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Habits of Highly Effective Biofilms: Ion Signaling

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Abstract

How do neighboring bacterial biofilms sense and communicate with each other? In a recent paper, Liu et al. (2017) demonstrate how electrical signaling allows communication of metabolic states between adjacent B. subtilis biofilms, providing a possible generalizable mechanism for communication in multispecies biofilms with interdependent metabolism.

When microorganisms adhere to a surface and form a biofilm, they make a tradeoff between a stationary and motile lifestyle. How do they coordinate their local behavior with their larger surroundings? Moreover, how does a particular species coordinate growth and maintain stable colonization as available nutrients change? In a recent paper in *Science*, the authors demonstrate that *B. subtilis* can coordinate growth between two neighboring biofilms using electrochemical signals (Liu et al., 2017). Intriguingly, this allows the biofilms to share resources by alternating their relative growth phase. This is mediated by a K^+ ion channel, and the authors hypothesize that this electrochemical signaling communicates the metabolic state of neighboring *B. subtilis* biofilms to each other. If generalizable, such signaling could serve as an essential component for the creation of stable and complex microbial communities by facilitating cooperation between microorganisms.

Previous work from the Süel laboratory demonstrated that electrochemical signals can propagate across a biofilm, allowing cells in the interior to communicate their metabolic state with cells on the periphery (Prindle et al., 2015). Since K^+ ion gradients were proposed to propagate the signal, this suggested that the same signal capable of propagating within a single biofilm could also reach adjacent biofilms. In this work, the authors extend their previous work by demonstrating that signal propagation by the same mechanisms can allow communication of glutamate limitation between two adjacent *B. subtilis* biofilms (Liu et al., 2017). This communication allows the two biofilms to share a limited nutrient (glutamate) by setting their growth phases accordingly. The K^+ ion gradient is dependent on the expression of YugO, a K^+ ion channel protein gated by a well-conserved TrkA domain (Lundberg et al., 2013). In the current study (Liu et al., 2017), the authors use a combination of experiments and mathematical modeling to study the relative growth of two biofilms

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under varied genetic back- grounds and nutrient availability. By doing so, they are able to create a predictive model in which the growth phase synchronization of the adjacent biofilms is dependent on K^+ signaling, competition strength, and glutamate availability. In a related recent work (Humphries et al., 2017), the authors demonstrate that K^+ ion signaling can also be used for interspecies signaling by showing that it mediates recruitment of motile cells of both *B. subtilis* and *P. aeruginosa* to *B. subtilis* biofilms. It is not currently known to what extent this signaling between species represents eavesdropping for competitive advantage or serves as an important component for creating a stable microbial community.

In addition to biofilms, bacteria such as *B. subtilis* can also exist in more loosely structured communities in the soil where there are extensive intra- and interspecies interactions. To take a recent example, germination of spores of the antibiotic producing bacteria *Streptomyces coelicolor* occurs in response to signals from nearby bacteria (Xu and Vetsigian, 2017). Although the identity of this signal(s) is not known, in *B. subtilis*, the YugO protein that mediates K^+ signaling in the biofilm is also expressed in sporulation and is found in the developing spore (Arrieta-Ortiz et al., 2015). Thus, an exciting possibility is that electrochemical signals could mediate communication even in non-biofilm settings such as that between vegetative cells and spores.

Interestingly, we observed that YugO has homologs in many environmental bacteria and archaea, including many thermophiles. This includes *Sulfurihydrogenibium yellowstonense*, which was isolated from a hot spring in Yellowstone National Park (Nakagawa et al., 2005), the site of some of the most famous large-scale microbial communities. In Yellowstone the bright colors and patterns on surfaces adjoining the hot springs are often microbial mats (Figure 1)—dense, multi-layered biofilms, composed of many microbial species that can span many square meters and often have cooperative metabolism (Flemming et al., 2016). The composition of the particular microbial mat is believed to be relatively stable and is dependent on the particular environment of the mat, including temperature, pH, and electrical conductivity (Inskeep et al., 2013). The importance of electrical conductivity for a given microbial mat may be a further hint that ion-based signaling plays an as yet underappreciated role in coordinating multispecies biofilms. In this context, the conservation of YugO in a large number of biofilm-forming organisms suggests that it may not just coordinate of the growth of same-species biofilms, but also influence coordination between different species as well. It remains an open question to what extent different microbes can use electrical signaling to cooperate in biofilms to gain a communal advantage or attempt to cheat and outcompete their neighbors.

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References

Arrieta-Ortiz ML, Hafemeister C, Bate AR, Chu T, Greenfield A, Shuster B, Barry SN, Gallitto M, Liu B, Kacmarczyk T, et al. Mol Syst Biol. 2015; 11:839. [PubMed: 26577401]

Flemming HC, Wingender J, Szewzyk U, Steinberg P, Rice SA, Kjelleberg S. Nat Rev Microbiol. 2016; 14:563–575. [PubMed: 27510863]

Humphries J, Xiong L, Liu J, Prindle A, Yuan F, Arjes HA, Tsimring L, Süel GM. Cell. 2017; 168:200–209.e12. e212. [PubMed: 28086091]

Inskeep WP, Jay ZJ, Tringe SG, Herrgård MJ, Rusch DB, YNP Metagenome Project Steering Committee and Working Group Members. Front Microbiol. 2013; 4:67. [PubMed: 23653623]

Liu J, Martinez-Corral R, Prindle A, Lee DD, Larkin J, Gabalda-Sagarra M, Garcia-Ojalvo J, Süel GM. Science. 2017; 356:638–642. [PubMed: 28386026]

Lundberg ME, Becker EC, Choe S. PLoS ONE. 2013; 8:e60993. [PubMed: 23737939]

Nakagawa S, Shtaih Z, Banta A, Beveridge TJ, Sako Y, Reysenbach AL. Int J Syst Evol Microbiol. 2005; 55:2263–2268. [PubMed: 16280480]

Prindle A, Liu J, Asally M, Ly S, Garcia-Ojalvo J, Süel GM. Nature. 2015; 527:59–63. [PubMed: 26503040]

Xu Y, Vetsigian K. Sci Rep. 2017; 7:699. [PubMed: 28386097]

Figure 1. Microbial Mat Adjoining a Hot Spring in Yellowstone National Park, WY, USA

Microbial mats such as this example are comprised of multiple species living in biofilms many layers thick. The diversity of microorganisms and their isolation to a particular niche result in the characteristic color patterns. These mats are also remarkable for the long-term stability of their microbial colonizers. Photograph provided by Elizabeth A. Libby.