Fiscal Year:	FY 2011	**Task Last Updated:**	FY 11/20/2013
PI Name:	Pennline, James Ph.D.		
Project Title:	Digital Astronaut: Bone Remodeling Model		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	Yes
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Bone Fracture**:Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (2) **Osteo**:Risk Of Early Onset Osteoporosis Due To Spaceflight		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	Directed Research
Start Date:	04/01/2011	**End Date:**	08/29/2015
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
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Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	Directed Research		
Performance Goal No.:			
Performance Goal Text:			

Background
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. The most commonly used countermeasure against bone loss in microgravity has been prescribed exercise. However, data has shown that existing exercise countermeasures are not as effective as desired for preventing bone loss in long duration spaceflight. This spaceflight related bone loss may cause early onset of osteoporosis to place the astronauts at greater risk of fracture later in their lives. Consequently, NASA seeks to have improved understanding of the mechanisms of bone demineralization in microgravity in order to appropriately quantify this risk, and to establish appropriate countermeasures.

In this light, NASA's Digital Astronaut Project (DAP) is working with the NASA Bone Discipline Lead to implement

Task Description:	well-validated computational models to help predict and assess bone loss during spaceflight, and enhance exercise countermeasure development. More specifically, computational modeling is proposed as a way to augment bone research and exercise countermeasure development to target weight-bearing skeletal sites that are most susceptible to bone loss in microgravity, and thus at higher risk for fracture. Methods The model consists of three major research areas, (1) the orthopedic science or mechanics of the removal and replacement of bone packets via remodeling units, (2) the biology and physiology of cellular dynamics of remodeling units, and (3) mechanotransduction which describes the function of skeletal loading and its role in maintaining bone health. The basic biological assumption used in the cellular physiology can be stated as such: Cell proliferation or anti-proliferation is respectively either directly proportional or inversely proportional to receptor occupancy ratio. In implementation, the bone remodeling model is based on a first principles physiological and mathematical description of the components of bone physiology, including responses by the endocrine, biochemical, autocrine, and paracrine systems. The model mathematically formulates the key elements based on well-accepted knowledge and experimental studies of bone. In particular, the model uses the RANK-RANKL-OPG signaling pathway to describe the cellular dynamics. For skeletal loading, the model includes the effects of nitric oxide and prostaglandin E2. In the computational model, reduced skeletal loading triggers a decrease in NO and PGE2, which in turn triggers an imbalance in the pathway in favor of resorption. This leads to a decrease in mineralized volume M and osteoid volume O, and hence a decrease in bone volume fraction (BVF). The loading portion of the model is based on the concept of a minimum effective strain stimulus, which takes into consideration strain rate as opposed to strain magnitude only. Specific Aims 1. For individuals in the age range of the astronaut corps, predict changes in trabecular and cortical volumetric bone mineral fraction and density as a function of time since measurement, gravity level, and applied loads 2. Support the bone fracture standard by accepting and providing data in the same form as that of a Quantitative Computed Tomography (QCT) scan
Rationale for HRP Directed Research:	This research is directed because it contains highly constrained research, which requires focused and constrained data gathering and analysis that is more appropriately obtained through a non-competitive proposal. This task meets the requirements for being tightly coupled with NASA efforts and therefore not amenable to solicitation because it: 1. Must be tightly coupled with integrated exercise biomechanical/device models that NASA is currently developing in-house. Otherwise, the bone remodeling model will have little utility for NASA because it will not be able to predict the time course change of vBMD in reduced gravity as a function of time and how exercise prescription can be optimized to counteract bone loss. 2. Must be tightly integrated with the QCT-based NASA bone strength standard. The bone remodeling model will provide valuable additional data via “forward prediction” simulations for during and after spaceflight missions to be used as input to the new bone strength FE analysis method to gain insight on how bone strength may change during and after flight. The bone remodeling model will be particularly be useful for providing data for time periods where QCT is not available, such as during flight. Under such cases, the model will be used to estimate the time course change of vBMD during an exploration mission and between the scans astronauts undergo after they return to Earth. This information can also be useful to help optimize exercise countermeasure protocols to minimize changes in bone strength during flight, and improve regain of bone strength post-flight.
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2011. [Editor's note (November 2013): Added to Task Book when information provided by HRP]
Bibliography Type:	Description: (Last Updated: 09/10/2018)