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MATERIALS INCOMPATIBILITY AS A MAJOR CAUSE OF HIP PROSTHESES REJECTION

Isabel Carvalho[1], Tomas Polcar[1,2], Mariana Henriques[3] and Sandra Carvalho[4,5]

[1]Department of Control Engineering, Faculty of Electrical Engineering, Czech Technical University in Prague, Technická 2, Prague 6, Czech Republic
[2]Engineering Materials, University of Southampton, Highfield, SO17 1BJ, Southampton, UK
[3]CEB, Centre of Biological Engineering, LIBRO-Laboratório de Investigação em Biofilmes Rosário Oliveira, University of Minho, Campus of Gualtar, 4700-057 Braga, Portugal
[4]GRF-CFUM, University of Minho, Campus of Azurém, 4800-058 Guimarães, Portugal
[5]SEG-CEMUC Mechanical Engineering Department, University of Coimbra, 3030-788 Coimbra, Portugal

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Abstract. The development of new multifunctional coatings to apply on medical biomaterials continues to be required, since materials commonly used in hip prostheses still presenting failures. Multifunctionality is the result of a synergy, on the nanoscale level, of good corrosion, mechanical and tribological properties. Additionally, a biomaterial must always be biocompatible. Besides these properties, the major challenge would be to get a material that also has antimicrobial activity. In this context, the development of advanced materials with the ability to present these properties is being regarded as a strategy to prevent the colonization of implant and biofilm formation by bacteria. So, in this review, the attention is focused on the description of the fundamental points of the natural synovial joint, since, its mechanical and tribological characteristics are the main causes that lead to the necessity of its replacement by an implant. Moreover, a contextualization was also performed on the hip replacement surgery and the biomaterials used, with a focus on their mechanical and tribological properties. Finally, it is explained the need of surface modification and the potential of TiCN coatings doped with silver.

1. INTRODUCTION

The increase of elderly population observed nowadays leads to a higher incidence of joint diseases such as osteoarthritis, rheumatoid arthritis and osteonecrosis, which in many cases leads to the need for total or partial replacement of the joint by artificial implants. Although these problems are more often associated with the population with a relatively advanced age, sometimes there are other conditions which lead to the need of joint replacement in the youngsters, such as epidemiological factors or situations of trauma caused by accidents. The surgical technique, which is presented as an immediate solution to this problem is hip replacement surgery, named hip arthroplasty, that could be primary or revision. Despite the arthroplasty of the hip is one of the greatest achievements of orthopaedic surgery in the past decades, different risk factors are still associated. Infection is the third most common cause of revision of total hip arthroplasty (THA) after instability/dislocation and mechanical loosening [1]. Therefore, the materials used in the implants production still require many developments given that their time in service is still low and the current average life span of these materials is about 15 years that is not sufficient for a population that may re-

Corresponding author: Isabel Carvalho, e-mail: isascarvalho@hotmail.com

quire 30–40 years of service [2]. Moreover it means a greater economic cost level. Thus, it is of major importance to overcome this problem, with the development of new coatings which will confer improved physical, mechanical, tribological and biological properties to the traditional biomaterials.

Titanium nitride (TiN) and Diamond–like carbon (DLC) have been used in industrial applications, however the first one shows high friction coefficient and relatively high wear rate [3,4] and the second one possesses moderate biocompatibility [5,6], which can represent a drawback in terms of multifuncionality. Transition-metal carbides, and metal nitrides, proved to be very attractive base materials due to a successful combination of high hardness [7], good wear and corrosion resistances [7–9]. The idea is to cover a wide range of mechanical/tribological properties outputs (high surface hardness and good lubricating performance, which translates into a low wear rate). Nevertheless, recent results demonstrated that, although there are some biomaterials presenting good mechanical properties and low cytotoxicity, they can be prone to microbial colonization [10,11]. This colonization is more frequently associated to *Staphylococcus epidermidis, being* one of the bacteria most commonly found in orthopaedic prosthesis [12,13]. Infections caused by this microorganism are often associated to implant failure [14]. Hence, this strengthens the urgent need of the development of new coatings with improved antimicrobial properties.

Several studies have been performed describing the use of silver with antimicrobial activity and for biomedical applications [15–20]. However, they only consider silver antimicrobial action disregarding other important factors, as silver cytotoxicity and materials' mechanical and tribological properties [18]. So, this highlights the importance of gathering all the materials properties, from mechanical and physical to biological properties, in order to develop a new material that is able to last long in patient and that is the most harmless possible.

2. HIP JOINT

2.1. Morphology

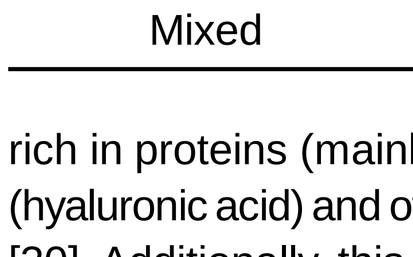
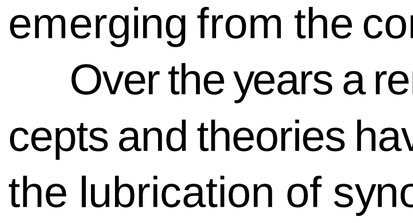
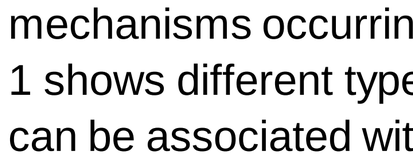
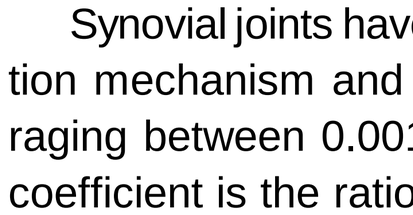
The hip is one of the joints in the human body which is subjected to most violent efforts. Its main function is to support the weight, balance the body in static postures (standing) and dynamic (walking or running), and protect the reproductive system and the lower part of the digestive system. The hip is the second most flexible joint in the body, after the shoulder, since it allows a great range of motion. These characteristics result from the configuration of ball-and-socket synovial joint where the roughly spherical femoral head is largely contained within the acetabulum [21–23]. Both articular surfaces are covered with a strong but lubricated layer called hyaline cartilage.

