Journal of the Mechanical Behavior of Biomedical Materials 77 (2018) 90–105

Contents lists available at ScienceDirect

Journal of the Mechanical Behavior of Biomedical Materials

journal homepage: www.elsevier.com/locate/jmbbm

Bioinspired surface functionalization of metallic biomaterials

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A R T I C L E I N F O

Keywords:
Metallic biomaterials
Bioinspired surface functionalization
Biocompatibility
Biofilm resistance
Corrosion resistance
Wear resistance

A B S T R A C T

Metallic biomaterials are widely used for clinical applications because of their excellent mechanical properties and good durability. In order to provide essential biofunctionalities, surface functionalization is of particular interest and requirement in the development of high-performance metallic implants. Inspired by the functional surface of natural biological systems, many new designs and conceptions have recently emerged to create multifunctional surfaces with great potential for biomedical applications. This review firstly introduces the metallic biomaterials, important surface properties, and then elaborates some strategies on achieving the bioinspired surface functionalization for metallic biomaterials.

1. Introduction

Metallic biomaterials are widely used for clinical applications due to an excellent combination of mechanical properties and durability when compared to the ceramic and polymeric biomaterials. However, they still lack satisfactory biofunctionalities for certain applications, such as blood compatibility for blood-contacting devices, bone conductivity in orthopaedic applications, and ultra-high wear and corrosion resistances for joint replacement. When a metallic biomaterial is implanted into the living tissue, the surface properties of the material play critical roles in the interactions between the biological environment and the implant (Nel et al., 2009; Planell et al., 2010). Therefore, surface functionalization is of particular interest and requirement to improve surface bioactivity and other biofunctionalities and hence enhance the cellular and tissue responses.

The morphology and properties of biological materials and structures have been developed by nature over millions of years, exhibiting unique characteristics and almost perfect functions to adapt to the harsh environment (Koch et al., 2009), such as the self-cleaning property of lotus leaves (Barthlott and Neinhuis, 1997), the structural colour (Kolle et al., 2010) and light trapping effect (Han et al., 2012) of butterfly wings, the superior combination of strength and toughness of bone tissue (Launey et al., 2010; Ritchie, 2011), and plastron property for underwater breathing (Shirtcliffe et al., 2006). These natural functions and strategies have recently emerged as a new source of inspiration to create multifunctional surfaces with high potentials to apply on the biomaterials. Many reviews have been published on bioinspired surfaces with special wettability for various applications (Wang et al., 2015; Liu et al., 2010; Yao et al., 2011; Zhang et al., 2008a; Shin et al., 2016; K Webb et al., 2011), but few addressed the other surface functions inspired by nature and their development on metallic biomaterials.

In this review, we focus on the functionalization strategy of bioinspired surface and their application on metallic biomaterials. Section 2 generally presents the inert metals and biodegradable metals for biomedical application. Section 3 introduces the relations between the surface properties and the cellular and tissue response. Before arriving into conclusion, Section 4 discusses the significant functionalization of bioinspired surfaces which have been or potentially be applied on metallic biomaterials using tailored morphology, chemistry, and wettability.

2. Metallic biomaterials

The record of metal's exploitation for biomedical applications can be traced back to 200 A.D. when the early European integrated an iron dental implant into human bone (Ratner et al., 2004). Compared to polymers and ceramics, metals can provide a combination of required

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http://dx.doi.org/10.1016/j.jmbbm.2017.08.035
Received 31 January 2017; Received in revised form 23 August 2017; Accepted 29 August 2017
Available online 01 September 2017

