

65. Live-cell Micropatterning for Analysis of Inter-cellular Behavior in Multi-species Systems

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Microorganisms exist in dynamic environments where nutrients, energy sources and signals are often in flux. Modeling cellular behavior within such environments is complex, and requires a fundamental understanding of substrate dynamics (i.e., concentration, location, and diffusion rate) and cellular responses to these substrates (i.e., uptake, biomass conversion, growth, efflux). We have used the open-source software platform COMETS (Computation of Microbial Ecosystems in Time and Space) to model metabolite resource sharing in multi-species bacterial systems and to generate predictions of spatiotemporal growth responses. To validate predictions made by COMETS, we have developed a microscale cell printing technology to produce complex patterns of bacterial micro-colonies. Micro-colonies printed with this system can be arranged two-dimensionally on agarose-based media to assess distance-dependent growth phenomena between multiple species. We have demonstrated the utility of this approach using combined COMETS modeling and cellular micropatterning for a synthetic consortium of an *E. coli* and *S. enterica* under conditions that require metabolite sharing between these organisms.

Micropatterning results strongly correlate with COMETS predictions, demonstrating the potential of this approach as a validation tool for computational modeling of bacterial growth within the context of resource sharing.