Department of Biomedical Engineering
UNIVERSITY OF WISCONSIN–MADISON

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Controlling multi-scale patterning for synthetic developmental biology

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Embryonic tissue-building processes must hierarchically pattern cells into life-sustaining structures while avoiding organizational defects that compromise organ function. Building mature and hierarchically complex synthetic organs in vitro from patient-derived cells would have a wide range of healthcare applications from personalized disease models to cell-based therapies and tissue replacement. Integrated cell engineering and biomanufacturing technologies have rapidly advanced the scale and structural complexity of synthetic tissues, yet current approaches still fail to capture fine-scale functional organization, such as repetitive niches, branching tubules, or compartment boundaries. This talk incorporates my work combining engineering and biology tools across scales to predict and control tissue organization. I will discuss my vision for synthetic developmental biology, in which I seek to adapt or create new molecular-to-tissue-scale tools to emulate embryonic tissue-building processes and guide reproducible tissue patterning. I will briefly cover work from my Ph.D., where I combined experiments and theory to understand how ensembles of molecular adhesions and force-generating cytoskeletal proteins enable cells to sense and respond to tissue stiffness and to predict the mechanisms of anti-invasion chemotherapy. While this work primarily focused on cancer, these general biophysical approaches can readily apply to tissue engineering and decoding embryonic cell behaviors alike. Next, I will present my postdoctoral work, where I explored how tissue-scale geometric and mechanical properties of the developing kidney affect the organization of branched collecting tubules and nephrons required for physiological function. The kidney is prone to congenital defects that affect tubule and nephron number and organization. Through combined experiments and geometric modeling I found that physical forces rearrange branching tubules to avoid organizational defects during development. I was able to predict and synthetically recapitulate conditions that cause defects, providing inspiration for future tissue engineering and disease modeling work. Finally, I will describe recent and ongoing work that bridges the molecular-to-tissue scales with optogenetic signaling tools to control three-dimensional tissue morphogenesis and multiplexed cell micropatterning to investigate the mechanical basis of tissue boundaries and interfaces. Further developing these multi-scale synthetic approaches will expand the tissue engineering design space, inspire new paradigms for tissue replacement, and improve models of congenital organ defects.

ABOUT the SPEAKER

Dr. Louis Prahl seeks to understand the engineering principles of embryonic tissue morphogenesis and to apply these insights to regenerative medicine, organoid engineering, and congenital disease modeling. As an NIH Ruth L. Kirschstein NRSA Postdoctoral Fellow in Dr. Alex Hughes' laboratory at the University of Pennsylvania, his work combines engineering and embryology to understand how geometry, tissue mechanics, and signaling impact kidney development. He has also contributed new tools and approaches to control in vitro tissue organization. Dr. Prahl received his Ph.D. in biomedical engineering from the University of Minnesota, where his dissertation work combined computational and experimental approaches to understand how brain tumor cells probe the mechanical properties of their environment, and how certain chemotherapy drugs can target this process to curb cancer progression. He is a recipient of the National Science Foundation Graduate Research Fellowship, a member of the Penn Postdoctoral Association leadership, and an alumnus of the 2021 Embryology Course at Marine Biological Laboratory. Prior to his Ph.D., he earned a B.A. in physics from Lewis & Clark College.

Monday, April 1 at Noon
1003 Engineering Centers (Tong Auditorium)