Chapter 2
Biomaterials: Characteristics and Properties

The design and selection of a biomaterial depend on its specific application in order to be useful and assure its properties as long as required, without rejection [1]. In order to be considered a biomaterial it should, besides not inducing inflammation, toxic reactions and allergenic symptoms in the body, be biocompatible, biofunctional, bioactive, bioinert and sterilizable (Fig. 2.1) [2, 3].

A further condition for a biomaterial is that the processes of hygienization and sterilization should not promote modifications in the properties of same [3].

The biomaterial surface, being directly exposed to the living organism, plays a crucial role as regards biocompatibility. When this issue is considered, the physical, morphological, and biologic characteristics can be adapted to promote improvement in the interaction of biomaterial and tissue [2].

The concept of biocompatibility has been deeply altered in these last few years. At first it was believed that a material was biocompatible by being completely inert to the human body, without any response from the biological medium to its presence. The idea of a totally inert material was abandoned when it could be observed that the presence of any kind of material always entails some response from the body, varying as a function of the kind of application and the patients' characteristics (age, sex, etc.). Thus, the concept of biocompatibility of a material, by emphasizing especially the tissue (or neighboring medium) material interface, could be defined only by encompassing the various forms of interaction of the body with the material [4].

Biomaterials can be utilized for various applications in a myriad of areas of the human body. However, for each of these applications, the commonly required feature is the degree of tolerance of these biomaterials when in contact with organs and tissues. In order to comply with this aspect, the biomaterials should undergo critical adjustments so as to serve each specific application in the best possible way. One mode of adjusting the surface characteristics of the biomaterials is by means of surface modifications, which keep the characteristics of internal properties of the material with a suitable surface in order to better meet the specification of the locus of application.

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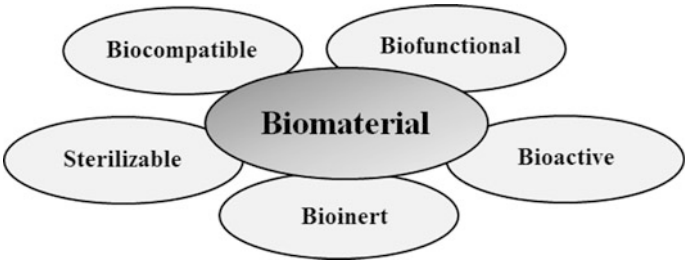


Fig. 2.1 Characteristics that a material must present to be a biomaterial

The use of medical implants increased in the last decades due to the population aging, boost in life expectancy and style of life and improvements in implant technology [5].

The development of biomaterials having the required characteristics to aid in the recovery of tissues damaged by accidents or disease is one of the major challenges in the scientific field involving medical and engineering areas [6].

Every material used as a biomaterial in the medical field, either by organ replacement, support for tissue growth or drug release should have specific characteristics in order not to stimulate or cause any level of allergenic or inflammatory response to the human body. The characteristics to be taken into consideration when it is meant a biomaterial used for implant include biocompatibility, biofunctionality, chemical, and mechanical stability. Besides these characteristics, the material should be sterilizable in order to avoid irritation, rejection, and/or problems at the locus of implant [7, 8].

Biocompatibility of a biomaterial as previously defined is related to the organism accepting the body, until then a foreign matter, and admitting it as part of the whole, as well as not exhibiting signs of harmful effects at its locus of operation. The expression biocompatibility comprehends different properties of materials, such as toxicity, tissues compatibility, blood compatibility (hemocompatibility), and biofunctionality properties [9].

Biofunctionality is essential for the material to perform the functions to which it has been designed for, at the required period of time and effectively. For materials of long-lasting biofunctionality the material should not degrade by contact with the tissue; since thus it would partly lose its functionality, it should also keep its chemical and mechanical stability throughout the whole process to which it has been enabled. For metals, degradation is related to corrosion which causes harmful effects to the body if these are not of a tolerable degree [4, 7].

