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A multiscale bone remodelling framework using the Physiome Project markup languages

Numerous computational bone models have explored remodelling and bone response at either the cell level, micro level or macro level (whole bone). However, there have been limited attempts to link information across these spatial scales [1]. Treatments such as milk-derived Lactoferrin therapy [2], have been shown to increase mineralised bone by modifiying the number of active bone absorbing cells (osteoclasts) and bone forming cells (osteoblasts). This, in turn, changes the micro bone architecture and the overall continuum strength observed at the whole bone level. A multiscale computational framework that passes information across the spatial scales will allow us to evaluate treatments and study disease progression. The focus of this study is to (i) outline the spatial linkages from the cell to the whole bone using the framework and markup languages developed for the Physiome Project [3]; and (ii) demonstrate this framework by looking at an anabolic treatment, Lactoferrin, and how it modifies osteoblast/osteoclast numbers, influences the strain pattern at the micro bone level and changes whole bone strength.

The multiscale modelling framework developed as part of the IUPS Physiome Project [4] was used to link the spatial scales. At the cell level the bone remodelling process describing the RANK-RANKL-OPG pathway [5] was implemented in the CellML markup language [6]. This describes the amount of osteoblasts (bone forming) and osteoclasts (bone resorbing) cells in response to a healthy, diseased or

treatment state. At the micro level a particulate method, 'Smooth Particle Hydrodynamics' (SPH) was used to model the micro strain of a bone cube (1mm x 1mm x 1mm) [7]. SPH has the ability to handle highly fragmenting solid structures, bone addition and removal. At the micro level a bone remodelling algorithm based on strain excitation adapted from the work of Prendergast [8] was used to add or remove bone in order to maintain bone density. At this level the osteon cortical pore structure was visible and the bone growth and resorption patterns based on the number of osteoclasts/osteoblasts lead to a changing architecture and overall bone strength. The macro model (whole bone) was a Femur geometry from the AnatML database, with material properties described using FieldML. A spatially varying density and Young's modulus was fitted from CT images using the CT number and a grey-scale mapping. The macro level models are physiologically loaded from muscle forces and ground reaction force data taken from gait experiments [9]. The whole bone model provides the boundary conditions for the micro models. The proposed computational framework has the potential to improve understanding of how cellular level changes influence whole bone strength.

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