## Forward Engineering of Multi-cellular Engineered Living Systems

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## **Extended Abstract**

The integration of living cells with 3D printed soft scaffolds can enable the realization of cellular machines for a range of applications in engineering and medicine. In this talk, I will present our group's efforts towards developing such centimeter scale biological robots that actuated by skeletal muscles cells and our efforts to integrate neural control in these biological machines. These machines are controlled via electrical or optogenetic signals and demonstrated improved healing after a damage when exercised via optical stimulation. We also explore their lifetime and degradation in performance due to breakdown of the matrix that contains the cells. We will also present an approach to form functional in vitro neural tissue mimic (NTM) of different shapes using stem cells, a fibrin matrix, and 3D printed molds. We used murine-derived embryonic stem cells for optimizing cell-seeding protocols, characterization of the resulting internal structure of the construct, and remodeling of the extracellular matrix, as well as validation of electrophysiological activity. We also characterized the effects of optogenetic stimulation during neural differentiation, by showing morphological changes in network formation. These cellular systems present many opportunities in the next decade and beyond with potential applications in drug delivery, power generation, and other biomimetic systems. As these cellular machines increase in capabilities, exhibit emergent behavior, and potentially reveal the ability for self-assembly and self-repair, important questions can also arise about the ethical implications for this direction of research, which are very important to consider and address.