



IU BLOOMINGTON

EMERGING AREAS OF RESEARCH

Abstract Template -- Due June 30, 2017

Title of initiative to be proposed:

From science fiction to science fact: informatics-driven cell reprogramming to create multicellular biodevices

Name of lead PI, with title, department/school:

Paul Macklin, Associate Professor, Intelligent Systems Engineering/SOIC

Key team member names and departments/schools (up to 10 names):

1. James Glazier (Intelligent Systems Engineering/SOIC),
2. Katy Borner (ISE/SOIC)
3. Geoffrey Fox (ISE/SOIC)
4. Luis Rocha (Computer Science/SOIC, CNetS)
5. James Sluka (ISE/SOIC)

Description of area to be proposed. What constitutes this area of research or creative activity as emerging?
(Word limit=500)

In the past decade, we have seen advances in manipulating cells at a molecular level that were previously in the realm of science fiction. New technologies such as CRISPR/Cas9, antibody-nanoparticle systems, and synthetic genes are emerging to change cell behaviors—to reprogram them—at a molecular level. In this emerging area of research, scientists are increasingly focusing on what to do with these new tools, and whether reprogrammed cells can solve problems in health, the environment, and society. Can cancer cells be reprogrammed to be less aggressive? Can we program stem cells to grow micro-organs that digest new toxins? Can we engineer bacterial colonies to fight pollution? Can we build multicellular biorobots that shuttle molecular cargo or repair damaged tissues?

Unfortunately, work to date has focused on developing individual technologies for single-cell manipulation, and not on overarching design principles for creating multicellular biodevices such as artificial tissues, complex microbial systems, or biorobots. There is a lack of knowledge on how to robustly reprogram single-cell behavior with molecular manipulations. There is a lack of insight on how systems of many reprogrammed cells (often of different types) interact to form small tissues, functional microbial communities, or simple organisms. And we lack design tools to choose multicellular functional design goals—and work backwards to single-cell programs to reach these design goals. Until we solve these problems, multicellular biodevices will remain science fiction.

IU is uniquely positioned to help resolve these outstanding needs and perform cutting-edge work at the forefront of this emerging area of research. Our faculty have leading expertise in bioinformatics and data mining (Wild), multicellular simulations (Macklin, Glazier, Sluka), high-performance and distributed computing (Fox), complex systems, machine learning, and bio-inspired computing (Rocha), single-cell microfluidic and mechano-acoustic manipulation (Guo), microbial environmental engineering (Picardal), visualization (Borner), and collaborative science (Borner, Fox). We have strong experimental collaborations at IU and other leading institutions. This EAR proposal would leverage our strengths to nucleate a new Center for Multicellular Design: a cross-cutting program to create and validate robust computational tools to reprogram cells, assemble them into multicellular biodevices, test their functions, and iteratively improve our cell programming choices to create useful and safe multicellular biodevices.

The team will develop:

- (1) bioinformatics tools to quantitatively map molecular-level reprogramming to cell behavior; [Wild, Hire1]
- (2) computational tools to virtually assemble and simulate multicellular biodevices in complex environments; [Macklin, Glazier, Sluka]
- (3) a language to quantify multicellular device form and function; [Macklin, Glazier, Sluka]
- (4) supercomputing techniques to test competing design choices; [Fox]
- (5) multicellular biodevices to validate the designs; [Guo, Hire2], and
- (6) a collaborative framework to work with domain experts across IU and beyond [Fox, Borner, Macklin].

With our collaborators in biological science and environmental microbiology (Picardal), we will test the tools on targeted problems in tumor-stromal dynamics, synthetic micro-livers that filter xenobiotics, and aquifer remediation. We anticipate new collaborations with COAS, SPEA, SPH, and SOIC to investigate the ethics and socioeconomic impact of engineered multicellular biodevices, and to control the security of multicellular biodevices.

Please submit to earprogram@indiana.edu