**Summer Research in the Duim Lab**

Email Professor Duim for details: wduim@g.hmc.edu

**Fluorescence Nanoscopy of Protein Aggregates**

The Duim lab uses single-molecule and super-resolved fluorescence nanoscopy to go beyond the diffraction limit of visible light (~250 nm) and probe molecular structures and interactions down to the 10-50 nm scale. Our techniques allow us to study biological and chemical processes on the small length scales and in the environments where they occur. We are specifically interested in the protein aggregates formed during the pathogenesis of neurodegenerative disorders such as Huntington’s, Parkinson’s, and Alzheimer’s diseases. These aggregates contain a great deal of fine structural detail below the optical diffraction limit and their morphology is sensitive to the conditions under which they form. Our goal is to elucidate the mechanisms underlying neurodegenerative disease.

**Opportunities for Students**

(1) *Optimization of our custom fluorescence nanoscope*

We will draw on optical principles to optimize the performance of our nanoscope, which includes lasers, lenses, filters, mirrors, and a high-sensitivity camera. Alignment of the laser beam and calibration using fluorescent beads will be essential parts of the process.

(2) *Characterization of the structures and growth of Huntington’s disease protein aggregates*

Continuing from previous studies, we seek to determine why Huntington’s disease protein aggregation differs from that of other disease proteins and what this difference means for the pathogenesis of Huntington’s disease. We will grow Huntington’s disease protein in the lab using bacteria, label the purified protein with fluorescence dyes, and image the aggregation under a variety of conditions.

(3) *Development of image processing algorithms and computer models of aggregation*

This project is in collaboration with Professor Levy of the HMC Mathematics Department. Please contact levy@g.hmc.edu for more details.

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**Super-resolved fluorescence nanoscopy of protein aggregates.** A) Each fluorescent molecule labeling the protein structure is imaged on the camera as a ~200 nm “blob.” The overlap of the blobs obscures the underlying structure. B) By separating the fluorescence in time, the position of each molecule can be determined to high precision (10-50 nm). The sum of the positions reveals the underlying structure. C) Overlay of nanoscopy (color) and atomic force microscopy (black) images of the same aggregate.