A. PROJECT SUMMARY

This proposal seeks to develop an integrated research and educational framework for simulating how changes in knee joint motions and loads due to anterior cruciate ligament (ACL) injury lead to development of osteoarthritis (OA). The three main objectives are to (1) develop and evaluate a novel adaptive simulation approach that can change the articular cartilage in a computational model of a patient's healthy knee into the articular cartilage in his or her ACL-deficient knee, (2) expose minority and female high school and college students to ways that engineering mechanics is being used to address clinically significant problems related to knee OA, and (3) involve college engineering students as tutors and mentors at a local high school with a low graduation rate and high percentage of economically disadvantaged students.

Computational models are valuable for developing and testing hypotheses that would be impossible to develop or test experimentally. They also provide a theoretical framework for explaining experimental observations. In the case of knee OA, a large number of animal and *in vitro* studies have been performed to improve our understanding of the disease process. However, our inability to measure cartilage contact conditions *in vivo* in human patients during disease progression makes it difficult to evaluate current hypotheses or develop new treatment paradigms. A computational model capable of reproducing the OA development process observed in human patients following ACL injury could provide a fast and inexpensive option for overcoming these limitations.

This project proposes to develop a state-of-the-art adaptive modeling approach that can simulate how articular cartilage thickness changes progressively over time in response to an altered mechanical environment. **The approach does not seek to capture every minute detail of the disease process with a highly complicated model but rather seeks to capture the first-order effects with a combination of simple models.** The approach will build on recent adaptive simulations that successfully predicted progressive surface wear in total knee replacements. Surface geometry, joint motion, and joint load inputs will come from individual patients, and an empirical cartilage adaptation law will be used in place of an empirical material wear law. The methodology will be evaluated by predicting the worn articular surface geometry for individual patients with a torn ACL starting from the geometry of the patient's healthy knee.

(1) Intellectual Merit of the Proposed Activity

The intellectual merit of the proposed research will be the creation of new adaptive simulation methods that can predict progressive changes in articular cartilage thickness. The success of recent adaptive wear simulations for artificial knees suggests that a similar adaptive simulation approach could work for predicting cartilage wear during the OA development process. This hypothesis will be investigated using a novel empirical cartilage adaptation law incorporated into iterative joint-level dynamic contact simulations. The proposed simulation approach is transformative in that they may open up an entirely new avenue for studying OA initiation and progression in the knee as well as in other joints.

(2) Broader Impacts Resulting from the Proposed Activity

If successful, the proposed computational technology may provide a valuable first step toward the development of new treatments for knee OA based on objective, theoretical knowledge of the mechanism by which altered motions and loads lead to cartilage degradation. Furthermore, if the approach can reproduce clinical observations for specific patients, it could potentially be used to design patient-specific interventions that produce the best long-term clinical outcome. Potential applications include identification of patients who are at greatest risk for rapid cartilage degeneration, design of personalized gait retraining strategies to minimize cartilage degeneration, and optimization of surgical design and placement of ACL grafts on a patient-specific basis.