Hyaline cartilage is a compact, transparent, elastic and soft substance known as, located between the contact surfaces of the acetabulum and the head femur, and in most moving joints. This cartilage also acts as a flexible shock absorber to prevent the collision of the bones during movement. Between the layers of hyaline cartilage, synovial membranes secrete synovial fluid to lubricate the joint. Surrounding the hip joint, many strong ligaments that prevent the joint dislocation are present. The strong muscles of the hip region also help to hold the hip joint together and to prevent dislocation [23].

2.2. Tribological properties

The synovial joints are remarkable systems as they form the base of movement, allowing the bones to slide against each other with the lowest degree of friction and wear [24,25]. This optimized tribological behaviour is owed to the existence of the joint cartilage. Its thickness and its transparency may vary in the same joint on account of the efforts it is subjected to, fluctuating between the micrometres and even a few millimetres. The hyaline cartilage thickness average values in the hip joints ranges between 2 and 4 mm [26,27]. This cartilage is enriched by its mechanical and physical properties, which confer viscoelastic behaviour to this material, responsible for: protecting the bone against abrasion (wear occurs between surfaces with a different relative hardness), absorbing the transmission/distribution shocks, reducing the contact efforts between opposing bonding surfaces and acting as a lubricating surface, favouring the motion between surfaces and reducing friction [28]. The hyaline cartilage is responsible for these tasks thanks to its highly organized cells and its structural heterogeneity. The cartilage is composed of chondrocytes in lacunae embedded within an extracellular matrix consisting mostly of collagen. Avascular, its nutrition is made by the diffusion of substances from the capillaries of fibrous connective tissue that surrounds the cartilage, named perichondrium and from synovial fluid secreted by the synovial membrane [29]. The synovial fluid has an extremely complex chemical composition, formed by an electrolytic solution

Table 1. Lubrication regimes, revised data from [32].

Lubrication Regime	Description
 Hydrodynamic	The surfaces are completely separated by a lubricating film. The characteristics of this contact are exclusively determined by the viscosity of the lubricant, and they are not influenced by its chemical properties
 Elastohydrodynamic	High contact pressures, provoked by the compression of the lubricant film, promote its elastic deformation in the contact area, which increases the viscosity of the fluid. This reinforcement produces a thick lubricant film that completely separates the two surfaces
 Boundary	The contact between the asperities in both surfaces is not prevented. However, these asperities are covered with a single coating of adsorbed lubricant molecules, which significantly reduces friction and wear coefficients
 Mixed	Friction and wear characteristics are controlled both by the viscosity of the lubricant (hydrodynamic lubrication area) and its chemical properties (absorption of a single layer of lubricant molecules)

rich in proteins (mainly albumin), polysaccharides (hyaluronic acid) and other water-solved compounds [30]. Additionally, this synovial fluid acts as a lubricant between articular surfaces, absorbing shocks emerging from the compression of these joints.

Over the years a remarkably high number of concepts and theories have been proposed concerning the lubrication of synovial joints, and this is fundamental to understand and predict friction and wear mechanisms occurring in artificial materials. Table 1 shows different types of lubricating layers which can be associated with lubrication regimes.

Synovial joints have an excellent natural lubrication mechanism and display a friction coefficient raging between 0.001 and 0.02 [31]. The friction coefficient is the ratio of the friction force and the normal load. Doubtlessly, the phenomenon responsible for the synovial lubrication is highly complex, and it is obviously very difficult to produce an artificial implant with a similar tribological performance. The viscosity of the synovial fluid is significantly different form the viscosity of the water, and it is believed that the synovial lubrication is explained by the hydrodynamic lubrication theory [32] (seen in Table 1). However, the operation mechanism of the hip is extremely complex, insofar as it is subject to several loads and velocities during the gait cycle [33], during which the thickness of lubricant film experiences fluctuations, as a consequence of its numerous macromolecules reacting to sheer stresses through viscosity, and its rheological properties change [30]. Consequently, the synovial fluid cannot be considered a Newtonian fluid [34].

Therefore, in synovial joints, it is possible that the only type of hydrodynamic lubrication that occurs, is the lubrication so called “weeping mechanism” [35], since this mechanism can be compared to a sponge. Owing to its permeability and a natural pumping system taking place during the motion, this fluid is able to lubricate the articular cartilage during the compression and decompression. In this way, when the cartilage is exposed to high loads the fluid is expelled (exudation), lubricating the joints, and, during the decompression, the fluid is absorbed (imbibition) [36,37]. However, this hydrodynamic lubrication is not so clear in certain situations, as when the foot is flat on the floor and the movement of the joint is initiated. In this case, the surfaces of the cartilage are very close to each other and a boundary lubrication (Table 1) takes place, possibly giving way to a direct contact between the cartilage surfaces [38–40]. This type of lubrication is favoured whenever the contact pair is subjected to extremely heavy loads, when the movement is initiated, or when the viscosity of the synovial fluid is very low, due to a certain medical condition. In these cases, synovial proteins may be adsorbed into the surface of the cartilage and form a semisolid film that impacts the friction coefficient [39]. Hyaluronic acid and phospholipids can behave in a similar way. According to Saikko et al. [41], the phospholipids found in the synovial fluid seem to occupy a signifi-

cant role in the boundary lubrication of the natural joint, reducing friction and wear.

