Title of the thesis: Bioactive organic-inorganic hybrid biomaterials for tissue engineering

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Summary:
The purpose of the thesis is to develop new organic-inorganic hybrid materials based on bioactive glasses for the repair of bone tissue and/or cartilage regeneration. Bioactive glasses exhibit remarkable properties which result from a dual action at both the chemical and biological levels. When intimately mixed at the molecular scale with a polymer phase through a bottom-up approach, a hybrid material capable of synergistic effects is obtained, which combines the bioactivity of the initial glass with the elastic and plastic properties of the polymer phase. In hybrids, the intimate entanglement of the two organic and inorganic phases allows them to behave as if they consisted of a single phase, resulting in a huge improvement of all the properties — in particular the mechanical ones — compared to composite materials.

Recently, the LPC group has patented a process demonstrating that the rate of bone regeneration of hybrids can be significantly increased and even reach record values though the incorporation in the hybrid matrix of nutrients usually used in nutrition for the prevention of osteo-articular damage. The process conducted under mild conditions ensures the preservation of dopants and their homogeneous distribution in the whole bulk of the hybrid matrix (and not limited to the matrix surface as with conventional adsorption methods). A first objective of the thesis is to apply this doping-strategy to a variety of dopants, whether of organic origin (derived from plants such as polyphenol molecules) or inorganic origin (metallic trace elements such as magnesium, copper, silver ions, etc.), all being chosen for their biological properties: stimulants of osteogenesis, angiogenesis, or even antibacterial activity. One of the challenges is to be able to reach the targeted biological effect without having to use traditional drug agents commonly employed for these purposes, which adverse effects are more and more debated (antibiotics developing bacterial resistance, or bone growth factors, hormones or cytokines with deleterious effects on the division and cell death processes). A second challenge of the thesis is to obtain class II hybrids, in which the polymer chains are grafted to the bioactive glass network through covalent bonds (mixed organomineral network). The silanisation of the polymer of interest (polycaprolactone) will allow its grafting on the silanol groups of the silicate network of the glass; bridging the two phases would enhance the mechanical properties and in vivo resorption kinetics of the hybrids. The third objective of the thesis is the additive manufacturing of hybrids using a 3D bio-printer based on mechanical and pneumatic extrusion which the LPC has recently acquired. The optimal extrusion modes and parameters (temperature, pressure, flow) will be determined in relation to the viscoelastic properties of the hybrids. Hybrids will be printed in the form of porous scaffold matrices capable of being colonized by cells and vessels; different scaffold designs (orthogonal meshes, gyroids, Schwartz surfaces, recursive Hilbert curves) will be studied and their influence on the cellular behavior (invasion, adhesion) and the mechanical properties (resistance, permeability) evaluated. In addition to this work, major multi-scale characterization work will be carried out including electron microscopy, vibrational spectrometry, thermal, rheological, mechanical, structural characterizations and large physics instruments which the LPC team can access (quantitative chemical imaging through ion beam analyses, and advanced high magnetic field NMR methods).