Bone remodeling performed by BMUs in a FEA

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SUMMARY
Bone quality is modified through the activity of bone cells which are responsible of bone formation and bone resorption. Those bone cells are triggered by mechanical loading and some biochemical agents. So far no one has attempted to unify into a FE model the bone cells kinetic driven by mechanical loading and biochemical agents in order to update bone mechanical properties. This work aspire to fulfill this lack by proceeding in three steps: (i) implementation of a BMUs model in a FE code; (ii) modeling the transduction phase which deals with mechanical and biochemical agents; (iii) coupling the BMUs with the transduction phase in order to drive bone cells to perform bone adaptation. The concept of the model is described in Figure 1 and displays how the mechanical and biochemical agents are managed. The FEA enables us to observe the evolution of bone tissue density, trabecular bone volume or the amount of active cells in a specific site.

INTRODUCTION
The demand of numerical model to simulate and predict clinical issues is increasing day after day. The goal is to diminish the cost of treatments by preventing disease and illness but also to improve life’s quality of people. Bone quality is an important factor regarding the risk of fracture that increases in osteoporosis or osteomalacia for example. Bone quality is mainly function of the density, the architecture and the mechanical properties. In turn those properties are updated by cells responsible of bone formation (osteoblasts) and bone resorption (osteoclasts). Those cells called Bone Multicellular Units (BMUs) are tightly coupled and are driven through a complex transduction phase [1]. The transduction consists in the interpretation of mechanical information such as loading cycles and biochemical agents like calcium, nitric oxide, prostaglandin E2 and much more. Many studies describe the relation between the applied load and the evolution of bone mechanical properties and its architecture [2, 3]. Some other studies focus on the modeling of BMUs [4, 5]. As far as we know no one has developed a unify model which fully integrate cells kinetic coupled with the mechanotransduction process into a finite element code. To do that we had to proceed in three steps: (i) implementation of a BMUs model in a FE code; (ii) modeling the transduction phase which deals with mechanical and biochemical agents; (iii) coupling the BMUs with the transduction phase in order to drive bone cells to perform bone adaptation. The concept of the model is described in Figure 1 and displays how the mechanical and biochemical agents are managed. The FEA enables us to observe the evolution of bone tissue density, trabecular bone volume or the amount of active cells in a specific site.

METHODS
1. Bone Multicellular Units (BMUs)
Many authors have developed different type of models to describe the interaction between osteoblasts and osteoclast. They differ by the degree of precision in the description of the interaction between the cells. For example Komarova S.V. [5] has developed the first model which can be easily implemented in a FEA but lacks of physical meaning. Whereas Pivonka et al., [6] is one of the latest and the most interesting model for us because it is based on Hill function which are well designed to express the binding mechanism between ligand and receptor. Moreover it describes osteoblastic and osteoclastic lineage. This implies the consideration of the differentiation coefficient from one state of cell to a more mature one and also the apoptosis coefficient.

2. Transduction phase
The transduction phase is based on the idea that osteocyte which is a cell embedded into the mineralized bone tissue is the orchestrator of BMUs by driving their activity. It is well known of the role of osteocyte in the transduction phase in
order to gather and manage mechanical information and biochemical agents such as parathyroid hormone [1]. Nowadays the only work modeling the transduction role of osteocyte in terms of mechanical and biochemical sensor is from Rieger et al., [7]. The concept of the model is well described by the upper part of Figure 1 which leads to output signals designed to drive BMUs in order to trigger bone remodeling.

3. Coupling BMUs to transduction
The idea is to influence the coefficient of differentiation and apoptosis by the signals coming from the transduction phase. This idea has already been initiate by Lemaire [4] and Pivonka et al., [6] who considered a sudden change in differentiation coefficient for a certain period in order to observe the impact in bone cell population and the bone volume. In our case the difference is in the dynamical variation of those coefficients induced by the variation of signals coming from the transduction phase. In summary what we have is differentiation and apoptosis coefficients function of the mechanical loading and biochemical agents gathered and managed by the osteocyte.

RESULTS AND DISCUSSION
Preliminary results show good qualitative results and responses in terms of bone volume and bone tissue density are highly sensitive to change in mechanical loading and biochemical factors. For example the concentration of serum calcium can diminish or favor bone formation/resorption since it is in a sufficient amount or not. Furthermore the model exhibit interesting qualitative correlation between the clinical effect of oxide nitric and prostaglandin E2 production alteration or external administration (Figure 2). Nevertheless the model is far from being complete and many important biochemical agents are missing. Also the BMUs model doesn’t differentiate differentiation of the bone cells the activation which is the real indicator of their action. Finally the model lacks of clinical data in order to quantitatively be validated.

CONCLUSIONS
The model exhibits FEA of mechanical properties and architectural evolution during bone remodeling. Bone remodeling which is performed by BMUs driven through different signals. In turn those signals are coming from the transduction phase which deals with mechanical loading and biochemical agents. Since the model has only been run with 2D trabecular architecture we project to test it with real 3D meshed trabecular images.

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REFERENCES