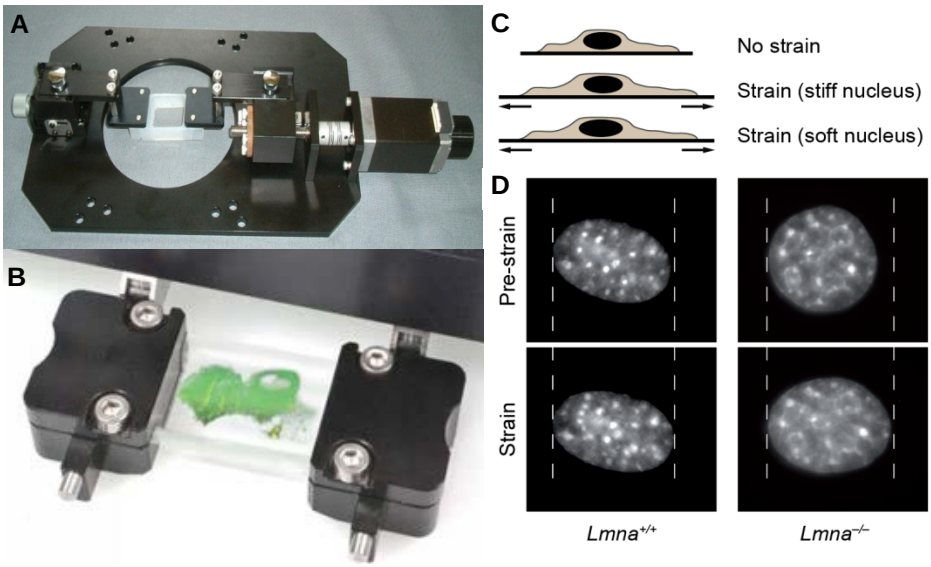
Design of a microscope-mounted cell stretching device

The ability of cells to properly sense and respond to mechanical forces has a major impact on both vascular and musculoskeletal health. Examples include muscle growth in response to exercise, bone remodeling based on their mechanical load, or endothelial cells aligning under fluid shear stress to protect against atherosclerosis. Recent discoveries provide compelling evidence that the physical properties of the nucleus are critical for a multitude of cellular functions, and that defects in nuclear structure and organization can contribute to a large number of human diseases including muscular dystrophies and cardiomyopathies. The Lammerding laboratory is developing novel experimental techniques to assess the impact of disease causing mutation on the structure and mechanical properties of cells, with the goal to determine how changes in the biophysical properties of the nucleus can render cells more vulnerable to mechanical stress and cause muscular dystrophy and heart disease. One major challenge in this research is to obtain precise measurements of the biophysical properties of the cell, including its nucleus, and the cellular response to mechanical stress.

The goal of this project is to design a microscope-mounted cell stretching device that can deliver biologically-relevant deformation to cultured muscle cells during simultaneous high-resolution imaging. The cell stretching device will attach to an inverted fluorescence and/or confocal microscope and apply precisely controlled mechanical strain to cells cultured on a thin, transparent elastic membrane (see Figure). The applied strain should be controlled through a computer interface, where the user can adjust the strain magnitude (up to 25%) and the strain application rate. Deliverables for this project include the motorized, computer-controlled strain device, a modular cell stretching chamber in which cells can be grown and transferred to the cell stretching device, and the creation of a user-friendly interface that allows fine control of the stretch magnitude, duration, and wave profile (e.g., ramp, sinusoidal, EKG, etc.).



Stretching cells to measure nuclear stiffness in diseased and normal cells. (**A-B**) Examples of commercially available cell stretching devices: STREX ST-150 (A) and EMS CS-10 series cell stretcher (B). (**C**) Schematic overview of nuclear deformations during applied substrate strain for cells with stiff and soft nuclei. (**D**). Cells lacking the nuclear envelope proteins lamin A/C (*Lmna*$^{-/-}$), which causes muscular dystrophy and heart disease, have softer nuclei that deform more than healthy control cells (*Lmna*$^{+/+}$) under the same applied membrane strain.

Students joining this project should have a background in mechanical engineering and some design experience. Students will learn additional design and fabrication techniques, advanced optical microscopy, computer-aided imaging and image analysis, as well as cell culture techniques. Experience with cell culture is a plus, but not required.

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