Titre : Modeling and simulation of bone reconstruction using a second gradient theory.

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Collaboration(s) (s'il y a lieu) : INSA Lyon, Université La Sapienza Rome, Polish Academy of Science

Rattachement à un programme (s'il y a lieu) :

Résumé :

In this work, we are interested in regenerative medicine and tissue engineering, and in particular, the bone reconstruction after a trauma or surgery. In these cases, it is often necessary to insert an implant in order for the patient to be able to recover from his/her injury. New reinforced polymer implants (micro or nano-structured porous scaffolds) are being developed to be bioresorbable which means they will mostly disappear with time as a function of the bone reconstruction. Numerous works exist on the subject for the modeling of bone reconstruction using high gradient theories and with efficient results. The proposed work will expand the existing works. We want to develop new 2D and 3D simulations coupling the long term reconstruction of bones together with the resorption of the scaffold. One of the difficulty is to precisely identify the model biological parameters which can be obtained using experimentations by efficient medical imaging facilities.

The final objectives of this work are to : (i) better understand and represent the biological effects taking place in bone reconstruction and (ii) develop a numerical model able to represent the bone reconstruction through a bioresorbable material and use as predictive and optimization tool.

This subject requires good knowledge of mechanics, numerical physics and a good taste for numerical modeling.

Descriptif du sujet (en complément, au format WORD impérativement)

"Modélisation et simulation de la reconstruction osseuse par une approche de second gradient"

1. Context

Regenerative Medicine aims at recovering injured or permanently damaged tissues, making use of laboratory-made compounds and materials, specially-grown cells (such as stem cells) and the rationalization of biochemical signals. Regenerative medicine is an inter-disciplinary field by definition, relying strongly on advances in materials science and engineering, tissue engineering, biology, chemistry, computer science, genetics, medicine, robotics, and other fields. As a consequence of aging, disease processes, or traumatic injury, tissues and organ systems lose their capacity to carry out their given physiologic function. While these degenerative processes are increasingly well understood, options for improving regeneration or restoration of function are all too often lacking. Important costs are involved in the process when the patient requires regular checking of his recovery and acceptance of the surgery that was involved. Shorter and more permanent solutions are therefore desirable. The global market for
tissue engineering and cell therapy products is set to more than quadruple from 2009 to 2018 with the largest segment for regenerative medicine and orthopaedic applications. One of the key components for tissue engineering approaches is the scaffold, or template, upon which cells are seeded or into which cells migrate after implantation into a defect site. In vivo, cells reside in a dense extracellular matrix network – a scaffold – from which they receive precisely-controlled cell-cell, cell-matrix, and cell-soluble factor signals which ultimately dictate activity. With the growing interest in tissue engineering substitutes, we first need to understand these interactions which may ultimately lead to more effective bio-mimetic scaffolds. In addition, the integration of these compounds into living organisms require the studies of their bio-compatibility, mechanical behavior, cells migration and development, and ultimately long life support within the body. This PhD proposal originated from existing collaborative works between the project partners. IMFS has been collaborating with the University of Aveiro on the development of materials for biomedical implants and on polymer nanocomposites (Singh et al. 2008, Shukufar et al. 2008, Nibennaoune et al. 2010, 2011, 2012, Baniassadi et al. 2011, Matadi et al. 2010, 2011, Ghazavizadeh et al. 2011) and with INSA Lyon on the modeling of bone resorption (Madeo et al. 2012)

3. Objectives

This work focuses on modeling the bone / scaffold interactions. The conception of a second gradient continuum mixture model accounting for the description of the effect of micro-structure on the overall mechanical behavior of both bone and bio-materials will be developed. Second gradient approaches have been widely recognized to be useful for these purposes. The model will be developed accounting for the local effects. It is clear that a parametric study of the most influencing biological parameters is required in order to validate the evolutions of both the bone reconstruction and resorption of the bio-material.Here, we propose to develop and extend further an existing 1D approach that was recently developed at IMFS and INSA Lyon (Madeo et al. 2011, 2012). The first step of this work requires the development of a theoretical and numerical model in order to be able to use it in a 2D environment. Indeed, the current model was developed in one dimensional case and in order to validate the cells deposition, aggregation and bio-resorption of scaffolds, we need to integrate it into a more general case. The numerical model will be written in a suitable language (C or FORTRAN) in order to be able to be integrated within a finite element analysis to represent the structural evolutions as a function of time. It is well established in the scientific literature (Buechner 2003, Harrigan 1988, Lakes 1981, Park 1986, Yang 1982) that classical Cauchy type continuum theories do not allow for the correct prediction of the mechanical behavior of bone, when considering sufficiently small scales and/or particular loading conditions. These scale-effects are related to the fact that bone is a hierarchically heterogeneous material, i.e. it can be considered as homogeneous at the scale of the millimeter, but it starts presenting heterogeneities at the scale of the micron and even at lower scales. The model developed will use second gradient theory in order to account for the local heterogeneous effects described. The conceived second gradient mixture model will be used to describe the mechanically driven process of reconstructed bone remodeling. We will apply the second gradient continuum model to suitable numerical simulations. This will permit to numerically test the effect of the heterogeneity at a microscopic scale on the overall process of bio-material resorption and of bone synthesis and resorption. Moreover, numerical simulations will allow for the determination of the crucial biological and mechanical parameters which intervene in reconstructed bone resorption and synthesis so guiding towards the conception of optimized bio-resorbable scaffolds. The first numerical simulations will be performed to start testing the different numerical and biological parameters. The simulations obtained via finite elements (Abaqus) will be used to validate the theory before producing more complex cases. Once the model will be validate, we will use it to predict the bio-resorption of the bio-degradable scaffold as a function of time.

Expected results and deliverables :

The expected outcomes of the numerical modeling and simulations are multiple. The prime objective is to develop a 2D theoretical and numerical model accounting for the mechano-biological effects at hand. Once the model will developed, it is expected to validate the biological kinetics using a parametric study in order to extract the most influencing parameters. Finally, we want to predict the evolution of the scaffold bio-resorption.
4. References