical properties [16]. Here, we extend our study to include the temperature-dependent protein conformation and clarify its behavior during adsorption and boundary lubrication in the UHMWPE/ceramic tribopair.

HSA consists of 585 amino acids and is comparatively rich in cysteine, which allow HSA to form a total of 17 internal disulfide bridges [17]. HSA has a rather high α-helical content [18], which can readily be detected using the circular dichroism (CD) technique. HSA consists of three domains with similar primary structure and is glycosylated at residues Asn-342 and Asp-518. The unfolding of HSA is known to proceed in several incremental steps [19].

In solution, proteins can be unfolded (i.e. denatured) by a change in chemical environment [20], pressure [21] or by changes in temperature [22].

Recently, it has been found that the temperature in articulated joints may rise up to 45°C below the cartilage surface in vivo [23,24] and up to 90°C in ex vivo hip-joint simulator tests [25,26]. Irreversible unfolding of proteins occurring under such conditions can significantly affect their boundary lubrication properties.

2. Experimental

2.1. Tribometer

A tribometer in pin-on-disc configuration was used to characterize the tribological properties of the test surfaces. Although this simple setup does not reproduce all clinical parameters relevant for the accurate simulation of wear (e.g. contact geometry, loading cycle, fluid entrainment or multi-directional sliding), it can give valuable fundamental information about the effects of interfacial protein adsorption on friction. The tribometer (CSEM, Switzerland) had a nominal loading range of 0.1–10 N (static weights) and a nominal velocity range of 10^{-4}–10^{-1} m/s. The sliding radius was set to either $r_1 = 3$ mm or $r_2 = 9$ mm, to extend the nominal velocity range. For comparison, the typical in vivo sliding speeds of the hip joint are known to be in the range of 0–10^{-1} m/s [27]. Friction was measured both in start–stop and steady-state sliding conditions. The friction data were recorded digitally at a sampling rate of 45 Hz. The nominal sensitivity of the friction–force measurement was 10 mN. A Plexiglas hood covered the tribometer, allowing physiological temperatures (37 ± 2°C) of pin, disc and lubricant to be maintained during all friction experiments. An IR heater with adjustable power and a DC fan inside the hood were used for this purpose. For some experiments, the model lubricant solution was independently heated to achieve higher temperatures: A peristaltic pump was used to continuously circulate the lubricant through a tubing system that passed through a heated water bath outside the tribometer. The temperature of the water bath could be adjusted in a range of 25°C to 90°C. Under typical circulation conditions, an individual protein molecule was thus repeatedly exposed to elevated temperatures by passage through the water bath. Typically, this amounted to $\approx 8\%$ of the total circulation time. Comparison between cyclic and steady tempering indeed revealed that the relevant parameter for irreversible protein unfolding was the integral exposure time to elevated temperature [28]. Multiplication of the time axis by a factor 0.08 was thus used to normalize the exposure times shown in Fig. 4 below.

2.2. Polymer and ceramic materials

We used flat-ended pins of ultra-high-molecular-weight poly(ethylene), (UHMWPE—medical-grade, DSM Stamylan, UH210). The dimensions of the square pins were 1.5 mm × 3.5 mm × 3.5 mm, as cut out of a larger block. The surface roughness of the pins was constant, $R_a = 1.5 \pm 0.5$ μm, after several hours of run-in, and a fixed pair of pin and disc was used for all measurements with each kind of lubricant composition. Rough pins were chosen because a statistical analysis of 20 independent friction measurements at 10 N load revealed superior reproducibility of the rough pins ($R_a = 1.5 \pm 0.5$ μm, $\sigma_{rough} = 50$ mN) as opposed to smooth pins ($R_a < 0.1$ μm, $\sigma_{smooth} = 180$ mN). Pins and disc were reused and thoroughly cleaned before each experiment (see below).

Medical-quality UHMWPE differs from the industrial polymer mainly in the smaller proportion of additives and trace elements. This is achieved by additional purification procedures and omission of antioxidants or stabilizers. This polymer is therefore susceptible to aging [29]. The ceramic discs used for