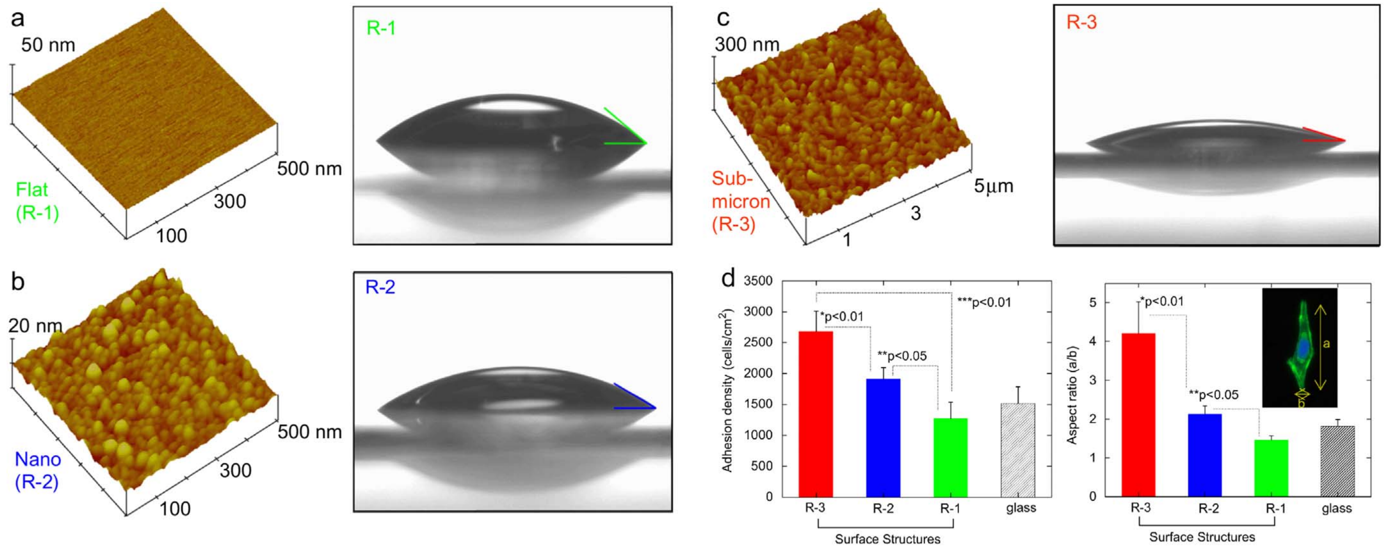

Fig. 1. Contact angles showed increased hydrophilicity on (a) flat, (b) nanometer and (c) sub-micron surface-featured titanium. (d) Adhesion density showed that sub-micron structures led to the best adhesion density (seeding density was 3500 cells/cm^2), and cell aspect ratios showed oriented cell morphology for flat, nanometer and sub-micron structures (increased right to left). Note that cell aspect ratios were calculated by the length of a single cell divided by its width (inset image of (d)). All error bars are mean ± SEM; n = 3; *p < 0.01 (compared to R-2) and **p < 0.05 (compared to R-1) Khang et al. (2008).

properties for the biomedical application, including the high ductility and fatigue limit, good corrosion and wear resistance. Metallic biomaterials account for approximately 70% implants including orthopaedic (knee joint, total hip joint, bone plates, fracture fixation wires, pins, screws, and plates) and cardiovascular (artificial heart valves, vascular stents, and pacemaker leads) (Niinomi et al., 2012).

Up to now, the three most used metallic biomaterials are stainless steels (SS), cobalt-chromium (Co–Cr) alloys and titanium (Ti) alloys (Niinomi et al., 2012). The 316 L type SS (SS316L) is the most widely used metal mainly for non-permanent implants such as bone plates and screws, whilst the more corrosion resistance Co–Cr- or Ti-alloys are used for permanent ones such as hip implants. The concern of nickel toxicity in SS316L has led to the development of a nickel-free high-nitrogen SS as a promising replacement in future for orthopaedic and cardiovascular stent applications. This new alloy has been proven to possess improved biocompatibility combined with excellent corrosion and wear resistance (Talha et al., 2013). Co–Cr alloys, mainly represented as Co–Cr–Mo and Co–Cr–W–Ni series, are characterised by their high corrosion and wear resistances (Yan et al., 2007). They have been used for making various implants such as artificial joints, denture wires, and stents (Narushima et al., 2013). Pure Ti and Ti–6Al–4 V have been used in orthopaedic and dental applications owing to their superior biocompatibility, pitting corrosion resistance and high strength to weight ratio to SS and Co–Cr alloys (Gepreel and Niinomi, 2013). A number of β-type Ti alloys with nontoxic and allergy-free elements and low Young's modulus (35–80 GPa) have been developed to avoid the harmful elements present in Ti–6Al–4 V and the stress shielding effect (Lin et al., 2016).

Apart of the three mentioned metals, biodegradable metals have been developed as ideal materials for temporary implants. They are expected to degrade safely in the body after fulfilling their function, thereby avoiding the need for removal surgery, accelerating the healing process, reducing risks from permanent presence of the implant, and eventually reducing overall hospitalisation time and costs (Zheng et al., 2014). Among the three most studied biodegradable metals (magnesium, iron, zinc), magnesium and its alloys are advancing to commercial products (Zheng et al., 2014; Zhu et al., 2017; Ma et al., 2016a, 2015a). They possess similar physical and mechanical properties to those of bones, i.e. Young's modulus, making them suitable for orthopaedic applications (Staiger et al., 2006). Magnesium alloys usually corrode too quickly in the human body, but various improvements have been made to retard its fast degradation, such as by using high purity Mg, proper alloying elements, composite structure, nanocrystalline and amorphous microstructure, and surface modification (Dorozhkin, 2014; Shadanbaz and Dias, 2012; Hornberger et al., 2012). Recently, a long-term clinical study found that the controlled degradation of an Mg-Zn-Ca alloy resulted in the formation of a "biomimicking calcification matrix" at the degrading interface to initiate the bone formation process (Lee et al., 2016).

3. Surface properties

When a metallic biomaterial is implanted into the living tissue, an interface is created between the implant material and the surrounding tissues. It is of significance to ensure the implants with specific surface features be recognised by the highly precocious ability of biological systems at the implant–tissue interface (Nel et al., 2009; Planell et al., 2010). The implant surfaces with different morphology, chemistry, and wettability will strongly influence the material-cell interaction and thereby tissue integration at the interface.

3.1. Surface morphology

The morphological features such as surface roughness (Deligianni et al., 2001) and its topography (Khang et al., 2008) can strongly influence the protein adsorption (Deligianni et al., 2001), cell adhesion (Khang et al., 2008), cell migration and differentiation (Zinger et al., 2005a). Generally, surface roughness can affect cell behaviour directly via enhanced formation of focal contacts or indirectly through selective adsorption of serum proteins required for cell attachment (Deligianni et al., 2000). The substratum topography with different scales and features have a direct effect on the abilities of cells to produce organised cytoskeletal arrangements (Shen et al., 2015). It has been reported that the adhesion and proliferation of vascular and bone cells increased on nanometer-scaled surfaces, as shown in Fig. 1 (Khang et al., 2008), nonetheless a few reports did not confirm such significant correlations (Izquierdo-Barba et al., 2015; Bagherifard et al., 2015). Bagherifard et al. (2015) suggested to consider additional roughness parameters, e.g. surface irregularities formation and their spatial distribution, to fully describe the precise surface morphological features. Moreover, it must be mentioned that cellular response to substratum topography may be different from one cell type to another.