2.3. Mechanical properties

Understanding the efforts applied to the hip joint in different movements and the requests to which the joint is subjected, is essential to the knowledge of its functioning and mobility, leading to the major cause of disease of the hip joint - osteoarthritis, as well as to predict potential complications in the development of artificial synovial joint.

Abnormal mechanical stress on joint cartilage is one of the main causes of osteoarthritis. Thus, it becomes crucial to evaluate the distribution of contact pressure and its maximum value along the articular surface [42]. The knowledge of the distribution of the contact pressure during daily activities is an important factor, because it allows predicting the mechanism of joint degeneration and wear of the joint replacement, providing valid planning of the biomechanical fundamentals before the surgery and rehabilitation. Yoshida et al. [42] resorted to methods of computer simulation and finite element analysis to forecast the contact area and pressure on the hip during different daily activities. To this end, it was generated an original three-dimensional surface, based on the assumption that the contact area between the pelvis and the femur is spherical and that the relationship between the femoral head and acetabulum is concentric. The results have shown that during standing up, sitting down and knee bending, the peak pressures were located at the edge of the posterior horn of acetabulum and the magnitude of the peak pressures during sitting down was the highest. For the other daily activities, the peak pressures were located at the acetabulum lateral roof. It was also shown the beyond the peak pressure value and location where maximum pressures were observed during different activities of daily living. It is also displayed the percentage of the contact area and the percentage of the cycle that is subject to this pressure.

Most models have assumed the hip joint to be a perfect ball and socket joint and have neglected deformation at the interface between bone and cartilage [42,43].

In a more recent study, Anderson et al. [44] used methods of finite element (FE) analysis with the objective to analyse finite element models of hip cartilage mechanics with varying degrees of simplified geometry and a model with a rigid bone material assumption to elucidate the effects on predictions of cartilage stress. The results demonstrate that simplifications to the geometry of the bone/cartilage interface, cartilage surface and bone material properties can have a dramatic effect on the predicted magnitude and distribution of cartilage contact pressures in the hip joint, underestimating peak and average contact pressures (50% and 25% lower, respectively) and overestimating contact area when compared with FE method. Models incorporating bone geometry with a constant thickness articulation cartilage also underestimated pressures and predicted evenly distributed patterns of contact.

2.4. Main problems of natural synovial joints

Despite human joints present excellent tribological characteristics, these structures have a limited capacity for regeneration. Therefore, the interaction of the femur with the acetabulum may result in damages that originate from hip joint diseases, given the high contact pressures to which they are subject. Since the hip joint is a contact interface between two bone surfaces, it is expected that any diseases that affect cells and bone mass affect also the articulation. The main reasons for total hip replacement derive in most cases from diseases such as rheumatoid arthritis, osteoarthritis, osteonecrosis, post-traumatic arthritis, benign and malignant tumours of the bone, femoral neck fracture [33]. Osteoarthritis, the major cause of failure of the hip joint, is a degenerative joint condition promoted by wear of the cartilage that covers and cushions the interior of joint combined with the decrease of synovial fluid leading to lubrication failure [45]. Understandably, as the bone surfaces are less protected by cartilage the patient will have pain, not only with the support of their weight, but also when it is in motion. Many people are affected by osteoarthritis after theirs 60s, due to the normal wearing out of cartilage that accompanies the aging body. In an early stage of osteoarthritis, cartilage joint becomes thinner, with a rough texture with fissures on the surface. With this aggravation, the cartilage and underlying bone crack and erode [44]. Depending on the development of this disease, the need to resort to surgery for joint replacement increases, because the pain, particularly the hip joint pain, drastically limits the ability to have an active life. This procedure, known for arthroplasty, is performed to deal with the problems caused by various diseases that affect many patients around the world, aged normally between 55 and 65 years. With the increase in average life expectancy, the hip joint replacement surgeries also increase, according with the National

Fig. 1. Hip prosthesis components: a) the stem femoral of titanium, b) the acetabular component of polyethylene with the cement and c) the stem and head femoral of titanium.

Joint Registry, during 2012 the total number of hip procedures was 86 488, an increase of 7% over 2011. Of these, 76 448 were primary and 10 040 were revision procedures [46].

3. HIP ARTHROPLASTY

Hip arthroplasty is a surgical procedure that consists fundamentally in the functional restoration of the joint through its replacement with an implant, preserving the synovial capsule [33]. Fig. 1 shows some hip prostheses components.

This substitution can be done in three ways: (i) only one part of the joint is damaged, with the replacement of the affected component, called hip hemiarthroplasty; (ii) the two parts are affected and the substitution is made at full articulation, named by total hip arthroplasty (THA); (iii) the existent prosthesis is replaced, which is called revision hip arthroplasty.