As for the response of the body, biomaterials can be characterized as biotolerable, bioinert, bioactive, and biodegradable [10].

Biotolerable is the way by which are designed materials that are tolerated by the body, being separated from the host tissue by the formation of a housing of fibrous tissue. This layer is induced by the release of chemical compounds, ions, corrosion products, and other ones resulting from the implanted material. Among the

biotolerable materials are highlighted the synthetic polymer materials and most of the metals [10].

Bioinert are materials which are also tolerated by the body, but where there is no chemical reaction between the material and the tissue. The material either does not release components in any significant amount or does not release components and the formation of fibrous housing is minimal. Common examples of bioinert materials are alumina, zirconia, titanium and alloys and carbon [10].

Bioactive are materials that can make chemical bonds with the bone tissue, characterized as an osseointegration process. Through this process the bone tissue connects to the implanted material promoting the coating by bone cells. Materials employed as bioactive are the calcium phosphate, hydroxyapatite, and calcium phosphate compound-based glasses and vitroceramics [10].

Biodegradable are materials which degrade, solubilize, or are absorbed when in contact with the body for a certain period of time. Their application is of deep interest since there is no need of a further surgery for the withdrawal of the implant. Within this class most important are the biopolymers [10].

A biomaterial which otherwise complies with all the characteristics required for its utilization can only be effectively employed if it can be sterilized. Sterilization is crucial since it is by means of this procedure that all impurities and microorganisms are eliminated, providing a material which is suitable for implant [11, 12].

According to regulating authorities such as the Therapeutic Goods Administration (TGA), Food and Drug Administration (FDA), European Commission on Health and Consumers (ECHC), and Medical Devices Bureau of Health Canada, medical devices are classed following their complexity and required control level to assure safety and effectiveness. In Australia, besides the cited classification is also attributed a class according to the degree of invasiveness and onto which tissue the device is applied to (e.g., class III corresponds to chronic diseases implantable devices). Non-implant (class I and II) medical devices (e.g., surgical and dental instruments) are manufactured from commercial-grade materials (Table 2.1). Biomaterials of higher interest for the scientific community can be found in the higher classes of Table 2.1, with characteristics suitable for prolonged contact with human tissues and thus require premarket approval [1].

The choice of the biomaterial is associated with the function it will perform and the period of time it will contact the human body, based on the combination of its physical, chemical, mechanical, and biological properties [13, 14].

2.1 Properties of Biomaterials

The biomaterial success for a certain application is related, besides the specific items for biomaterials cited above, to its physical, chemical, and mechanical properties. According to the effort demanded from the material and the region to which it will be applied, such properties can be modified and thus they deserve careful attention when choosing a material.

Table 2.1 Some accepted classifications and description of medical devices [1]

Authority	Class			
TGA	I	IIa, IIb	III	–
FDA	I	II	III	–
ECHC	I	IIa	IIb	III
Health Canada	I	II	III	IV
Description				
General description	Non invasive and/or transient use (e.g., dermal)	Minimally invasive, short term (e.g., eyes, ear canal)	Short to medium term contact with blood, oral/nasal mucosae	Medium to long term contact, chronic implants, control systems
Restrictions	General	General and specific	General control and premarket approvals	–
Health risk	Low	Low/moderate	Moderate/high	High
Example	Surgical instruments, mechanical barriers	Contact lenses, ultrasound probes	Orthopedic implants, dialysis machines	Pacemakers, perfusion pumps, vascular stents

2.1.1 Physical Properties

The physical properties of the biomaterial are fundamental for the response of cell adhesion. When cells adhere to the biomaterial surface physical chemical reactions between cell and biomaterial occur, such reactions being influenced by factors such as cell behavior, biomaterial surface properties, and environmental factors. The biomaterial surface properties include wettability, filler, roughness, softness, and chemical composition [15].

