

# Mechanisms, Current Methods and Future Prospects of Biomimetic Surface Functionalization for Bone-Integrating Orthopaedic Implants

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## Abstract

The incidence of orthopaedic implants is rising worldwide, with hundreds of thousands of surgeries performed each year. However, due to inadequate bone integration, a sizeable fraction of these surgeries fail. Numerous research directions have been looked at to address this problem and enhance the biocompatibility of orthopaedic devices by altering the body's reaction to the implant surface. Orthopaedic surfaces with biomimetic functionalization can signal through immobilised proteins and other biomolecules to influence the biological response. By encouraging osteoblast development and bone growth at the implant surface, this strategy hopes to integrate the orthopaedic surface with the surrounding bone tissue. The requirement for biomimetic functionalization is first highlighted in this review from a materials and biological standpoint. The characteristics of the surface that control protein-surface interactions are subsequently explained. We review and discuss developments in the biomolecule functionalization of orthopaedic surfaces through adsorption, chemical covalent immobilisation, and physical covalent immobilisation. Each approach's immobilisation mechanisms are looked at, and the tactics are rated for complexity, effectiveness, reproducibility, and scalability. Then, new and promising directions for the multi-functionalization of biomimetic surfaces and the conversion of 2D substrates to 3D substrates are investigated.

**Keywords:** Surface bio-functionalization; Biomolecules; Osseointegration; Titanium

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## Introduction

Worldwide, the use of orthopaedic or bone implants has significantly increased. For instance, since 1999, about a million total hip and knee replacement procedures have been carried out in Australia alone; about 10% of these procedures required revision surgeries because of issues related to inadequate bone integration [1]. Even with initiatives like improved surgical implant techniques, sterile operating rooms, and increased postoperative care, a sizable portion of implants fail because of insufficient bone tissue integration [2]. Implants become vulnerable to the foreign body reaction, where fibrotic tissue encapsulates them and biofilm formation due to bacterial colonisation when

fresh bone is not quickly encouraged to grow on their surface. implantable material. The presence of fibrotic tissue at the bone-implant interface frequently interferes with implant attachment and function, necessitating recurring surgical intervention. Biofilm buildup causes infections that are frequently only treated by surgically removing the implant [3]. A compelling demand for surface changes that speed up Osseointegration, or the formation of new natural bone on and around the implant surface, is created by the expenses, hazards, and discomfort that revision surgery causes patients. The requirement for optimally Osseointegration bone implants is growing due to the rise in orthopaedic implants performed each year around the world and the demand for longer implant lifetimes as human life spans lengthen.

## Surface Chemistry

Depending on how they will be used, orthopaedic implants are divided into load-bearing and non-load-bearing categories. Devices like screws or maxillofacial plates that provide structure but do not sustain weight are known as non-load bearing implants. Resorbable ceramics that are chemically comparable to bone, such as hydroxyapatite (HA), or biodegradable polymers, such as polycaprolactam, are preferred materials for non-load bearing devices (PCL). In this instance, the implant's function is to promote the growth of natural bone, which eventually fills the space left by the implanted scaffold as it deteriorates. On the other hand, load-bearing implants, such as prosthetic knees and hips, must be able to support the patient's weight while moving. These implants' construction materials must be able to maintain their shape when intense mechanical pressures are applied repeatedly [4]. Ceramic materials lack the required flexibility because of their extremely strong ionic bonding. In general, polymeric materials lack the strength to withstand repeated stress without undergoing plastic deformation. The exception is polyether (ether ketone) (PEEK), which has uses in spinal implants and mechanical qualities similar to those of natural bone. PEEK has been used in orthopaedic applications, including bioactive surface changes. For load-bearing orthopaedic applications, metallic materials have traditionally been the preferred option because they exhibit the necessary mechanical strength to support physical loading and the degree of elasticity required to resist failure under cyclic physiological loads.

