

# COMPUTER SIMULATIONS OF BONE REMODELING, BASED ON A MATHEMATICAL MODEL CONSIDERING BIO-CHEMO-MECHANICAL REGULATION, AS WELL AS THE INFLUENCE OF THE VASCULAR POROSITY

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## **Introduction**

Bone remodeling comprises resorption of mature bone tissue and formation of new bone tissue [Martin et al., 1998]. The actions of involved cells (osteoclasts and osteoblasts) are driven by a number of biochemical factors, and they are also sensitive to the mechanical loading applied onto the skeleton. Here, we aim at contributing to prediction of the bone remodeling progress, by means of a multiscale mathematical model integrating systems biology, in order to take into account the biochemical governance of bone remodeling, and multiscale bone mechanics, in order to adequately consider the mechanical loading to which the studied piece of bone is subjected.

## **Methods**

The model is based on a bone cell population model, which considers the densities of osteoclasts and osteoblasts within a representative volume element of cortical bone, and their development from uncommitted progenitor cells, via precursor cells, to active cells. This development is driven by (i) biochemical factors, such as the receptor activator of nuclear factor kappa B (RANK), the ligand of RANK (RANKL), osteoprotegerin (OPG), parathyroid hormone (PTH), and transforming growth factor beta (TGF-beta); and by (ii) changes of the prevailing mechanical loading [Scheiner et al., 2013].

Furthermore, the model takes into account that the supply of the studied piece of cortical bone with progenitor cells (which, over time, develop into active bone cells) is governed by the available pore space, quantified by the corresponding volume fraction, that is the vascular porosity.

## **Results**

The model is then employed to study two different mechanical loading regimes. Firstly, a microgravity scenario is simulated, with the simulation results being in reasonable agreement with related experimental data. Secondly, mechanical overuse is simulated, that is the mechanical loading is increased compared to normal mechanical loading. Because of the implemented dependence of the osteoclast and osteoblast progenitor populations on the vascular porosity, bone gain decays with decreasing vascular porosity, which is physically reasonable and also agrees with experimental observations.

## **Discussion**

The numerical results confirm that the integrated mathematical model soundly considers key features of biochemically and mechanically regulated bone remodeling. Thus, refining the considered mechanobiology of bone remodeling and further experimental validation will eventually allow for utilization of the model as interpretative and predictive instrument.

## **References**

Martin, R.B. *et al.* Skeletal Tissue Mechanics, Springer Verlag, 1998.  
Scheiner, S. *et al.* Comput Method Appl M, 254: 181-196, 2013.

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