3D-Printable Functional Living Composite Materials: Living cells, Polymer scaffold, and Engineered proteins

Natural materials– such as wood, bone, and skin –are composites of living cells, effector biomolecules, and a variety of polymeric scaffolds. The living, autonomous nature of these natural composite matters realizes emergent properties, such as self-regulation, adaptation to various environmental changes, and the capacity for wound healing. In order to accomplish such complex biological tasks, 3-dimensional hierarchical organization and morphological heterogeneity are required. We see this in bone as it provides structural support, serves as a mineral reservoir, and nurtures hematopoietic stem cells at the same time. ***The Sim laboratory's research centers on integrating living entities and protein assemblies as functional components of smart polymeric materials in 3D architectures*** (**Figure 1**). Living cells possess ideal attributes for creating emergent materials: they can assemble, communicate, adapt to variable environments, and can be programmed to perform novel functions with tools from synthetic biology. A key idea here is to employ engineered living microbial cells to function as an active component of materials for mechanical reinforcement, biochemical sensing, and functional protein synthesis *in situ*. In recent years, a myriad of genetically encoded biological modalities useful for therapeutics, imaging, sensing, and communication over various length-scales have been discovered and engineered in the fields of molecular and synthetic biology. Repurposing these modalities operated by living cells for generating a new class of biomaterial with 3D complexity would open a new paradigm to engineer unprecedented functions.

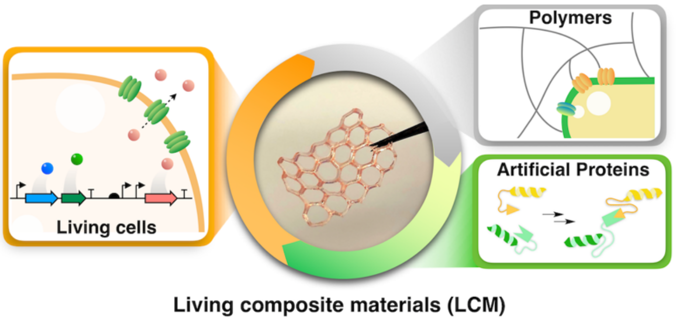

Figure 1 | Three major components in living composite materials (LCM).

The Sim laboratory seeks to develop 3D-printed living composite materials (LCM) comprising immobilized, yet metabolically active, living microbial cells that perform engineered tasks. Specifically, we aim to develop (1) LCMs producing and eluting therapeutic biomolecules *in situ*, (2) microfluidic LCM devices for facile, reusable, and multiplexable detection of biomarkers, and (3) a novel soft robotic system using controllable mechanical actuation and reconfiguration of LCMs. (**Figure 2**). Although recent studies have shown that living bacterial cells can be engineered to produce their own matrix, in order for such LCMs to be a platform technology, they must be self-contained, user-friendly, and perform useful functions. We will ambitiously tackle this challenge by integrating genetically programmed living cells and spores, carefully designed functional polymeric networks, and engineered artificial proteins. The outcome of this research will be functional materials directly contributing to human health and will manifest the powerful synergy of **polymer chemistry, protein engineering, and bioengineering**. This work will also contribute to expanding our currently limited knowledge regarding the cell-material interface and its impact on cellular physiology, an important facet of LCMs which has not yet been systematically studied due to the lack of a proper experimental platform. The ability to translate cellular behaviors to the materials' function and property will give birth to new insights for a broad spectrum of scientific fields, including microbiology, biophysics, and systems biology.

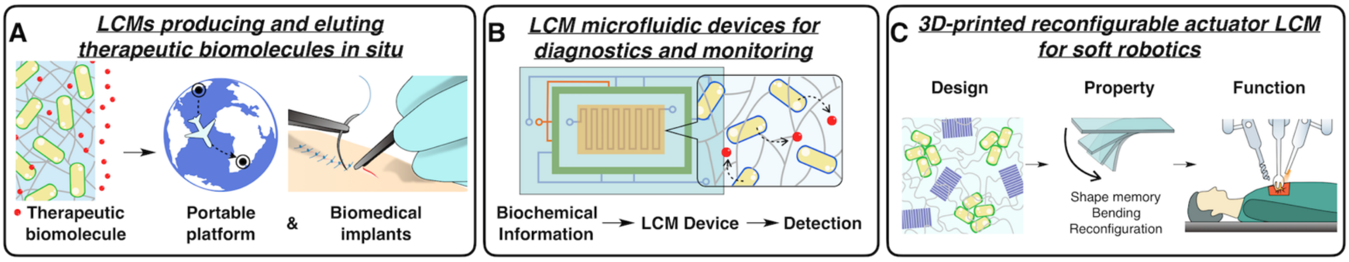

Figure 2 | The Sim laboratory's specific research goals