Wettability (hydrophobicity/hydrophilicity) is one of the parameters affecting the biological response of the biomaterial and describes the balance between the solid surface intermolecular interactions with a liquid. Among the affected properties are protein adsorption, platelet adhesion/activation, blood coagulation, and cellular and bacterial adhesion. Hydrophobic surfaces are, generally, considered as more protein-adsorbent than hydrophilic surfaces due to the hydrophobic interactions occurring at the surface in contrast with the solvation forces which are water repellent relative to the water linked to the hydrophilic surface [16].

As relates to surface charge, researchers reported improved biocompatibility, cellular affinity, and cellular differentiation on surfaces of biomaterials implanted utilizing positive ions and negative ions. For example, 2-hydroxyethyl methacrylate (HEMA) gels incorporated with positive charges promoted better adhesion and spreading of fibroblasts and osteoblasts when compared with negative or neutral charges [15].

The roughness of the biomaterial also plays an important role in the adhesion and cellular behavior and exerts direct influence both in vitro and in vivo. Smooth surface and rough surface have different contact areas with molecules and cells and this difference in contact influences the kind of biological units' links and therefore, conformation and function. In most of the cases cells prefer rough surface to smooth ones, due to the fact that rough surfaces favor proliferation [15].

For low friction applications, such as in implants of orthopedic joints, biomaterials with mirrored finishes are preferred. And when tissue-implant integration is desired, as is the case of endobone implants, high roughness is preferred [17].

The surface roughness of a biomaterial should be studied in terms of amplitude and organization. Studies revealed that low-amplitude surface grooves induce orientation of groups of cells or individual cells along its axis this being the basis to state that the best parameter for the orientation of cells would be the groove's width and not its depth. Still, oriented osteoblasts tend to mineralize more quickly, favoring the tissue/implant osseointegration process [18]. Still, for cases where the biomaterial is used for dental implants, high roughness surfaces could show risks of increased peri-implantitis, peri-implantar mucositis, or ionic release in case of alloys [19].

Case Study: Relationship between surface properties (roughness, wettability) of titanium and titanium alloys and cell behavior [20]

A study performed on a titanium-based biomaterial reports data on wettability, surface free energy, interfacial free energy, and roughness aiming at determining which of these parameters had the strongest influence on the response of human fibroblasts proliferation.

Titanium samples contained neat titanium (Cp-Ti), titanium–aluminum–vanadium alloy (Ti–6Al–4V) and titanium–nickel (Ni–Ti). Ni–Ti had different roughness values, Ni–Ti80 (Ra = 1.02 ± 0.17 μm), Ni–Ti400 (Ra = 0.15 ± 0.015 μm), and Ni–Ti2400 (Ra = 0.057 ± 0009 μm), Ti–6Al–4V (Ra = 0.068 ± 0.007 μm), and Cp-Ti (Ra = 0.064 ± 0.008 μm). Upon evaluation of cellular proliferation at the several roughness values, results indicated that cells showed preference for surface roughness values lower than 1 μm.

Wettability was evaluated for the rough surfaces and for smooth surfaces. For rough surfaces wettability exhibited higher contact angle for the highest roughness sample (Ni–Ti80), both in the parallel (69 ± 11°) and in the perpendicular (73 ± 5°) direction. For smooth surfaces of the Cp-Ti, Ni–Ti, and Ti–6Al–4V samples with roughness below 0.015 μm (mechanical polish), the contact angle with water was of hydrophilic nature with close values for Cp-Ti (53.9 ± 5.1°) and Ti–6Al–4V (50 ± 3.1°) and higher values for Ni–Ti (60.4 ± 5.8°), proliferation being bigger at the Ni–Ti surface.

In accordance with the Owens–Wendt calculations, the total surface free energy was 46 ± 3 mJ/m^2 for Ni–Ti and 52 ± 2 mJ/m^2 for Cp-Ti and Ti–6Al–4V. As

regards fibroblasts proliferation, it was bigger for the Ni–Ti sample, this being possibly related to the lower value of total surface free energy. Interfacial free energy had extremely low values (Ni–Ti: 2.36 ± 0.15 mJ/m^2, Cp-Ti: 2.4 ± 0.05 mJ/m^2, Ti–6Al–4V: 2.17 ± 0.07 mJ/m^2) which could be attributed to hydrogel formation at the metal surface.