The hip replacement, beyond knee prosthesis, is the most common used in orthopaedic surgery and it is estimated that annually more than 1 million procedures are undertaken worldwide [47]. Despite the hip arthroplasty be considered one of the greatest achievements of orthopaedic surgery in the last decades, hip implants are not a complete success and still need further developments. This poor performance is reflected in the number of revision arthroplasties realized in the United States, which surrounds the 20% [1,48]. The materials used in conventional prostheses are designed to perform their duties for a period of at least 15 years [2,33,49,50]. However, these realities for younger patients, with a high average life expectancy, are far from satisfactory. Besides, there is the fact that the revision arthroplasties of the hip are significantly more complicated than the total primary arthrosplasties [51,52]. One of the main reasons for these complications is the loss of bone, in adjacent areas to the primary prosthesis getting thinner and more fragile. This may lead to bone grafts, or other materials, around the implant replacement to strengthen the bone. These grafts can come from the patient's body or from other donor if the amount of the patient's bone to remove is large. These complications also may result on failure of prosthesis materials, translating in aseptic loosening, instability, wear, and infection caused by implant [51,52].

3.1. Biomaterials for hip replacement

Currently, the importance of biomaterials is recognized around the world, driven by market need. An effort to achieve higher standards of living, in search of a greater longevity, was made in the area of biomaterials, which has gained increasing importance in the repair and replacement of living tissues victimized by trauma or pathology [53–55]. There are many definitions, in the literature, to express biomaterial concept, given the wide range of areas involved in the design and characterization of the materials used in biomedical applications [53]. Consequently, a biomaterial can be considered as "a synthetic or natural material that comprises whole or part of a living structure or a biomedical device which performs, augments or replaces a function that has been lost through disease or injury with no negative influence on the biological environment" [56]. Associated with the definition of biomaterial, the concept of biocompatibility arises, since only biocompatible materials may be used in implants under the risk of failure. However, it is difficult to find a definition of biocompatibility because it covers various aspects related to material, function and biological response. Some authors define biocompatibility of a material as "the ability to perform a particular function in the human body, inducing an adequate response in biological organisms" [57,58].

The deployment of biomaterials in the human body enables the restoration of biological and mechanical functions, increasing the quality of patients' life. These biomaterials are now commonly used as prostheses in cardiovascular, orthopaedic, dental, ophthalmological, and reconstructive surgery, and in other interventions such as surgical sutures, bioadhesives, and controlled drug release devices.

Among the possible applications of biomaterials, hip replacements must be pointed out by its importance, since it often presents itself as the only solution to restore the quality of life of the patient.

Table 2. Wear rates and average wear particles size resulting from in vitro simulation of several materials pairs, revised data from [62].

Materials pairs	Wear rates ($mm^3/10^6$ cycles)	Average wear debris size(nm)
Metal / UHMWPE	35-45	300 ± 200 (of UHMWPE)
CoCrMo alloy / CoCrMo alloy	1.23 ± 0.5	30 ± 2.25 (of CoCrMo alloy)
ZrO_2 / UHMWPE	31 ± 4.0	300 ± 200 (of UHMWPE)
Al_2O_3 / Al_2O_3	0.05 ± 0.02	9 ± 0.5 (of Al_2O_3)

Researches in the area of biomaterials for use in hip prostheses date from the first half of the XIX century. Nowadays, it is one of the most explored areas of the branch orthopaedic biomedicine, due to the growing increase of the necessity for replacement of the hip joint. So, it is essential to explain the inherent requirements of biomaterials used in the hip joint, as well as the limitations associated to the joint material combinations.

All materials used in hip replacements must display certain properties that enhance their life span. Considering the aggressive environmental conditions to which they are subjected to, these materials must meet several requirements, as biocompatibility, tribologial resistance, corrosion and mechanical strength.

Biocompatibility

Biomaterials must not cause any damage to the cells of the organism in which they are implanted. So, their physical and chemical properties must not interact negatively with the living tissue interface [55].

Tribological Resistance

A small friction coefficient favours the sliding motion between contact surfaces and generally leads to a lower wear rate, also preventing the release of potentially toxic debris. Considering the repeated cyclic loads to which these devices are subjected to, fatigue strength is crucial determining the long-term success of the implant [50].

Corrosion Strength

The chemical environment inside the human body is highly aggressive. Given the nature of certain materials used in orthopaedic prosthesis, this environment can act as an electrolyte and trigger electrochemical reactions. The products released from this corrosion can be toxic, and they can interfere with the normal functioning of the organism [59–61]. High corrosion and wear resistance is indispensable in the development of implants to ensure the longevity of the material in the human body [50].

Mechanical Strength

The prostheses must possess adequate mechanical properties to withstand the forces involved in the movement. The formation of wear debris is dependent on those properties, including paramount as hardness, tensile strength, modulus and elongation [50]. The hardness in so far that harder materials tend to produce less particles, the modulus and elongation to provide some elasticity to materials to make them less brittle and finally the tensile strength important in the study of the deformation of the materials.

3.2. Joint material combinations

The type of implant and its constitution are carefully selected by surgeons, pondering several variables such as the patient's age, lifestyle and activity level. The combinations of materials applied in replacement of femoral and acetabular components have different friction coefficients and wear rates. Accordingly different combinations of materials are available: metal-on-polymer (MoP); metal-on-metal (MoM); ceramic-on-polymer (CoP) and ceramic-on-ceramic (CoC).

Metal-on-polymer

UHMWPE (ultrahigh molecular weight polyethylene) is still the most commonly used material in prostheses as acetabular component with a metal for femoral component [38]. UHMWPE is recognized for its biocompatibility [23] and hence it has been used as a biomaterial. Of all the combinations of materials, this is one which has a higher wear rate value. Table 2 shows the wear rate values of the different combination and the respective size of particles released.

