Simulating Emergent Behavior in Host-Microbiome Systems using Robots and Synthetic Biology

Keith C. Heyde[1], Patrick W. Gallagher[2], and Warren C. Ruder[3]

***Short Abstract* — The microbiome's underlying dynamics play an important role in regulating the behavior and health of its host. In order to explore the details of these interactions, we created an *in silico* model of a living microbiome, engineered with synthetic biology, that interfaces with a biomimetic, robotic host. By analytically modeling and computationally simulating engineered gene networks in these commensal communities, we reproduced complex, emergent behaviors in a physical robotic within an arena. Our system is a novel tool for exploring inter-kingdom ecological relationships while potentially impacting fields ranging from ecology to medicine.**

***Keywords* — Synthetic Biology, Computational Biology, Microbiome, Inter-kingdom, Robotics, Biomimicry**

I. BACKGROUND

COMMENSAL microbes, and in particular the microbiome, have been shown to play a critical role in regulation the behavior of their hosts, with influence ranging from reproductive affinity[1] to anxiety and motility[2]. Although targeted microbiome engineering remains challenging, synthetic biology and biomimetic robotics provide us with two invaluable tools for understanding host-microbiome interactions. Using these two tools, we designed a robotic host with a synthetically engineered simulated microbiome in order to create a model system for studying host-microbiome interactions [3].

II. RESULTS

Our system architecture relied upon information exchange between an engineered cell population and the onboard robotic microcontroller. We conceptualized this system as having three different modules. (1) Inducer chemicals enter the cell population and activate gene circuits encoding for fluorescent proteins. (2) Changes in cell coloration are converted into a digital signal via a microscope. (3) The digital signal is processed by the robot microcontroller and converted into robot subroutines. Here, we computationally simulated modules 1 and 2 in MATLAB® and built and programmed a physical robot for module 3.

We designed the cells to contain plasmids with canonical gene circuits from synthetic biology [4]. The cells were modeled and simulated using a system of differential equations based off of first principles.

Upon interfacing our physical robot with the simulated cell population, we found that simple engineered gene networks caused nuanced emergent robot behavior. These behaviors included preferential resource selection as well as predation behavior similar to those found in vertebrates [3,5]. It should be noted that at no point was the robot's firmware altered, and all variations in robot behavior were a direct result of changes in the cell's morphology.

III. CONCLUSION

By engineering and testing a robot that could interface with a simulated cell, we designed a novel tool for understanding host-microbiome interactions in nature. Our simulated cell population provides a predictive tool for effectively engineering living cell lines for selective robotic behaviors.

Acknowledgements: This work was funded by AFOSR award FA9550-13-1-0108 and NSF IGERT award #0966125.

[1]Department of Biomedical Engineering and Mechanics, Virginia Polytechnic Institute and State University, Blacksburg VA USA. E-mail: kch2118@vt.edu

[2]Department of Biological Systems Engineering, Virginia Polytechnic Institute and State University, Blacksburg VA USA. E-mail: patgall@vt.edu

[3] Department of Biological Systems Engineering, Virginia Polytechnic Institute and State University, Blacksburg VA USA. E-mail: wruder@vt.edu

REFERENCES

[1] Sharon G, et al. (2010) Commensal bacteria play a role in mating preferences of Drosophila melanogaster. *PNAS* **107**, 20051-20056.

[2] Neufeld K, et al. (2011) Reduced anxiety-like behavior and central neurochemical change in germ-free mice. *Neurogastroenterol. Motil.* **23**, 255-264.

[3] Heyde KC, Ruder WC (in press) Exploring host-microbiome interactions using an *in silico* model of biomimetic robots and engineered living cells. *Sci. Rep*.

[4] Gardner T, Cantor C, Collins, C (2000) Construction of a genetic toggle switch in Escherichia coli. *Nature* **403**, 339-342.

[5] Moermond T. (1981) Prey-attack behavior *oiAnolis* Lizards. *Zeitschrift fur Tierpsychologie* **56**, 128-136.