The Digital Astronaut Project Bone Remodeling Model

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INTRODUCTION: Under the conditions of microgravity, astronauts lose bone mass at a rate of 1% to 2% a month, particularly in the lower extremities such as the proximal femur [1]. The most commonly used countermeasure against bone loss has been prescribed exercise [2]. However, current exercise countermeasures do not completely eliminate bone loss in long duration, 4 to 6 months, spaceflight [3,4], leaving the astronaut susceptible to early onset osteoporosis and a greater risk of fracture later in their lives. The introduction of the Advanced Resistive Exercise Device, coupled with improved nutrition, has further minimized the 4 to 6 month bone loss. But further work is needed to implement optimal exercise prescriptions [5]. In this light, NASA’s Digital Astronaut Project (DAP) is working with NASA physiologists to implement well-validated computational models that can help understand the mechanisms of bone demineralization in microgravity, and enhance exercise countermeasure development.

METHODS: The objective of the DAP computational modeling effort is to enable simulations in time of changes in bone mineral density (BMD) and Bone Volume Fractions (BVF) under the conditions of skeletal unloading and changes in physiological processes encountered in microgravity. Since the geometry of the remodeling units or bone packets that are removed and replaced during remodeling differ, separate modules for trabecular bone and cortical bone are developed. Key elements of the computational model include: Bone resorption (formation) rate varies with activation density, volume of remodeling unit removed (replaced), and active osteoclast (osteoblast) population. The active osteoblast and osteoclast populations vary according to the cellular dynamics mediated by hormones, proteins, ligands and receptors. The well-known adaptive response theory of Frost drives the bone response to variations in skeletal loading. Within the expressions for rates of changes of the cellular populations, assumptions for the ligand and receptor expressions are modeled in accordance with the American Society of Bone and Mineral Research educational literature.

INITIAL MODEL DEVELOPMENT: The model’s initial development focuses on the femoral neck. Remodeling unit dimensions for the femoral neck (particularly for cortical bone) were identified in the literature to make the model specifically applicable to the femoral neck, although many other model parameters were based on general bone knowledge. For model validation, we used BMD changes of control subjects in the current 70 day bed rest study and available data from the 17-week bed rest studies conducted in the past (Figure 1). Volumetric bone densities for the 70 day rest were obtained at pre and post bed rest via Quantitative Computed Tomography (QCT). However, bone densities from past bed rest studies were obtained via Dual-energy X-ray Absorptiometry (DXA). Given that DXA is 2-D integrated cortical and trabecular, and the computational model tracks BVF changes, the DXA values were mapped to equivalent QCT integral volumetric density values in order to run simulations with the DXA data. Our poster will discuss in detail how the model tracks BVF and the preliminary model validation results.

DISCUSSION AND FUTURE WORK: Our results show that a good foundation has been laid for establishing a physiologically accurate bone remodeling model. For example, mean BMD data for the 70-day bed rest is well within the 95% confidence interval of the model prediction. Future work will integrate the bone remodeling model with DAP’s biomechanical exercise models to predict the benefits of exercise induced load stimulus from different exercise prescriptions for maintaining bone at the femoral neck. The model will also be extended to include predictions for the lower lumbar spine, calcaneus, trochanter and the integrated proximal femur.

### Background

**Why Quantifying Change in Bone via Bone Remodeling is Objective of NASA Digital Astronaut Project (DAP)**
- One of the main objectives is to provide a tool to help scientists address Bone Gap Fraction.
- We don’t know the contribution of each role factor on bone loss and recovery of bone strength and which factors are the most critical for countermeasure application.
- **Importance for the New Finite Element-Based Strength Standard**

### Bone Remodeling Model Implementation Plan

**Model Representation of Bone Loss Due to Insufficient Mechanical Loading**

#### Mathematical Description

- System of ordinary differential equations
- Expressions for Osteoprotegerin (OPG), RANKL, and their ligand osteoclast activating factor (Osteocalcin)
- Complete detailed set of cellular dynamics in a coherent framework of the type of Lemaire et al. [1] and Pivonka et al. [2]
- Relates to realistic to skeletal loading.

#### Converting Experimental Data to Model Variables

- **Definitions**
  - Adiposity
  - Apparent density
  - Bone mineral content
  - Bone volume fraction

#### Preliminary Validation Results for Bone Reconditioning Simulations

- **Bone adaptation prediction for more than 180 days of spaceflight**
- **Develop model for predicting bone adaptation for trochanter, total body, and head**
- **CFT70 study**

#### Future Work

- **Mathematical model of the Mechanostat.**
- Integrates with DAP Biomechanics.
- Model includes bone properties and cell populations.

### General Description of the DAP Bone Remodeling Model

**What does it do?**
- It tracks changes in the bone when the balance between formation and resorption in the bone remodeling process becomes unbalanced.

**How does it do it?**
- The cellular physiology, remodeling unit mechanisms, and mechanotransduction theory that drive the process are described mathematically.

**How does the computational algorithm work?**
- Rates of change of bone volume fraction and cell populations are set to zero (Balanced healthy state with steady bone density).
- Balance is broken by skeletal unloading, and rate of change is no longer 0.
- System including bone properties and cell populations are integrated in time to estimate the change.

**NOTE:** Model parameters and methodology are currently focused on the femoral neck.

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#### State Variables and Definitions

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