Therefore, the wear particles released from the UHMWPE component cause serious adverse reactions within the human body, as osteolysis (tissue bone destruction) in the surrounding tissues [63]. In this combination of polymer materials with metal, most of the wear debris comes from the grooves of smoother surface (polymer). As a result, these polymer residues can be transferred to the metal material, forming a film that promotes wear adhesive type. Generally, the harder material (metal) exhibits a

Table 3. Young's modulus of natural or synthetic materials in joints, revised data from [75].

Joint material	Young's modulus, *E* (GPa)
Articular cartilage	0.001-0.17
Bone	10-30
Ti6Al4V alloy	100-110
Stainless steel 316L	190
CoCrMo alloy	210
UHMWPE	0.8-2.7
ZrO_2	150-208
Al_2O_3	350-400

higher resistance to abrasive wear, being the softer material which suffers, typically, greater wear. For this reason, the presence of imperfections in metal surface may promote abrasive wear on the polymeric component surface.

Metal-on-metal

Total hip prostheses type MoM have aroused interest because of the problems highlighted by the pair MoP [64], mainly by presenting wear rates that are significantly lower than those of the prostheses type MoP [62]. Some studies have reported that the wear rate of MoM hip prosthesis is 1–6 mm^3 per year, comparing to 30–100 mm^3 for MoP hips [65–67]. The wear rate value of MoM hip prosthesis is lower than MoP type once materials with similar chemical properties usually exhibit high adhesion forces, forming chemical bonds more quickly, causing its reduction. However, there is a serious problem associated with this materials pair, since the ions released are toxic to the blood. In the case of cobalt-chromium alloys, metal ions, which are released to synovial fluid, produce water-soluble metal salts which migrate to blood and posteriorly are excreted in the urine [68]. Nickel, ion released by stainless steel, is usually eliminated through the urine, but cobalt and chromium remain longer in the body and may even be retained in organ tissues [45].

Ceramic-on-polymer

In prostheses CoP, the polymeric component wear may be reduced by 50 % when using a ceramic femoral head, however it still involves a large number of particles released [62]. Therefore, due to this problem there is an emergent interest in the study of CoC materials.

Ceramic-on-ceramic

Prostheses CoC produce a low number of wear particles (1 mm^3 / year) [66,69], this being fairly value lower than the joint articular MoP wear rate (100 mm^3 / 10^6 cycles) [70]. The most widely used ceramic materials in the field of prostheses are alumina (Al_2O_3) and zirconia (ZrO_2), featuring biocompatibility, wear and corrosion resistance. Oxides correspond to the maximum state of oxidation of a metal, being stable in harsh environments, providing this way a weak degradation [71]. In the 70s, it was developed the first hip prosthesis of Al_2O_3. Studies revealed that the concentration of wear particles generated in the joint pair CoC (Al_2O_3 / Al_2O_3) was around 20 times lower than that observed in the joints of MoP [72–74]. In addition to the number, also its size is fairly inferior when compared to the size of the polymer particles resulting from the action of wear (Table 2). However, this material exhibits a brittle tendency and is sensitive to microstructural flaws [74]. Consequently, the interest in zirconia, a material with a fracture resistance much higher than alumina, arises. ZrO_2 was recognized for its high strength and surface finish, becoming suitable for the highly loaded environments found in joint replacement [74].

Long-term results with this type of combination (CoC) can be considered interesting, especially in younger patients. In older patients with pathology of rheumatoid arthritis or osteoporosis, it has been found sometimes the occurrence of osteolysis and, therefore, dislocation of the acetabular component, which may be related to the effect of "stress-shielding" induced by the high elasticity module of alumina [57,75,76]. Table 3 shows elasticity modules values of two natural materials comparatively with some materials used in artificial synovial joints.

This effect is caused by the discrepancy between elasticity modulus of the bone and the materials used in implanted devices (Table 3). The ceramic component is significantly stiffer than bone and consequently promotes an uneven distribution of the load on the bone [77]. As the regenerative and remodelling processes in bone are directly triggered by loading, over time, the reduction in the loading leads to the deterioration in its quality, causing a weakening, mass loss and eventually the dislocation of the prosthesis [77]. Considering only the low wear rates of these materials, these could be considered the most suitable materials for use in orthopaedic implants such as hip case. However, since Young's modulus values are very high, this suggests that are poorly deformable and more susceptible to fracture, causing the unbalanced release of particles, preventing surgical removal of the implant [73].

The main cause of hip implants failure is the degradation of the biomaterial surface, caused by the combination of electrochemical corrosion effects and mechanical effects of cyclic loads, which pro-

mote the debris release. The release of particles in the form of ions can induce accumulation in tissues, causing inflammation, and discomfort in the patient, and in extreme situations implant rejection. Such release occurs in the form of debris which they are treated by the organism as foreign bodies. However, while these enzymes attack these particles also kill adjacent bone cells, a process known as osteolysis. This process causes bone re-sorption and aseptic implant dislocation which eventually leads to the necessity for a revision arthroplasty [61].

4. SURFACE MODIFICATION

The need to prevent the release of wear debris into the body reflects the importance of the optimization of the implant surface. However, the development of a biomaterial is a very complex challenge, especially regarding its surface. So, a biomaterial must be carefully designed and characterized in order to facilitate the understanding of its interaction with the biological environment, which is quite complex and not fully understood. Numerous studies are continuously carried out with a view to solve this kind of problems leading to a competitive and diverse hip prostheses market. Accordingly, and given the difficulty in developing a material that meets all the requirements for the application in question, the research in this field has been strongly directed to the surface modification of biomaterials, allowing not only the improvement of the mechanical and tribological properties, the minimization of the production of wear debris, but also the increase of the materials' biocompatibility [50]. Within the various techniques that enable the surface modification, those that permit to obtain new materials from the vapour phase should be highlighted. The most important techniques are chemical vapour deposition (CVD), physical vapour deposition (PVD), ion deposition and plasma discharge [50]. Through these techniques, and through the selection of the deposition parameters, it is possible to create materials with virtually all of the desired properties. Changing the parameters of suitable deposition it is possible to obtain crystalline structures with varied grain sizes and different growth preferential orientations, and eventually amorphous structures for a material with the same chemical composition.

