2021 NSF CYBER-PHYSICAL SYSTEMS PRINCIPAL INVESTIGATORS' MEETING CPS: Frontier: Collaborative Research: bioCPS for Engineering Living Cells Calin Belta¹ (Lead PI), Doug Densmore¹ (Co-PI), Vijay Kumar² (PI), Ron Weiss³ (PI) Boston University, ²University of Pennsylvania, ³Massachusetts Institute of Technology

Award number: 1446607

Challenge:

Next-generation biological cyberphysical system (bioCPS) in which desired global behaviors can be achieved in populations of living cells through design of local behaviors

Solution:

- equip cells with sensing, communication, and decision making capabilities using methods from synthetic biology.
- micron-scale mobile robots assist in optimizing the formation of patterns by affecting communication through optogenetic triggering of genetic circuits or by moving cells and signals
- mathematical modeling, machine learning, formal methods, and optimization techniques to quantify and create patterns

Key Innovations:

- computational techniques for pattern formation
- micro-robot technology
- top-down synthesis of synthetic circuits and biological protocols for pattern formation





Robot combines organic and inorganic substrates

Scientific Impact:

Areas of immediate impact

- Differentiation of stem cells into specific tissues and organs
- Support technologies such as drug design tissue and organoid-on-a-chip
- Novel techniques for actuation and interaction at the micron level
- Define interfaces between living / non-living matter
- Proposed BDA advances standardization and automation in synthetic biology
- Better understanding of morphogenesis and developmental biology Broader and long term impact:
- General framework for synthesis of desired global behaviors from local dynamics and interactions
- · Anomaly monitoring, detection, and mitigation in maritime and automotive systems

Broader Impact:

Robot Assistant for Communication, Sensing, and Control in Cellular Networks

- Technology transfer
- MIT iGEM Teams, MIT
- Museum Education Days, MIT **High-School Summer** Program, Cambridge Science Festival, Chelsea High School Science Fair, UROP at BU, Penn - GRASP First Lego League, Penn - GEMS Girls in Engineering, Math, and Science







S. Das et al., "Cellular expression through morphogen delivery by light activated magnetic microrobots," J. Micro-Bio Robot., pp. 1–12, Jun. 2019. E.E. Hunter et al., "Nanoliter Fluid Handling for Microbiology via Levitated Magnetic Microrobots", IEEE Robotics and Automation Letters, vol. 4, no. 2, pp. 9971004, Apr. 2019. N. Mehdipour et, al., Spatial-temporal pattern synthesis in a network of locally interacting cells, 57th IEEE Conference on Decision and Control (CDC), Miami, Florida, 2018 Bartocci et. al., A Formal Methods Approach to Pattern Recognition and Synthesis in Reaction Diffusion Networks, IEEE Transactions on Control of Network Systems, 2016

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