



## **EINLADUNG**

zum Gastvortrag

von

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am

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## Investigation of bone remodelling based on a systems biology approach

**Abstract**: The conceptual model employed by bone scientists today is based on the dynamic balance between two main bone cell types, the osteoclasts and osteoblasts, which continuously resorb bone and form new bone. This process is referred to as "bone remodeling". This conceptual approach has given many new insights into how bone structure and function is influenced by a variety of factors including hormones, cytokines, mechanical loading, and gene mutations to name only a few. But these two cell types do not work independently, but rather work in a coordinated way in so-called basic multi-cellular units (BMUs). There is cross-talk between the cell types to coordinate their functional behaviours. Given this interaction, it is very difficult to predict what might happen given some changes of the bone microenvironment. To date there have been few attempts to integrate all the key observations into a theoretical framework, which allows theoretical predictions and subsequent investigation experimentally. Mathematical modelling, provides the basis for "translation" of conceptual models into theoretical models which can then be employed to quantitatively investigate various hypotheses and study system behaviour as a whole rather than single-component behavior (Pivonka and Komarova 2010). Mathematical models can be built at different spatial and temporal scales.

In this presentation, we demonstrate how present conceptual knowledge of signalling pathways in bone remodeling can be integrated into a bone cell population dynamics model (Pivonka, Zimak et al. 2008). This model incorporates key interactions, including the RANK-RANKL-OPG signalling cascade together with the regulating action of TGF- $\beta$  on bone cells. Using cell numbers and bone volume as output functions we can then investigate how various therapeutic agents such as parathyroid hormone (PTH), bisphosponates, etc. impact on overall bone volume (Pivonka, Zimak et al. 2010).

**References :** Pivonka, P. and S. V. Komarova (2010). "Mathematical Modeling in Bone Biology: from Intracellular Signalling to Tissue Mechanics." Bone: in press.

Pivonka, P., J. Zimak, et al. (2008). "Model structure and control of bone remodeling: A theoretical study." Bone **43**(2): 249-263.

Pivonka, P., J. Zimak, et al. (2010). "Theoretical investigation of the role of the RANK–RANKL–OPG system in bone remodeling." Journal of Theoretical Biology **262**(2): 306–316.