## Protein – Surface Interactions

Over the past century, the development of orthopaedic implants has involved extensive research into three metallic alloys: titanium, cobalt chromium, and stainless steel (Ti). First put forth in the 1940s, extremely strong ionic bonding. In general, polymeric materials lack the strength to withstand repeated stress without undergoing plastic deformation. The exception is polyether (ether ketone) (PEEK), which has uses in spinal implants and mechanical qualities similar to those of natural bone [5]. PEEK has been used in orthopaedic applications, including bioactive surface changes. For load-bearing orthopaedic applications, metallic materials have traditionally been the preferred option because they exhibit the necessary mechanical strength to support physical loading and the degree of elasticity required to resist failure under cyclic physiological loads [6].

The latter half of the 20th century saw practically sole use of titanium and its alloys. Numerous Ti alloys have been studied and in-depth reviews of them have been published elsewhere. The fabrication of porous Ti alloys, which exhibit improved Osseointegration but have reduced mechanical strength due to the pores acting as stress concentrators, is one of the more recent advances [7]. Due to their higher biocompatibility and lower elasticity modulus, titanium alloys are better to stainless steel and CoCr alloys for orthopaedic implants. According to the table, the elastic modulus of titanium alloys ranges from 50 to 118 GPA. This modulus is 2 to 5 times higher than hard cortical bone, although being half that of stainless steel (216 GPA) and CoCr alloys (240 GPA) (10–30 GPA). While PEEK's elastic modulus

of 3.6–3.9 GPA is closer to that of Ti, its yield and tensile strengths are much lower, indicating that fibre reinforcing may be necessary for skeletal implants subjected to high levels of cyclic loading. A situation known as "stress shielding" occurs when there is an imbalance between the elastic moduli of the implant and the bone [8].

## Results

Where the implant-surrounded bone is resorbed According to Wolff's Law, the stresses that the bone experiences determine the shape of the bone tissue, which goes through a continuous cycle of production and resorption [9]. The surrounding hard tissue is resorbed when a titanium implant is placed because the hard bone tissue no longer receives the essential mechanotransductive pressures for bone growth. Implant loosening brought on by a lack of physiological feedback need revision surgery to fix. In contrast to stainless steel and CoCr alloys, which have negative effects on the surrounding tissue due to the leaching of metallic ions, titanium-based alloys are typically well tolerated in vivo [10]. Ti ions are substantially less harmful to the surrounding cells than Fe, Co, and Cr ions are. Due to these benefits, titanium-based alloys are now the main component of load-bearing orthopaedic implants. Due to the development of an unreactive oxide layer with a thickness of about 5 nm on the surface (also known as the passive layer), titanium is physiologically inert.

## Discussion

*In vivo*, titanium is well tolerated, but on a cellular level, it does not actively promote osseointegration. As mentioned in the context of dental implants, both additive and subtractive surface modification methods have been researched to enhance osseointegration. Proteins from the biological environment quickly adsorb on the implant surface once titanium has been inserted into the body, reducing the interface's free energy. Protein adsorption will lower the free energy of a more hydrophobic interface's concentrating their hydrophilic domains in the aqueous medium and unfolding to expose their inner hydrophobic areas to the surface. A layer with a varied content and shape may result from proteins arriving later displacing or aggregating with proteins on the surface. The interactions between the surface and the biological environment are controlled by the adsorbed proteins, which serve as markers and signalling molecules. An unstable protein layer that contains molecules in non-native conformations causes a foreign body reaction that causes fibrotic tissue to surround the implant. A possible strategy to overcome the bioinertness of the surface and increase osseointegration is the functionalization of a titanium implant through the immobilisation of desired proteins or their bioactive fragments.

The underlying issue of elastic modulus mismatch cannot be resolved by protein immobilisation since elastic modulus is a feature of bulk materials. However, by promoting more effective bone integration, protein immobilisation can lessen the overall effects of stress shielding in areas sensitive to bone resorption.

## Conclusion

Peptide immobilisation gave rise to protein immobilisation, which

was initially carried out on glass substrates. A small number of studies, which date back to 1990, were released before the year 2000. Since then, numerous processes and proteins have been studied in the area of protein immobilisation. The proteins that act as signals to stimulate bone formation and the extracellular matrix (ECM) proteins that serve as cell adhesion sites make

up the two types of proteins that are thought to improve osseointegration. BMP-2, which is known to drive cortical bone formation during surgical procedures, has been immobilised on Ti surfaces and has been demonstrated to stimulate osteoblast-like cell proliferation and differentiation.

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