Modeling the effects of viral (Hiv) and bacterial infection (Staphylococcus aureus) in bone dynamics

This work focuses on viral (Hiv) and bacterial (staphylococcus aureus) infection of bone tissue causing the alteration of the remodelling process.
In the first part we present a mathematical model (ODE) of the infection and the formation of R5 and X4 strains HIV strains. Then we introduce a second model that describes the HAART therapy. The infection with the human immunodeficiency virus-1 (HIV) and the resulting acquired immune efficiency syndrome (AIDS) affect not only cellular immune regulation but also the bone metabolism through the NF-kB pathway. It is observed that significant number of HIV-1 infected patients exhibit bone loss with osteopenia and osteoporosis, leading to higher incidence to develop weak and fragile bones during the course of disease. The HAART therapy is also responsible for a significant loss of bone density. The models parameters are fitted using available gene expression data. Our models are able to explain the emergence of the IRIS (Immune reconstitution inflammatory syndrome) which can be tested experimentally.
In the second part we present a model of osteomyelitis, a bone pathology caused by bacteria infection (mostly Staphylococcus
aureus). The infection alters the RANK/RANKL /OPG signalling dynamics that regulates osteoblasts and osteoclasts patterns of bone remodelling, i.e. the resorption and mineralisation activity. We first perform meta analysis on a large ensemble of related gene expression data. We mainly focused on RANKL/OPG signalling and the NF-kB pathway which is a master switch in inflammatory processes. Given the lack of models for bone loss diseases, we first analysed gene expression profiles of differences between normal and osteomyelitis bone conditions. Using information from the gene expression data we estimate parameters that we have used in a novel model of osteomyelitis. This model could be seen as part of a hybrid ODE and probabilistic verification modelling framework which aims at investigating the dynamics of the infection with respect to both normal bone and osteoporotic bone. We compare the effects of viral and bacterial infection. Finally we discuss the use of probabilistic verification methodology in supporting different statistical estimators for multidiagnosis (infection versus osteopenia versus osteoporosis versus other pathologies). Together with a statistical estimator based on bone mineral density, we introduce new statistical estimators that detects rapid (months scale) decreases and the variance of the bone density. We show that these clinical bioinformatic estimators are meaningful and could be used in practice.