Adventures in Cell Herding: Engineering and Control of Multi-agent Cellular Swarms

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Abstract
We are working to accomplish for cells something akin to what a shepherd and sheepdogs bring to flocks of sheep: control over large-scale collective cellular motion. As coordinated cellular motion is foundational to many forms of multicellular life, being able to ‘herd’ or program large-scale cell migration raises exciting possibilities for accelerated healing, tissue engineering, and novel biomaterials. We treat tissues as living, multi-agent systems allowing us to combine approaches from disparate fields—control theory, active matter mechanics, tissue engineering, and materials—both to better understand the rules of cellular crowds and to build new tools to ‘herd’ large-scale cell behaviors. One approach we use is guided self-assembly of tissues, where we establish precise initial conditions and let the tissues develop spontaneously. Here, we combine machine learning, biomechanical modeling, and tissue micropatterning to characterize the rules of collective migration within tissues of different types; connect cell-cell mechanics to large-scale collective dynamics; and build complex ‘tissue tessellations’ through precise control of healing boundaries between tissues. In contrast to self-assembly, we are also developing tools that allow for true, interactive control of tissue growth and form at the multicellular level. Here, we use a unique bioelectric cue—electrotaxis—to literally program large-scale collective cell migration, enabled by our ‘SCHEEPDOG’ bioreactor. In this case, ionic currents manipulate cellular signaling allowing control of both cell direction and speed, allowing us to: accelerate the ‘healing’ of gap injuries with in vitro tissues; investigate how cell-cell interaction mechanics modulate ‘controllability’; and manipulate the growth of 3D tissues and organoids.

Bio
Daniel Cohen is an Assistant Professor of Mechanical and Aerospace Engineering at Princeton University and a founding member of the new Princeton Bioengineering Institute (PBI). He trained first in Mechanical Engineering at Princeton, followed by a joint Ph.D. in Bioengineering at UC Berkeley/UCSF, the Physiology Course at the MBL at Woods Hole, and as a Life Sciences Research Foundation Fellow at Stanford University. He started his lab at Princeton in 2018, where his work has been awarded an NIH Early Career MIRA award and an NSF CAREER award. His works span dinosaur and organismal mechanics, tissue engineering, biomaterials, and bio-electromechanics. Outside the laboratory, he is heavily engaged in science communication, running both theatrical performances for the public and the yearly, week-long Lab Tales workshop at Princeton to train researchers in the hidden histories and human stories behind modern scientific research.