The development of ceramic coatings has been perceived as one of the solutions to increase the average life span of orthopaedic prosthesis. The strong characteristics displayed by ceramic materials, such as the resistance to corrosion and a high mechanical strength and resistance to wear, have outweighed their biggest limitation, brittleness [7]. Amongst the different coatings under study, the nitrides, the transition metal carbonitrides (mainly Cr and Ti) and the DLC's (Diamond-like carbon) stand out. These materials have been subject to several scientific investigations concerning biomaterials, as well as in other fields demanding strong mechanical and tribological characteristics, and a high level of resistance to corrosion [78–80]. DLC coatings have been proposed as surface alternatives in orthopaedic implants, owing to the excellent properties they have displayed in several *in vitro* studies, namely an increased hardness (ranging between 1 – 60 GPa), a solid resistance to wear and corrosion, a low friction coefficient and a high biocompatibility [5,81]. However, the main downside of these coatings, generally produced with PVD and CVD techniques, concerns their adhesion problems that are connected to high residual stresses, especially when deposited in steel or titanium substrates, the most commonly used in biomaterials [2,80]. TiNbN (titanium niobium nitride) is one of the commercially available coatings used in hip replacements**.** However, the number of tribological studies focused on this type of surface is very scant. From what is known concerning these coatings, the wear and the release of metal ions have been significantly reduced when compared with a MoM prosthetic implant [82].

Titanium nitride coatings (TiN), on the other hand, have been known and studied for several decades, owing to their inherent properties and, above all, because they display high levels of hardness [83,84]. Additionally, the oxidized TiN increases the resistance to corrosion and promotes the nucleation of calcium phosphates, favouring the integration of the implant in the human bone [4]. However, TiN is known for a high friction coefficient and consequently a weak resistance to wear, an unwanted characteristic in hip replacement prosthetics [85]. The development of TiC coatings with an increased hardness has tried to overcome this limitation. Despite their solid tribologic properties, these coatings pose adhesion problems [86]. Over in the last few years, the TiCN system has been subject to some investigation, with the purpose of bringing together the isolated qualities of both the TiN and the TiC. TiCN forms a solid TiN-TiC solution with an increased hardness (intrinsic to TiC and TiN), a friction coefficient 3 to 4 times lower than TiN and a wear rate 5 to 7 times lower than TiN [7,50,80,87–89]. Therefore, TiCN coatings are widely applied in medical

