PhD Dissertation Defense Announcement
Mechanical and Aerospace Engineering Department
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LONG-TERM SIMULATION OF STEM CELL MECHANOBIOLOGY

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Abstract

An accurate representation of cellular mechanobiology necessitates the inclusion of subcellular elements characterized by minute masses and dimensions. These minute objects yield multiscale dynamic models with disproportionate terms, which require inordinate amounts of computational time to simulate. The computational requirements limit the time span of the simulation to time histories shorter than one second, even when employing supercomputers. This work presents a high-speed, long-term, approach to simulating the mechanobiology of stem cells. The proposed approach separates the computational time from the size, and distribution, of masses of the subcellular elements, enabling the simulation of weeks-long cellular processes within hours on a typical desktop computer. The accuracy of the approach is verified by the agreement between the computational results and the experimental data.

This work examines adipogenesis, the transformation of human bone marrow-derived mesenchymal stem cells (hMSC) into adipocytes, fat cells, a biochemically-induced differentiation process that spans two weeks. Stem cells undergo drastic morphological alterations during differentiation. The cytoskeletal remodeling, morphological changes of the nucleus, and in-crease in lipid expression during adipogenesis are studied herein.

Several physics-based, coarse-grained, biomechanical nuclear and cellular models of the adipogenic differentiation process are presented. These models include subcellular elements characterized by masses from femtogram to picogram in size and lengths from nanometers to microns in size. The forces acting on these elements will be orders of magnitude larger than the masses. The correspondingly large accelerations necessitate the use of small time steps to obtain an accurate solution. Numerically integrating this multiscale model for such a long time period is computationally infeasible with conventional methods. A novel scaling approach, based on method of multiple scales, is developed herein to resolve the disproportionality in terms of the dynamic model. This new approach drastically reduces computational time to several hours, on a typical desktop computer, for the two-week duration of adipoge