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UNDERSTANDING THE PROCESS OF FORCE-INDUCED BONE GROWTH AND ADAPTATION BY A MATHEMATICAL MODEL

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INTRODUCTION

Mathematical modeling offers a powerful tool to predict the influence of multiple and simultaneous factors on biological processes. It also offers the possibility to study and to analyze bone tissue as a dynamic complex system. Additionally, mechanical stimulation has been recognized as a potential regulator factor involved in development, growth, maintenance and function of the skeleton [1]. Our research is focused on understanding the process of force-induced bone growth and adaptation. In this work, a mathematical model is employed to consider multiple and simultaneous effects of mechanical force and local factors during a bone remodeling cycle.

Bone as a living tissue, has the ability to self-repair and adapt in response to new biophysical demands. The complex and hierarchical bone structure has attracted the interest of different scientific communities, studying and developing conceptual and computational models trying to shed light into the phenomenon of bone growth, development and maintenance. Additionally, research studies have been conducted in order to understand and identify the mechanisms bone uses to transduce the mechanical loads (gravity, physical activity) into biochemical signals.

Taking the conceptual framework of bone as a highly regulated system, proposed in the mechanostat theory and the functional adaptation concept, we constructed a mathematical model describing the bone dynamics at the tissue, cellular and signaling transduction level [7]. The model encompasses three layers of abstraction, from the biochemical signaling in response to mechanical stimulation, passing through the formation and resorption activities of bone cells (*metabolic mechanisms*), up to a basic description of the bone *thickness* growth and adaptation at the tissue level (*mechanical part*). The mechanobiological phenomena of the bone tissue is based on the hypothesis of osteocyte cells functioning as the bone mechanotransducers. Specifically, osteocytes formed an interfacing layer between the functional

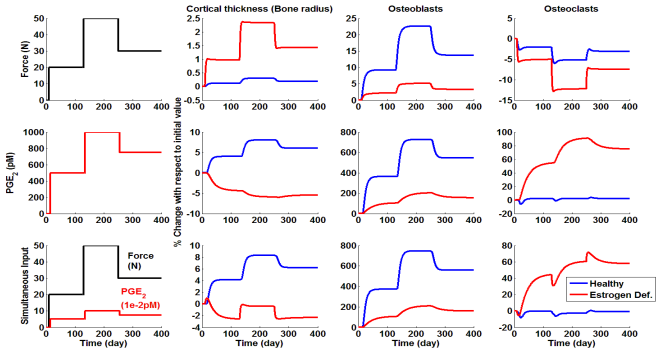

Figure 1: Responses to force-loads, drug-based medication PGE_2, and simultaneous input.

loads acting on the tissue by means of mechanical stress, and the biochemical signaling occurring during a bone remodeling cycle. In this sense, osteocytes sense changes in the average functional loads and release Nitric Oxide (NO) and Prostaglandin E_2 (PGE_2) factors to the bone microenvironment. These local factors influence the RANKL-RANK-OPG cytokine system, which regulates the coupled interactions between osteoclasts and osteoblasts during the bone remodeling cycle.

Figure 1 shows the bone response to increases in the average of mechanical force-load, to a external doses of PGE_2, and the effects of combined inputs. Bone tissue response is considered in the presence of *Healthy* and *Estrogen deficiency* condition [7]. The achieved results capture qualitatively very well the bone adaptation response to combined and simultaneous effects of mechanical force and external inputs, such as PGE_2. The potential power of the model lays in the fact that it enables one to examine the effect of metabolic changes together with the influence of functional loads. This allows for exploration of new therapeutic approaches targeting optimal therapeutic treatments design with anabolic and anti-resorptive effects to certain bone diseases.

REFERENCES

[1] D. Carter and G. Beaupré. *Skeletal Function and Form: Mechanobiology of Skeletal Development, Aging an Regeneration*. Cambrigde Univ Press, Cambridge, 2001.

[2] T. Skerry. "One mechanostat or many? Modifications of the site-specific response of bone to mechanical loading by nature and nurture". *Musc Neu Int*, Vol. **6**, 122–127, 2006.

[3] A. Parfitt. "Osteonal and Hemi-Osteonal Remodeling: The Spatial and Temporal Framework for Signal Traffic in Adult Human Bone". *Cell Biochem*, Vol. **55**, 273–286, 1994.

[4] V. Lemaire, F. Tobin, L. Greller, C. Cho, and L. Suva. "Modeling the interactions between osteoblast and osteoclast activities in bone remodeling". *J Th Biol*, Vol. **229**, 293–309, 2004.

[5] H. Frost. "A 2003 Updated of Bone Physiology and Wolff's Law for Clinicians". *Angle Orthod*, Vol. **74**, 3–15, 2004.

[6] E. Burger and J. Klein-Nulend. "Mechanotransduction in bone-role of the lacunocanalicular network". *FASEB J*, Vol. **13**, 101–112, 1999.

[7] S. Maldonado, R. Findeisen and F. Allgöwer. "Phenomenological Mathematical Modeling and Analysis of Force-Induced Bone Growth and Adaptation". *Proc. of 2nd FOSBE*, 147–152, 2007.