The study evidenced that roughness influences human fibroblasts proliferation, as well as the wettability characteristic. However, surface free energy can be a dominant parameter for fibroblasts proliferation.

2.1.2 Chemical Properties

The physical properties, composition, and chemical properties also influence the kind of cell bond and determine the biomaterial chemical stability and reactivity.

The corporeal ambience is harsh and may cause corrosion of biomaterials. On account of this fact, the biomaterials' chemical stability becomes a relevant factor as regards biocompatibility.

Corrosion products may cause adverse reactions to the implant neighborhood. Body fluids are in balance with specific ions under normal physiological conditions. When a biomaterial is implanted the concentration of these ions increases significantly around it and may cause swelling and pain, besides the fact that the corrosion wastes may migrate to other parts of the body and cause undesirable reactions, both for the tissues and the implant [21].

Corrosion of biomaterials alters not only chemical stability, but also affects the mechanical integrity, with possible premature failure of the material [21].

As with corrosion, the corporeal ambience may cause and/or accelerate the biomaterial degradation. Degradation can also be influenced by sterilization processes to which materials are submitted [22–24]. When the biomaterial is degraded, modifications occur at the material structure and, consequently, modifications in its properties.

Surface functional groups can also influence the biomaterial response, since the surface chemical functionality affects adsorbed protein and cell/protein interactions. Commonly investigated functionalities as relates biomaterials are carboxyl (–COOH), hydroxyl (–OH), amino ($–NH_2$), and methyl ($–CH_3$) groups [25].

2.1.3 Mechanical Properties

Advances in engineering and medicine require the development of ever more specialized properties for biomaterials. For a biomaterial utilized for a specific

mechanical application, some of the requirements studied are Young's modulus, ductility, tensile strength, yield strength, compression strength and fatigue, and wear debris. These properties are evaluated on account of the fact that the human body has different properties for each tissue. For example, elasticity varies from very soft as is the case of brain tissues ($\sim$0.1–1 kPa) up to extremely hard or stiff (30 kPa and above), which is the case for the completely mineralized bone [26].

Biomaterials having Young's modulus close to that of the bone are recommended since they assure uniform tensile distribution and avoid stress shielding after implant placement; high values for yield and compression strength properties avoid fractures and improve functional stability; ductility is important for modeling the biomaterial formation and for dental biomaterials. The ductility minimum value is 8%; hardness and tenacity also evaluate the biomaterial response; the increase in hardness reduces the wear incidence; and increase in tenacity renders fracture more difficult [27]. These features, besides defining the processing ability of the biomaterial, are used to evaluate the success and biocompatibility of same.

Still as relates mechanical properties, biomaterials used for hip implant or articulation replacement should bear cyclic loads without failure or fracture for a long period of time, the same being true for cardiac valves. Besides numerous cyclic loads, failure by fatigue can also occur if tensile variations are high [2]. Biomaterials which should bear cyclic efforts without allowing cracking propagation are made up chiefly of polyurethane, polyester, and metals in general. The biomaterials which bear the desired characteristics are mainly applied for orthopedic, dental, and cardiovascular implants [17].

Wear causes material surface removal and this process occurs by the movement of two surfaces in contact. Failure by fatigue and wear can occur, for example, in biomaterials used for hip prosthesis, where the contact movement of the biomaterial parts is imperative. Besides, the physiological medium may aggravate these phenomena [2].

Biomaterials used for replacement of intervertebral disk should have fair properties of compression strength since the backbone undergoes compression caused by the body weight besides those due to the contraction loads of the muscles surrounding the backbone. For example, compression forces during dynamic lifting were estimated in up to 2500 N and the intradiscal pressure of approximately 1 MPa during routine activities, such as climbing steps (0.5–0.7 MPa) and jogging (0.35–0.95 MPa) [28]. Table 2.2 lists the load applied in different activities on the lumbar intervertebral disk (L-3) for a 70 kg individual [29].

