Title: **Muscular and Fascial Instrumentation and Anatomy Using Reflected Light Polarimetry and Contrast-Enhanced MicroCT**

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Research Location: NEOMED

Abstract: Smooth muscle plays a critical role in the function of many organ systems, but our ability to understand the effects of smooth muscle contraction are limited by our current inability to directly record smooth muscle activity *in-vivo*. Unlike skeletal muscle, smooth muscle does not depend on cell-membrane depolarization to coordinate contraction, so standard techniques such as electromyography (EMG) will not work. Current research in Hieronymus lab is focused on two major aims: (1) developing new methods of measuring peripheral smooth muscle optical properties to record activity, and (2) developing selective, localized, and reversible interventions to manipulate smooth muscle contraction for functional studies. This summer research project has two available tracks: one track will prototype and test components of a direct polarimetric probe system with the aim of developing *in vivo* instrumentation; the other will make use of recent advances in microCT imaging to characterize the architecture of smooth muscle tissue in bird skin (our lab's experimental model system for smooth muscle polarimetry and manipulation), with particular attention to its relationship to the superficial and deep fascia of the human-comparable musculoskeletal elements of the forelimb.

Significance: In addition to the smooth muscle lining the GI tract, airways, and vasculature, avian skin contains bundles of smooth muscle responsible for moving the feathers, similar to the arrector pili muscles in human skin. Because they are abundant and comparatively large, these muscles form a readily accessible experimental model for studies of smooth muscle physiology. My lab is developing a contact polarimetry instrument to record smooth muscle activity *in vivo* and investigating means to locally and reversibly knock down smooth muscle function—both of these aims feed into the broader goal of testing hypotheses of smooth muscle function *in vivo* during normal behavior. Current electrophysiology-based methods do not allow for direct measurement of smooth muscle contraction, and instead rely on indirect measures of correlated skeletal muscle contraction, which are only present in some systems. The ability to directly measure and reversibly manipulate smooth muscle function *in vivo* has implications across urogenital, gastrointestinal, and cardiopulmonary physiology.

Goals & Objectives: The goals of these paired studies are to develop new instrumentation components for measuring smooth muscle activity, and to provide the first tomographic characterization of smooth muscle bundles in avian skin. Students' research experience in the first track will focus on prototyping and testing optical and electronic instrumentation. The specific question to be addressed in this track is whether expected variation in optical properties of smooth muscle can be detected by reflected light polarimetry. Students' research experience in the second track will focus on assessing interconnections between dermal smooth muscle bundles, superficial fascia, and underlying deep fascia and skeletal muscle of the forelimb. The specific question to be addressed is whether the unusual connections of dermal smooth muscle to underlying bone in the avian forelimb are mediated by deep fascia and associated muscular tissue.

Research Methods: For prototyping, the student will use basic small electronics etching and soldering techniques, together with basic biocompatible materials approaches such as PDMS casting. For imaging, the student will apply Diffusable Iodine Contrast Enhancement (DICE) and Selectively Perfused Iodine Contrast Enhancement (SPICE), both recently developed techniques for imaging normally radiolucent tissues with X-ray computed tomography (CT). These techniques employ the radiodensity of iodine as a contrast agent for CT imaging, and are thus comparable to the use of injectable iodinated contrast

media for angiography. Paraffin histology of focal samples will be used to confirm tissue relationships in areas of interest.

Data Analysis: Analysis for this project will include signal processing in R and RStudio to assess instrument function and segmentation using Avizo CT analysis software to generate computer models of the musculature and surrounding tissues.

Contribution to Overall Research Effort: Completion of this project will augment continuing experiments with avian feather muscles. This work will also produce stand-alone methods and anatomical results suitable for student-led publication.

Student Fellow Mentoring Plan: Student fellows will take part in weekly lab meetings with all lab members to identify and address lab-wide issues and tasks. If both tracks are filled, students will have the opportunity to work collaboratively on all phases of both projects. Student fellows will also be expected to attend the weekly journal club for the Musculoskeletal Research Focus Area, providing exposure to a broad range of research topics as well as a chance to interact with researchers at different career stages—typical attendance in summer includes 2-4 summer fellows, 2-3 technicians, 1-4 graduate students, 3 postdocs, and 3-4 faculty PIs. Timely completion and reporting of the student fellows' projects will be ensured by biweekly one-on-one meetings with the PI, not only to organize work but also to work through main tasks side by side (*e.g.,* worked examples of analysis, drafting, editing and presentation) both during the summer and through the following year as needed. Materials and equipment for the proposed research are currently available in the PIs lab.