# Multifunctional bioinspired surfaces for different host responses

## Abstract

In short, the topic of this thesis is the functionalization of biomaterials for bone contact applications with different biomolecules to confer multifunctional surface properties. Biomolecules are chemical compounds that play an important role in living being. The here used biomolecules are both natural such as polyphenols and vitamin E (α-tocopherol (αT)) and its derived compound α-tocopherol phosphate (αTP) or artificially synthesized, such as peptoids. The use of natural biomolecules for the functionalization of biomaterials brings advantages, such as lower immune response, different functionalities, natural native ligands, natural degradation process, wide availability, and cost-effectiveness but may have some issues such as the high variability of properties and composition, difficult industrial processes and standardization, control of degradation profiles, sterilization. This is also why it is interesting to compare different biomolecules that have completely different origins. The chosen biomolecules differ in properties and chemical structures; they have antibacterial, anti-inflammatory, antioxidant, and osteoinductive properties, and the challenge of this work is to exploit their ability to give effective functionalities and new capabilities to biomaterial surfaces. Indeed, nowadays the main medical need of biomedical devices is a multifunctional activity able to induce rapid and physiological osseointegration, counteract bacterial biofilm formation, and prevent in situ chronic inflammation at the same time. The substrates used for functionalization were chemically treated titanium surfaces to become bioactive: they have nano-textured surfaces and, in one case, a calcium titanate layer doped with iodine ions to confer antibacterial properties to the surface. Different functionalization protocols were investigated and improved, from a thick, homogeneous coating to a single molecular layer. The method of functionalization was selected case by case, depending on the molecule used, varying the pH, solvent medium, and temperature, with the aim of optimizing the adhesion and amount of the molecule on the substrate. A protocol of a physical/chemical and biological characterization was also investigated, using different techniques such as Z-potential titration curve, UV-VIS spectroscopy, FTIR, KPFM, contact angle, photospectroscopy

measurements with the Folin&Ciocalteu method, release tests, and so on. For biological characterization, samples were tested *in vitro* with bacterial and cellular assays. Of course, the same characterization techniques were not used for all molecules, but for each molecule, the right suitable protocol was explored.
The different physicochemical characterizations revealed a continuous homogeneous coating for α-tocopherol and molecular functionalization for peptoids and polyphenols. The grafting of α-tocopherol phosphate, on the other hand, was explored in both ways, either as a homogeneous coating or through molecular functionalization.
Biological tests revealed different properties for each molecule: α-tocopherol has an antifouling effect, through which it provides an antiadhesive coating for both cells and bacteria. α-tocopheryl phosphate and peptoids have an effective antibacterial activity and polyphenols have shown a successful antioxidant ability in a chemically-induced pro-inflammatory environment, thus showing a scavenger activity towards toxic active species responsible for inflammation.
According to the results, surface functionalization of biomaterials is a promising strategy to achieve multifunctional surfaces that combine the properties of the substrate with those of the grafted biomolecule