Differentiated cells or stem cells of different organs and tissues of the body can feel the properties of biomaterials, such as the matrix elasticity and convey the mechanical signs as physiological responses, such as strain specification, cell orientation, morphological alterations, and growth factor. The development of bio-adaptive materials having mechanical properties similar to those of damaged tissues or organs could favor cell adaptation [30].

Table 2.2 Load applied on the intervertebral disk as related to different activities [29]

Activity	Load on disk (N)
Supine position	294
Standing	686
Seated right	980
Walking	833
Rolling the trunk	882
Inclining laterally	931
Coughing	1078
Jumping	1078
Stretching out	1176
Laughing	1176
Lifting 20 kg with upright column, flexed knees	2058
Lifting 20 kg with bent column, stretched knees	3332

2.2 Surface Modification—Biomaterial–Tissue Interactions

Modifications at the biomaterial surfaces are considered as a promising alternative to improve biomaterial–tissue interactions and promote better biocompatibility and biofunctionality results without altering the materials' bulk properties [31].

Surface modifications can be of the following kinds: physicochemical modifications (related to modifications involving changes of atoms, constituents, or surface molecules) and surface coating (involving different materials for underlying support). Physical–chemical modifications can be obtained by means of chemical reactions (oxidation, reduction, utilization of organosilanes, acetylation), etching, mechanical roughening/polishing, and patterning; and surface coatings include grafting, non-covalent, and covalent coating, besides thin film deposition [31]. Figure 2.2 illustrates a few surface modification techniques.

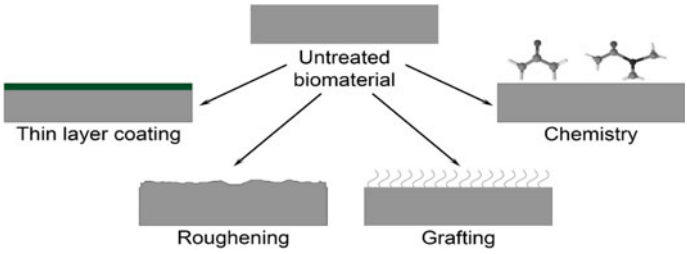


Fig. 2.2 Illustration of surface modification techniques for biomaterials

Table 2.3 Different techniques and coating characteristics with apatite deposition

Technique	Thickness	Advantages	Disadvantages
Thermal spraying	30–200 μm	High deposition rates, low cost	Line of sight technique, high temperatures induce decomposition, rapid cooling
Sputter coating	0.5–3 μm	Uniform coating thickness on flat substrates, dense coating	Line of sight technique, expensive time consuming, produces amorphous coatings
Dip coating	0.05–0.5 mm	Inexpensive, coatings applied quickly, can coat complex substrates	High sintering temperature, thermal expansion mismatch
Sol–gel	<1 μm	Can coat complex shapes, low processing temperature, relatively cheap as coatings are very thin	Process require controlled atmosphere processing, expensive raw materials
Electrophoretic deposition	0.1–2.0 mm	Uniform coating thickness, rapid deposition rates, can coat complex substrates	Difficult to produce crack-free coatings, requires high sintering temperatures
Pulsed laser deposition	0.05–5 μm	Coating with crystalline and amorphous, coating with dense and porous	Line of sight technique
Biomimetic coating	<30 μm	Low processing temperatures, can form bonelike apatite, can coat complex shapes, can incorporate bone growth stimulating factors	Requires replenishment and a constant pH of simulated body fluid

Adapted [32]

In the group of coatings those listed in Table 2.3 are highlighted. These surface coatings are obtained by deposition of hydroxyapatite, a bioactive material which favors the osseointegration process [32, 33].

