Culture Environment Impacts Synthetic Microbial Consortia Behavior

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***Short Abstract* — In nature, microorganisms grow in consortia that help them adapt to changing environments by cooperating and communicating. Expanding traditional synthetic biology gene circuits to two or more bacterial strains can lend the same advantages. These synthetic microbial consortia can be used to produce desired products in an assembly line fashion, measure intercellular communication, study the evolution of natural consortia, and eventually lend insights to engineering probiotics. To successfully engineer cooperative synthetic microbial consortia, we must examine how engineered strains communicate and cooperate in different environments.**

***Keywords* — Synthetic microbial consortia, microfluidics**

I. Purpose

TRADITIONALLY synthetic gene circuits have been studied in a single engineered bacterial strain. Expanding these gene circuits to multiple cooperating strains in synthetic microbial consortia can yield more robust population level phenotypes, enhance bioprocessing, and reveal insights to the evolution of natural consortia [1, 2]. We aim to examine the effect of different growth environments on the cooperation and communication of strains in synthetic microbial consortia.

Microfluidic devices allow for measuring single cell gene expression over time using fluorescent proteins as reporters [3]. However, they may introduce spatial patterns when used to grow multiple bacterial strains. Here, we examine which cell trapping regions provide a better microfluidic environment for synthetic microbial consortia to allow for cooperative growth and proper communication. The main attribute being overall size and shape of the cell trap.

In addition, we examine how the same microbial consortium behaves differently when grown in a fluidic device, in bulk culture, and on agar plates. The main differences that affects the population phenotype in these three environments is the presence of spatial patterns and any limitations on communication via small molecule diffusion.

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II. Results

Multiple synthetic microbial consortia are studied in this work including non-communicating strains, communicating strains, and strains that exchange nutrients. Their growth rates, communication distances, and cooperation are measured and compared in different environments.

A. Microfluidic devices affect strain stability and spatial patterning

We used non-communicating strains to determine that microfluidic devices with larger cell trapping areas allow for greater stability of two strains over time. We also observed that in these larger cell traps, spatial patterns arise that depend on the number of cells seeded into the trap.

B. Spatial patterns affect communication

We then examined how these spatial patterns affect communicating strains in microfluidic devices. We measured how far quorum sensing molecules can diffuse in the cell trapping region to determine the necessary proximity of cells from different strains for proper consortia behavior.

C. Synthetic consortia in different environments

We grew the consortia in microfluidics, bulk culture, and on agar plates and compared growth, cooperation, and communication. While bulk culture does not allow for single cell measurements, it eliminates spatial patterning. In agar plates, we can measure population level phenotypes and control the spatial patterns. In each environment the distance of quorum sensing signaling and nutrient exchange differs.

III. Conclusion

Synthetic microbial consortia need to be grown in environments that allow for strain stability over time, intercellular communication, and exchange of nutrients. Microfluidic devices, bulk culture, and agar plates each have attributes that can affect these. Here we've quantified the limitations and strengths of each environment depending on the synthetic microbial consortia being evaluated.

References

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