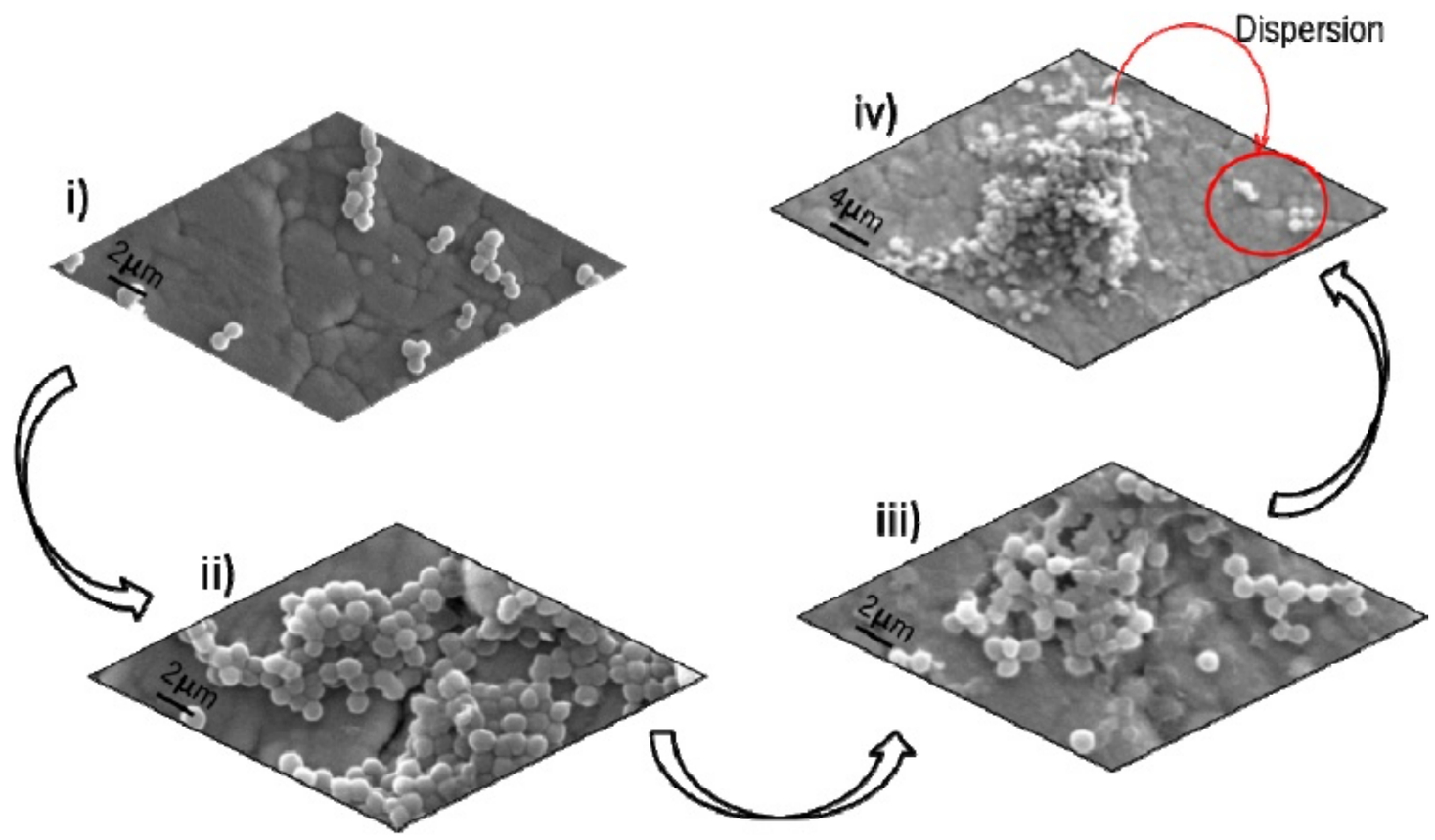


Fig. 2. Stages of biofilm development i) initial attachment of microbial cells to surface; ii) multiplication of the microbial cells forming microcolonies; iii) maturation of the biofilm of cells and production of an extracellular matrix and iv) detachment of some biofilm cells leading to colonization in other parts of surface.

tools, owing to their great biocompatibility and their excellent tribological behaviour [78]. However, according to the available literature, these coatings have never been applied in hip replacement prosthetics [82]. Notwithstanding, biotribological *in vitro* ball-on-disk short-term tests, using Hanks' balanced salt solution as lubricant, have revealed that the TiCN/TiCN pair has a higher wear resistance than the pair that is currently available, TiNbN/TiNbN. The wear rate observed in the pair TiCN/TiCN, by Serro et al. [82], correspond to 6.3 x 10^{-17} m^3/Nm in comparison to the 3.1 x 10^{-16} m^3/Nm of the pair TiNbN/TiNbN. A study of Martínez-Martínez et al. [90] reported that in TiCN coatings deposited by magnetron sputtering, a C enrichment led to the formation of an amorphous carbon phase that can help to decrease the friction coefficient and the wear rate, although promoting a hardness reduction. A similar behaviour is reported by Silva et al. [91] that used ZrCN coatings deposited by magnetron sputtering with N_2 flows ranging from 2 to 10 sccm. These results show that an amorphous phase CN_x formation could act as a lubricant resulting in a low coefficient of friction (0.1 – 0.2). In a previous study [92], the incorporation of silver into TiCN coatings to be used in implant and medical devices must be limited up to 6 at.% to ensure a good tribological behaviour.

5. ANTIMICROBIAL COATINGS

Infections, as already referred, are one of the main causes of hip replacement failure, and are triggered by the microbial adhesion and biofilm formation on the surface of biomaterials. In fact, in the U.S.A., studies developed by the *Centers for Disease Control and Prevention,* concluded that 60% of biofilm induced infections are associated with biomedical implants [93]. Biofilms are characterized by communities of microorganisms strongly attached to each other and to a biomaterial surface, embedded in an exopolymeric matrix. Biofilm matrix is composed by a mixture of components, such as extracellular polymeric substances (EPS), nucleic acids, and other substances [94]. The EPS constituted mainly by polysaccharides and proteins [95] are produced by a wide variety of bacteria. These substances are very important for intercellular binding during surface colonization [96] and protection against the host immune system and resistance to antibiotics [97]. For these reasons, biofilms are difficultly eradicated making them important in infections. The process of biofilm formation which included several steps is illustrated in Fig. 2.

One of the microorganisms associated to biofilm formation and consequent implant rejection is *Staphylococcus epidermidis* [12,98–100]. Fig. 3 shows a *Staphylococcus epidermidis* biofilm.

Staphylococcus epidermidis belongs to the genus *Staphylococcus* and is characterized to be gram-positive bacteria (presents violet coloration after Gram staining method, due to the thick peptidoglycan layer in the cell wall, while gram-negative have a thin peptidoglycan layer incapable to retain the Gram stain), coagulase-negative (they do not produce the enzyme coagulase responsible by the blood plasma coagulation) and present a rounded shape with about 1 mm in diameter. This species