A huge variety of techniques for surface modifications is to be found in the literature; however, no universal technique is known that could be used for any type of biomaterial. What are known are process variations and those depend on the desired application and the kind of biomaterial. For example, for bone implant biomaterial quick bone conductivity is required and stents should be structured to avoid cell proliferation provoking restenosis, while a cardiovascular device should have blood compatibility or antithrombogenicity [34].

The choice of the surface modification technique is a function of factors such as the substrate material, components and geometry design, application and surface aspects of engineering processes which include coating thickness and process temperature [34].

References

1. Chen, Q., Thouas, G.A.: Metallic implant biomaterials. Mat. Sci. Eng. R. **87**, 1–57 (2015)
2. Bauer, S., Schmuki, P., Von Der Mark, K., Park, J.: Engineering biocompatible implant surfaces Part I: materials and surfaces. Prog. Mater Sci. **58**, 261–326 (2013)
3. Domanska, A., Boczkowska, A.: Biodegradable polyurethanes from crystalline prepolymers. Polym. Degrad. Stab. **108**, 175–181 (2014)
4. Oréfice, R.L., Pereira, M. de. M., Mansur, H.S.: Biomateriais: fundamentos e eaplicações. Cultura Médica, Rio de Janeiro (2006)
5. Holzapfel, B.M., Reichert, J.C., Schantz, J.T., Gbureck, U., Rackwitz, L., Noth, U., Jakob, F., Rudert, M., Groll, J., Hutmacher, D.W.: How smart do biomaterials need to be? A translational science and clinical point of view. Adv. Drug Deliv. Rev. **65**, 581–603 (2013)
6. Lasprilla, A.J.R., Martinez, G.A.R., Lunelli, B.H., Jardini, A.L., Maciel Filho, R.: Poly-lactic acid synthesis for application in biomedical devices: a review. Biotechnol. Adv. **30**(1), 321–328 (2012)
7. Ravaglioli, A., Krajewski, A.: Bioceramics—Materials, Proprieties Applications. Chapman & Hall, Nova York (1992)
8. Silver, F., Doillon, C.: Biocompatibility: interactions of biological and implantable materials. VCH, New York (1989)
9. Wang, Y.X., Robertson, J.L., Spillman Jr., W.B., Claus, R.O.: Effects of the chemical structure and the surface properties of polymeric biomaterials on their biocompatibility. Pharm. Res. **21**(8), 1362–1373 (2004)
10. Hench, L.L., Wilson, J.: An Introduction to Bioceramics. World Scientific Publish, Singapore (1999)
11. Rai, R., Tallawi, M., Roether, J.A., Detsch, R., Barbani, N., Rosellini, E., Kaschta, J., Schubert, D.W., Boccaccini, A.R.: Sterilization effects on the physical properties and cytotoxicity of poly(glycerol sebacate). Mater. Lett. **105**, 32–35 (2013)
12. Ratner, B.D., Hoffman, A.S., Schoen, F.J., Lemons, J.E.: Biomaterials science: an introduction to materials in medicine, 3rd edn. Academic Press, Amsterdam (2013)
13. Kawachi, E.Y., Bertran, C.A., Reis, R.R. dos., Alves, O. L.: Biocerâmics - tendências e perspectivas de uma área interdisciplinar. Quim. Nova. **23**(4), 518–522 (2000)
14. Zuleta, F.A., Velasquez, P., Aza, P.N. de.: Effect of various sterilization methods on the bioactivity of laser ablation pseudowollastonite coating. J. Biomed. Mater. Res. B Appl. Biomater. **94B**(2), 399–405 (2010)
15. Chang, H.I., Wang, Y.: Cell Responses to surface and architecture of tissue engineering scaffolds. In: EBERLI, D. Regenerative Medicine and Tissue Engineering—Cells and Biomaterials, pp. 569–588. INTECH, Croatia (2011)
16. Xu, L.C., Siedlecki, C.A.: Effects of surface wettability and contact time on protein adhesion to biomaterial surfaces. Biomaterials **28**(22), 3273–3283 (2007)
17. da Silva, M.H.P.: Apostila de biomateriais. CBPF, Rio de Janeiro (2006)
18. Wieland, M., Chehroudi, B., Textor, M., Brunette, D.M.: Use of Ti-coated replicas to investigate the effects on fibroblast shape of surfaces with varying roughness and constant chemical composition. J. Biomed. Mater. Res. **60**(3), 434–444 (2002)
19. Chen, W.C., CL, K.O.: Roughened Titanium Surfaces with Silane and Further RGD Peptide Modification in Vitro. Mat. Sci. Eng. C. **33**(5), 2713–22 (2013)
20. Ponsonnet, L., Reybier, K., Jaffrezic, N., Comte, V., Lagneau, C., Lissac, M., Martelet, C.: Relationship between surface properties (roughness, wettability) of titanium and titanium alloys and cell behavior. Mat. Sci. Eng. C. **23**, 551–560 (2003)
21. Smith, W.F., Hashemi, J.: Fundamentos de engenharia e ciência dos materiais, 5th edn. AMGH, Porto Alegre (2012)
22. Holy, C.E., Cheng, C., Davies, J.E., Schoichet, M.: Optimizing the sterilization of PLGA scaffolds for use in tissue engineering. Biomaterials **22**(1), 25–31 (2000)

