

Invited Speaker Abstract

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Review of computational modeling in bone biology: from intracellular signaling to tissue level

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Computational modeling provides a powerful tool for description of complex biological systems such as bone tissue and allows one to test various experimental and theoretical hypotheses “in-silico”. This paper will review a variety of distinct mathematical modeling approaches which can be applied to advance our current knowledge on bone biology at various scales of observation. The two examples described below have been chosen based on our current research projects, but stress analysis and the ‘mechanostat’ model is also reviewed.

The first example deals with modeling the dynamic response of bone cells within the framework of ordinary differential equations. It is now well established that cells of osteoblastic and osteoclastic lineage “cross-talk” via a variety of different signalling pathways. Among these the RANK-RANKL-OPG pathway has been identified as most crucial. Many factors have been identified increasing the RANKL/OPG ratio and, hence, bone resorption including parathyroid hormone, prostaglandins, interleukins, and vitamin D₃. Recently we and others proposed integrated mathematical models describing interactions of various cell lines of the osteoblastic and osteoclastic lineage utilizing the RANK-RANKL-OPG pathway together with growth factors [1]. Many characteristics of bone diseases can quantitatively be reproduced by these models. Furthermore, application of these models to the design of drug therapies allows identification of optimal strategies to restore bone mass.

The second example deals with computational modeling of tumor metastasis in bone. Based on various interactions between tumor cells, bone cells and cells in the bone microenvironment tumor growth and bone destruction can be simulated. A simplified version of this type of modeling has been used previously to monitor tumor morphology and phenotypic evolution driven by selective pressure from the microenvironment [2]. For this simplified problem the chosen mathematical model is a coupled continuum-discrete model where the continuum part is employed to model the evolution of variables of the microenvironment such as oxygen concentration and extracellular matrix macromolecule concentration. The discrete part accounts for cell motility, cells proliferation, differentiation and apoptosis.

References

- [1] P. Pivonka, J. Zimak, D.W. Smith, B.S. Gardiner, C.R. Dunstan, N.A. Sims, T..Martin, G.R. Mundy. Model structure and control of bone remodeling: a theoretical study. *BONE*, 2008. (available online 15 April 2008)
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