***in silico* and *in vitro* analysis of resource allocation in a chronic wound biofilm consortia**

Ross P. Carlson1, Michael Henson2, Luke Hanley3, Matthew Fields4

1. Department of Chemical and Biological Engineering, Center for Biofilm Engineering, Montana State University, Bozeman, MT 59717
2. Department of Chemical Engineering, University of Massachusetts, Amherst
3. Department of Chemistry, University of Illinois, Chicago
4. Department of Microbiology and Immunology, Center for Biofilm Engineering, Montana State University, Bozeman

Biofilms are ubiquitous in medical, environmental, and engineered microbial systems. The majority of naturally occurring microbes grow as mixed species biofilms. These complicated consortia are comprised of a large number of cell phenotypes with complex interactions and self-organize into three-dimensional structures. While foundational to the vast majority of microbial life on the planet, the basic design principles including resource allocation strategies of consortia biofilms are still poorly understood.

Multiscale, spatiotemporal models were developed to investigate the intersection of resource gradients, resource competition and metabolism in a multispecies biofilm comprised of two common chronic wound isolates: the aerobe *Pseudomonas aeruginosa* and the facultative anaerobe *Staphylococcus aureus*. By combining genome-scale metabolic reconstructions with partial differential equations for metabolite diffusion, the models provided both temporal and spatial predictions with genome-scale, metabolic resolution. The models analyzed the phenotypic differences between monoculture and coculture biofilms and demonstrated the tendency of the two bacteria to spatially partition in the multispecies biofilm, along resource gradients, as observed experimentally.

The *in silico* research was supported with detailed experimental analysis of *P. aeruginosa* and *S. aureus* resource usage when grown as monocultures or cocultures. Analysis considered both planktontic and biofilm growth conditions and measured mass and energy fluxes in monocultures and the potential exchange of resources in cocultures, quantifying how nutrient gradients and resource availability influenced ecologically competitive metabolisms. The two bacteria used very different, yet complementary, metabolisms to partition available resources resulting in the emergent property of enhanced biomass productivity. This enhanced productivity represents a challenge to treating chronic wounds. The studied ecological theories, including the maximum power principle, are believed relevant to many naturally occurring consortia and will be fundamental to preventing or managing consortia in medically relevant environments.