23. Hooper, K.A., Cox, J.D., Kohn, J. Comparison of the effect of ethylene oxide and g-irradiation on selected tyrosine-derived polycarbonates and poly(L-lactic acid). J. Appl. Polym. Sci. **63**(11), 1499–510 (1997)
24. Loo, S.C.J., Ooi, C.P., Boey, Y.C.F.: Radiation effects on poly(lactide-co-glycolide)(PLGA) and poly(L-lactide) (PLLA). Polym. Degrad. Stab. **83**(2), 259–265 (2004)
25. Thevenot, P., Hu, W., Tang, L.: Surface chemistry influence implant biocompatibility. Curr. Top. Med. Chem. **8**(4), 270–280 (2008)
26. Rehfeldt, F., Engler, A.J., Eckhardt, A., Ahmed, F., Discher, D.E.: Cell responses to the mechanochemical microenvironment: Implications for regenerative medicine and drug delivery. Adv. Drug Deliv. Rev. **59**, 1329–1339 (2007)
27. Saini, M., Singh, Y., Arora, P., Arora, V., Jain, K.: Implant biomaterials: a comprehensive review. World J. Clin. Cases **16**(3), 52–57 (2015)
28. Walter, B.A., Illien-Junger, S., Nasser, P.R., Hencht, A.C., Iatridis, J.C.: Development and validation of a bioreactor system for dynamic loading and mechanical characterization of whole human intervertebral discs in organ culture. J. Biomech. **47**, 2095–2101 (2014)
29. Hamill, J., Kwutzen, K.: Bases biomecânicas do movimento humano. Manole, São Paulo (1999)
30. Wang, Y.: Bioadaptability: an innovative concept for biomaterials. J. Mater. Sci. Technol. **32** (9), 801–809 (2016)
31. Garcia, A.J.: Surface modifications of biomaterials. In: Atala, A., Lanza, R., Thomson, J.A., Nerem, R.M. (eds.) Foundation of Regenerative Medicine, pp. 368–377. Academic Press, San Diego (2010)
32. Yang, Y., Kim, K.H., Ong, J.L.: A review on calcium phosphate coatings produced using a sputtering process—an alternative to plasma spraying. Biomaterials **26**, 327–337 (2005)
33. Ciobanu, G., Ilisei, S., Luca, C.: Hydroxyapatite-silver nanoparticles coatings on porous polyurethane scaffold. Mat. Sci. Eng. C. **35**, 36–42 (2014)
34. Nouri, A., Wen, C.: Introduction to surface coating and modification for metallic biomaterials. In: Wen, C. (ed.) Surface Coating and Modification of Metallic Biomaterials, pp. 3–60. Elsevier Woodhead Publishing, Cambridge (2015)

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