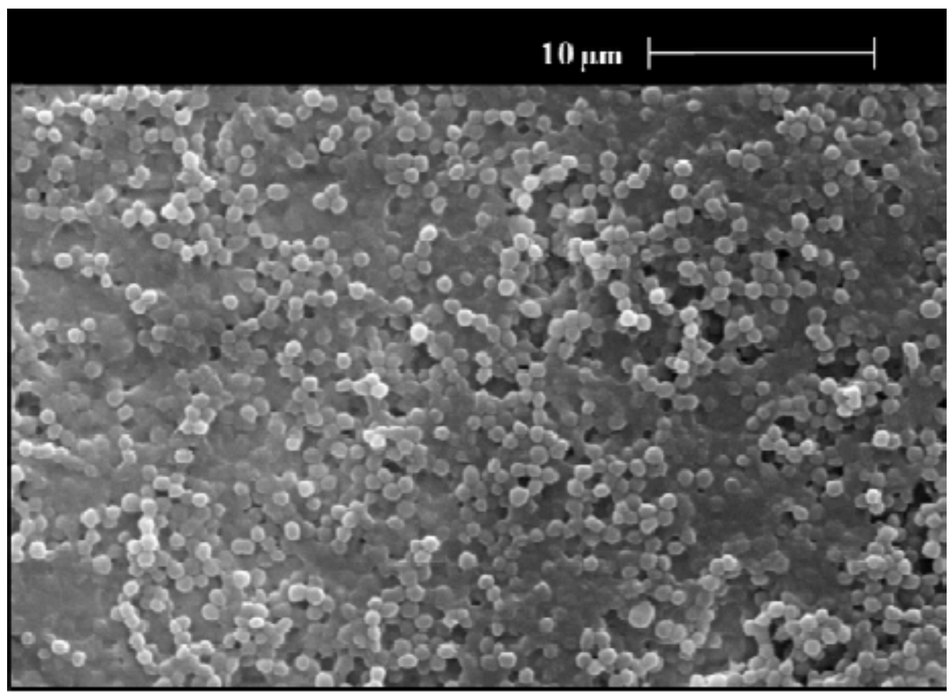


Fig. 3. Biofilm of *Staphylococcus epidermidis.*

colonizes the skin and mucous membranes of the human body, and represents an important part of its normal microflora [13,101], and is one of the major nosocomial pathogens associated to infections of implanted medical devices [102]. These microorganisms easily come in contact with the implant during surgeries [103] and are responsible for chronic and profound infections, which can occur months or even years after the prosthesis implantation [101,104]. Prosthetic heart valves, central venous catheters, urinary catheters, contact lenses and prosthetic joints (hip prostheses and other orthopaedic devices) are the medical devices mostly affected by *S. epidermidis* [96,101,104,105].

In addition to their role in infections, biofilm also promotes corrosion, namely in metal surfaces, which leads to their degradation once the change of electrochemical conditions at the metal/solution interface induces or accelerates the corrosion process. This change occurs by the attachment of bacteria to the metal, which release metabolites within biofilms, including several acids that influence the anodic and cathodic reactions, creating conditions for corrosion [106]. Therefore, several strategies have been studied in order to avoid biofilm formation in medical prostheses. The main line of research has focused on reducing the attractive forces between bacteria and the surface of the biomaterial, optimizing the physical and chemical properties of the latter. These studies have shown that the interactions between the biological environment and the biomaterial are influenced by the surface properties of the material [107]. However, the alteration of surface properties alone does not effectively eliminate the production of biofilm [97,108]. It is therefore necessary to adopt different approaches that hinder microbial adhesion. This can be achieved with biomaterials that are capable of releasing antimicrobial agents. There are several papers discussing antimicrobial agents such as Ag, Au, Cu, Zn, among others [109–111], however the most commonly used is silver. The incorporation of silver, Ag clusters in transition metal carbonitrides systems may be a solution. The antimicrobial properties of this metal are widely known since ancient times and have been mainly attributed to its oxidized form, Ag^+. The antimicrobial action of the silver ions (Ag^+) is effective in fighting different types of bacteria and fungus, since Ag^+ destabilize microbial cell walls, interrupting the metabolism of their cells and inhibiting their reproduction [110,112,113]. In addition to its antimicrobial properties, the incorporation of controlled percentages of silver has revealed solid tribological properties, acting as a solid lubricant, raising the interest around this metal [114–116]. In this sense, the development of coatings with good tribological properties and an antibacterial character can be crucial to overcome the main limitations of hip replacements.

In the last few years, different systems have been the target of several studies for the development of prostheses replacement coatings, such as Ag doped TiN [85,117,118], CrN [117,119], ZrN [117], TaN [17,120], TiCN [121] as well as DLC's [5,122]. Although the results observed by different authors revealed that the Ag incorporation leads to the development of antimicrobial properties, Kelly et al. [117] observed that the incorporation of Ag percentages above 10 at. % in TiN, CrN, ZrN coatings promotes an antibacterial activity verified by NBT (nitroblue tetrazolium) assays resulting in a decrease in *Staphylococcus aureus* colony forming units. Moreover it leads to a significant decrease in the hardness, wear and corrosion resistance, unwanted effects in a tribological behaviour. Tseng et al. [123] observed an identical behaviour in TaN-Ag systems when Ag was introduced in percentages close to 10 at.%. Accordingly, the incorporation of high silver contents does not favour these applications. In addition to its impact on tribological properties, the incorporation of high silver contents can promote cytotoxicity, leading to the rejection of the biomaterial [17,124]. In fact, few studies have reported that concentrations of silver above 10 mg/L can be toxic to some types of human cells [125,126]. Other authors have shown that the size of silver nanoparticles can influence antimicrobial activity[127]. Studies done by Kelly et al. [85,117] with TiN/Ag coatings, showed that in addition to the quantity and size there is also a relationship between shape and distribution density of the silver particles and the nature of the surrounding matrix, which could also influence the antimicrobial activity. The high chemical stabil-

ity in the formation of Ag^+, responsible for the antimicrobial properties, may not be meaningful. In a previous study [121], the Ag-TiCN coated SS 316 L showed no antibacterial effect, even for relatively large quantities of silver (15 at.%), conflicting with other published results [85,120,128–134]. Furthermore, it is still necessary a better understand the silver action mode as an antimicrobial agent.

So, the improvement in the development, design and production of materials and techniques for implants is imperative to maintain a good quality of patients' life. Moreover, an accurate characterization of the materials and their interaction with host tissues is required, so that the main property of a biomaterial, which is the absence of any adverse reaction in the body, is satisfied.

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