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Modeling Mechano-chemical Couplings in Bone Adaptation by Remodeling

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Abstract: Bone adaptation by remodeling is a process to change its outer shape and internal structure to the changing mechanical environment by osteoclastic bone resorption and osteoblastic bone formation. These cellular activities are regulated by mechanosensory network of osteocytes embedded in bone matrix. An imbalance between bone resorption and formation due to low loadings or disuse results in metabolic bone disorders such as osteoporosis. Many studies have identified various signaling pathways that regulate these cellular activities; however, the physiological and pathological conditions of bone as a system remain difficult to understand because of the complexity of the signaling networks including mechano-biochemical couplings.

We have developed a novel mathematical model of bone remodeling that enables us to conduct *in silico* experiment by which the effects of perturbation of the biochemical and mechanical factors on the spatiotemporal dynamics of bone adaptation by remodeling can be observed.

Effects of disruption of the signaling molecules were investigated through computational simulations for cancellous bone remodeling using image-based cancellous bone models. Mechano-adaptive behaviors of trabecular bone under mechanical loading were investigated by considering a mechano-sensory network of osteocytes in bone matrix, in which the pathological bone states due to low mechanical loadings and abnormal expression of signaling molecules were reproduced. The developed platform was applied to conduct *in silico* perturbation experiment to observe the effects of specific signaling molecules on bone remodeling dynamics over time including distribution of signaling molecules, cell behaviors, and trabecular microstructure.

Keywords: Bone adaptation; computational biomechanics; *In silico* experiment

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