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MULTIPHYSICS TWO-SCALES ANALYSIS OF BONE REGENERATION IN TISSUE ENGINEERING PROBLEMS

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ABSTRACT

Bone Tissue Engineering aims to cover the classical drawbacks of allo- auto- grafting in orthopaedic illnesses, or attemps to promote bone regeneration in situations where the individual lost his innate regeneration capacity. Moreover, it is intended for accelerating bone frature healing in trauma processes. Under this perspective, cell-cultured porous biomaterials, i.e., *scaffolds* are implanted *in-vivo* to serve as a guide for bone regeneration and withstand early loads. The rate of bone regeneration within scaffolds depends on the cell migration, attachment, differentation and bone maturation which are a processes that take place in the pore scaffold scale. Furthermore, cells are sensitive to the mechanical environment induced by the loads generated by joints and muscles at the tissue scale. Consequently, different biophysical phenomena occurs at different coupled scales. In addition, the overall rate of bone regeneration within the scaffold is highly inlfluenced by its geometrical features as pore size, microarchitecture, and porosity, as well as the biomaterial properties as stiffness or resorption kinetics due to hydrolysis. The elucidation of the effect of each scaffold feature *in-vivo* requires costly protocols and long-term experiments, being therefore the computational modeling of the problem an inexpensive and attractive tool for scaffold design once properly validated with experimental results.

In this work we present the mathematical modeling and computer implementation of bone regeneration using scaffold in a specific *in-vivo* example (see Fig. 1) [1]. The

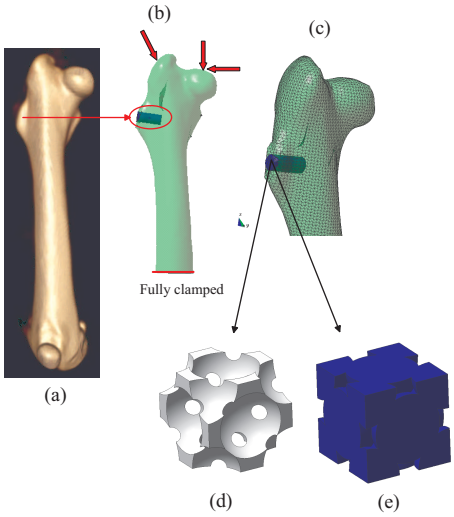

Fig. 1. Multiscale approach for *in-silico* simulations taken from the experimental model shown in [1]. (a) CT of the rabbit femur and (b) CAD macroscopic model (tissue level) of the femur and scaffold implantation, showing boundary loads and prescribed displacements whereas a detailed FE mesh of that zone is magnified in (c). Figs. (d) and (e) belong to a unit cell of the idealised scaffold microstructure (pore level) both the solid scaffold and fluid domains, respectively.

model involves different physical or biophysical phenomena at two scales, e.g., the pore scale (microscopic) and the tissue scale (macroscopic). At the tissue scale, bone and scaffold are treated in a different manner (Fig. 1b,c). Since we are interested in the scaffold region, bone is modelled only macroscopically but considering a heterogenous material with mechanical properties experimentally fitted as a function of its density [2]. Moreover, the density is considered to be an internal variable of the model which depends on the state of loading according to a phenomenological model of bone remodelling [2]. On the other hand, the scaffold (Fig. 1d,e) is modeled at both scales. The macroscopic mechanical state and cell density at each Gauss point of the finite element scaffold mesh (Fig. 1c)—featured by the macroscopic strain tensor and Fick's diffusion, respectively—is given to the scaffold microstructure (Fig. 1d) where a bone growth model is implemented using the voxel-Finite Element Method (Voxel-FEM). Here we simulate bone growing by adding voxels to the scaffold boundary according to a model derived from [2]. Scaffold resorption is modeled as a hydrolysis process [3] and is simulated removing voxels (Voxel-FEM) once a certain thresold has been overeached. Mechanical and flow properties, i.e., permeability are macroscpically derived from the underlying scaffold microstructure (Fig. 1d,e) by invoking the assimptotic homogenization [4]. The computer implementation is accelerated using parallel performance. As an example of application, the problem shown in Fig. 1 is solved varying several scaffold parameters from a baseline (reference) scaffold configuration as: porosity, a lower pore size (–), a higher pore size (+), a lower stiffness of the base material (–), a higher stiffness of the base material (+), a faster resorption kinetics and the effect of the scaffold cell pre-seeding. Furthermore, different bone growth models are investigated in this work. Results are presented in Table 1 and show an increasing rate of bone regeneration with increasing scaffold stiffness, scaffold mean pore size and pre-seeding whereas the collapse of the scaffold occurs for a faster biomaterial resorption kinetics. Requiring further experimental validation, the model can be useful for the assessment of scaffold design and for the analysis of scaffold parameters in tissue regeneration.

	4 weeks		8 weeks	
	Bone reg.	Scaff. deg.	Bone reg.	Scaff. deg.
Reference	2.6	100.0	27.5	51.3
Porosity	2.2	100.0	27.4	62.6
Pore size (–)	0.0	100.0	12.5	52.1
Pore size (+)	3.5	100.0	35.9	100.0
Stiffness (–)	0.0	100.0	0.0	49.6
Stiffness (+)	31.3	100.0	54.1	100.0
Res. kinetics	0.6	100.0	–	–
Pre-seeding	3.0	100.0	28.0	51.5

Table 1. Local percentage at the middle point of the scaffold midsection of tissue regeneration and scaffold resorption for the different cases at four and eight weeks after implantation.

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